JOURNAL OF SLEEP AND SLEEP DISORDERS RESEARCH
ISSN 0161-8105

SLEEP

VOLUME 30, 2007
Abstract Supplement

Official publication of the
Associated Professional Sleep Societies, LLC

A joint venture of the
American Academy of Sleep Medicine
and the Sleep Research Society

SLEEP 2007
21st Annual Meeting of the
Associated Professional Sleep Societies, LLC

June 9-14, 2007

Minneapolis Minnesota

Scientific Highlights/Abstracts of Original Investigations

MINNEAPOLIS
SLEEP
2007

SLEEP (ISSN: Print 0161-8105; Online 1550-9109) is published monthly by the Associated Professional Sleep Societies, LLC, a joint venture of the American Academy of Sleep Medicine and the Sleep Research Society located at One Westbrook Corporate Center, Suite 920, Westchester, Illinois, 60154, phone (708) 492-0930 and fax (708) 492-0943. Periodicals postage paid at Maywood, IL and additional entries.

ANNUAL SUBSCRIPTION RATES: Subscription rates for Vol. 30, 2007: Individual subscriptions $205, outside U.S. $275, Institutional subscriptions: $305, outside U.S. $380. New subscriptions and renewals begin with the January issue of the current year. Subscriptions should be secured as early in the year as possible as the publisher cannot guarantee the supply of back issues. Journal issues prior to the current volume, when available, may be ordered at the single issue rate. Air delivery included for countries outside of the USA, Canada, and Mexico. Single copy: $36. Payment should accompany all orders. Claims for missing issues must be received within 60 days of the publication date. Questions about subscriptions (including payments, billing procedures, or policy matters) should be directed to the APSS office at (708) 492- 0930. Changes of address should be submitted four to six weeks in advance of the change to ensure uninterrupted service. Send us your current mailing label (including the old address), along with your new address and the effective date of change.

POSTMASTER: Send change of address to APSS, One Westbrook Corporate Center, Suite 920, Westchester, IL 60154.

SLEEP

JOURNAL OF SLEEP AND SLEEP
DISORDERS RESEARCH
Volume 30, 2007
Abstract Supplement
Official publication of the Associated Professional Sleep Societies, LLC
A joint venture of the American Academy of Sleep Medicine and the Sleep Research Society

EDITORIAL

This abstract supplement unites the journal *SLEEP* and the science of the SLEEP 2007 21st Annual Meeting of the Associated Professional Sleep Societies, LLC in a convenient format. This special issue includes all abstracts presented at SLEEP 2007, on June 9-14 in Minneapolis, Minnesota. The supplement provides all AASM and SRS members, including those unable to attend the meeting, a glimpse into the new ideas and latest research taking place in the field of sleep disorders medicine and sleep research.

Of the 1,124 abstracts accepted, 250 will be presented in oral presentation format and the remainder as poster presentations. Similar to prior meetings, the Program Committee elected to:

1) Group posters into thematic groups.
2) Display each poster on one of the three schedule poster days (June 11, 12, 13).

New this year, the poster sessions have been expanded to a full two hours, allowing attendees greater opportunity to view posters and interact with presenters. Each poster has a unique 4 digit number and is assigned to one of the 19 categories listed below to facilitate identification and location.

Category A – Neuroscience
Category B – Physiology/Phylogeny/Ontogeny
Category C – Pharmacology
Category D – Circadian Rhythms
Category E – Pediatrics
Category F – Aging
Category G – Sleep Deprivation
Category H – Sleep Disorders – Breathing
Category I – Sleep Disorders – Narcolepsy/Hypersomnia
Category J – Sleep Disorders – Insomnia
Category K – Sleep Disorders – Parasomnias
Category L – Sleep Disorders – Movement Disorders
Category M – Sleep Disorders – Neurologic Disorders
Category N – Sleep in Medical Disorders
Category O – Sleep in Psychiatric Disorders
Category P – Instrumentation & Methodology
Category Q – Healthcare Services, Research & Education
Category R – Molecular Biology & Genetics
Category S – Behavior, Cognition & Dreams

Attendees of the SLEEP 2007 meeting will experience a forum for the discussion of new ideas and key research in the field of sleep medicine and research. Our hope is that this experience fosters an environment in which members and attendees obtain education on the latest basic science, clinical science and technologies in the sleep field, further promoting the continued growth of the field through the dissemination of new knowledge. We look forward to sharing in the success of this pivotal event.

David F. Dinges, Ph.D.
Editor-in-Chief

Author Index

Author **Abstract Number**

A

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

V

W

X

Y

Z

0001

MICRODIALYSIS DELIVERY OF AN ADENOSINE A2A RECEPTOR AGONIST TO THE PREFRONTAL CORTEX OF C57BL/6J MOUSE DECREASES ANESTHESIA WAKE-UP TIME AND INCREASES ACETYLCHOLINE RELEASE

Van Dort C, Baghdoyan H, Lydic R
University of Michigan, Ann Arbor, MI, USA

Introduction: Acetylcholine (ACh) (Anesthesiology 103:1268, 2005) and adenosine (Nat Neurosci 8:858, 2005) are important regulators of arousal. The prefrontal cortex (PFC) modulates arousal and executive functions such as selective attention and working memory (Neuron 30:319, 2001). Prefrontal cortical function is negatively affected by sleep deprivation (Trends Cogn Sci 6:475, 2002) via unknown mechanisms. Dialysis delivery of adenosine A1 receptor agonists and antagonists modulate anesthesia wake-up time and PFC ACh release (Sleep 29:0010, 2006; Soc Neurosci Abstr 32:157.14, 2006). The present study is testing the hypothesis that dialysis delivery of the adenosine A_{2A} receptor agonist 2-p-(2-Carboxyethyl)phenethylamino-5'-N-ethylcarboxamidoadenosine hydrochloride (CGS) to the PFC of C57BL/6J (B6) mouse causes a concentration-dependent decrease in anesthesia wake-up time and increase in PFC ACh release.
Methods: Adult male B6 mice (n=21) were anesthetized with isoflurane. A CMA/7 dialysis probe was placed in the PFC and perfused with Ringer´s (control) followed by Ringer´s containing CGS (0, 0.3, 1, 3, 10, or 30 μM) or CGS and the adenosine A_{2A} receptor antagonist 4-(2-[7-amino-2-(2-furyl)[1,2,4]triazolo[2,3-a][1,3,5]triazin-5-ylamino]ethyl)phenol (ZM). ACh release was quantified by HPLC. Following each dialysis experiment anesthesia was discontinued and the mice were placed in dorsal recumbency. The time to resumption of righting was recorded (wake-up time). Data were analyzed using one way analysis of variance and Tukey-Kramer multiple comparisons test.
Results: CGS caused a concentration-dependent decrease in anesthesia wake-up time ($F_{(5,12)}$=11.2; $p<0.05$) and increase in PFC ACh release ($F_{(5,102)}$=25.0; $p<0.01$). Both the decrease in anesthesia wake-up time and the increase in ACh release caused by CGS (10 μM) were blocked by coadministration of ZM (0.1 μM). Histology confirmed dialysis probe placement in the PFC.
Conclusion: Adenosine A_{2A} receptors in the PFC of B6 mouse modulate arousal and ACh release. The previous and present data support the conclusion that both A_1 and A_{2A} receptors in the PFC modulate arousal.
Support (optional): National Institutes of Health grants HL65272, HL57120, HL40881, MH45361 and the Department of Anesthesiology.

0002

NMDA RECEPTORS MEDIATE SLEEP-DEPENDENT PLASTICITY IN THE DEVELOPING VISUAL CORTEX

Aton S, Jha S, Coleman T, Frank M
University of Pennsylvania, Philadelphia, PA, USA

Introduction: Recent studies have revealed a critical role for sleep in processes dependent on synaptic plasticity, such as learning and memory. Previous studies from our lab have shown that sleep enhances a canonical form of in vivo synaptic remodeling in the visual cortex (V1), triggered by monocular deprivation (MD) during a critical developmental window (known as ocular dominance plasticity [ODP]). The effects of sleep on ODP are mediated by unknown, activity-dependent mechanisms.
Methods: We investigated the role of NMDA receptors (NMDArs) in this process by infusing the NMDAr antagonist APV into V1 during a 6-hour sleep period following MD. Effects of this treatment on ODP were assessed by intrinsic signal imaging and single-unit recording of responses in V1 to stimuli presented to the deprived and non-deprived eyes (DE and NDE, respectively).
Results: A large shift in neuronal responses toward the open eye occurred when V1 was infused with vehicle during post-MD sleep, but this shift was abolished in V1 infused with APV. Further analyses revealed that V1 changes underlying ODP in sleeping, vehicle-infused cats involved both depression of DE responses and potentiation of NDE responses. Critically, MD alone without subsequent sleep induced only depression of DE responses, and failed to potentiate NDE responses. APV treatment during post-MD sleep appeared to selectively block the sleep-dependent potentiation of NDE responses.
Conclusion: These findings indicate that sleep promotes synaptic remodeling by specifically strengthening synapses via NMDAr-dependent cellular mechanisms.
Support (optional): Supported by the National Institutes of Health (R01 MH067568; MGF) and a National Sleep Foundation Pickwick Postdoctoral Fellowship (SJA).

0003

MOBILE PHONE `TALK-MODE´ SIGNAL DELAYS SLEEP ONSET

Hung C,[1] Anderson C,[2] Horne J,[3] Mcevoy P[3]
(1) Loughborough University, Leicestershire, United Kingdom, (2) Loughborough University, United Kingdom, (3) Loughborough University, Loughborough, United Kingdom

Introduction: Mobile phone signals are microwaves, pulse-modulated at extremely low-frequency (ELF), which differ between `talk´ and `listen´ modes, as do their respective specific absorption rates (SARs). Previous studies have shown ELF components are more important than microwave carriers for sleep/wake EEG effects, but no sleep study has differentiated these two modes.
Methods: We used a standard GSM 900 MHz mobile phone, operating at 12.5% (23dBm) of maximum power and controlled by a base-station simulator with a test SIM card. ELF components and SARs of talk-mode are: 8, 217/1736 Hz with SAR=0.133 mW/g and for listen-mode: 2, 8, 217/1736 Hz with SAR=0.015 mW/g (for a 10g averaged tissue). 10 right-handed healthy young men (mean age: 22±2.7y), sleep restricted to 6h, were exposed (blind) to talk, listen and sham (nil signal) modes at weekly intervals. Ss lay in a sound-proof bedroom, with a thermally insulated phone attached beside the right ear and a silent signal generated for 30 min, starting at 13:30h. Ss remained silent and stared at a wall marker. Bipolar EEGs were recorded continuously, and subjective ratings of sleepiness obtained every 3 min (only during exposure). After exposure the phone and base-station were switched off, the bedroom darkened, and a 90-min sleep opportunity followed. Results are focused on sleep-onset using : i) visually scored latency to onset of stage 2 sleep, ii) EEG power spectral analysis.
Results: Post-exposure, sleep latency after talk-mode was markedly and significantly delayed beyond listen- and sham-modes. This condition effect was also evident in 1-4Hz EEG left frontal power across time, and 12-16Hz EEG right frontal power was different between talk and listen modes during waking before the first appearance of stage 1 sleep. There was no condition effect for subjective sleepiness.
Conclusion: Talk mode shows an alerting effect. It is possible that 2, 8, 217 Hz modulation may differentially affect sleep-onset.

0004

DEEP BRAIN RECORDING AND STIMULATION OF THE HUMAN PEDUNCULOPONTINE NUCLEUS: IDENTIFICATION OF PGO WAVES AND MODULATION OF REM SLEEP

Lim A, Moro E, Lozano A, Hamani C, Dostrovsky J, Hutchison W, Lang A, Wennberg R, Murray B
University of Toronto, Toronto, Ontario, Canada

Introduction: Animal data supports an important role for the pedunculopontine nucleus (PPN) in production of ponto-geniculo-occipital (PGO) waves, and rapid eye movement (REM) sleep. PGO waves have previously never been recorded in humans. Moreover, stimulation of the PPN in humans to modulate REM sleep has previously been impossible.
Methods: Four patients underwent PPN deep brain stimulation (DBS) as part of a study of treatment of Parkinson´s Disease/Progressive Supranuclear Palsy. PPN position was determined with MRI and microelectrode recordings. DBS location was confirmed with MRI. We obtained polysomnography pre-/post-operatively, with DBS turned off/on after DBS settings were optimized for mobility. Post-operatively, we also obtained intracranial extracellular field recordings from electrodes near the PPN. We present results on the first subject to complete the study.
Results: 3 of our 4 subjects reported changes in sleep or alertness.

In our first subject, we observed sharp wave transients occurring during REM and pre-REM sleep with a striking resemblance to PGO waves recorded in animals. Waveforms were localized to the axial plane of the PPN at the level of the inferior colliculus. They were observed in REM/pre-REM more frequently than during NREM (χ^2=494, p=1.9x10^-9).

Postoperatively, the subject spontaneously reported vivid dreaming and reduced daytime sleepiness. Between the DBS-off and DBS-on nights, REM sleep increased (11-36% of total sleep), REM latency decreased (314-0 min), and the REM phasic electromyographic metric increased in the contralateral leg.
Conclusion: PGO waves were seen from the region of the PPN. Moreover, PPN-DBS substantially increased REM sleep and REM phasic electromyographic activity. These findings support an important role of the PPN in modulation of REM sleep in humans, and support the unity of sleep control mechanisms among mammals.

0005

MORPHINE INCREASES PRINCIPAL SENSORY TRIGEMINAL NUCLEUS (PSTN) ACETYLCHOLINE (ACH) RELEASE IN ANESTHETIZED WISTAR RAT VIA GABAERGIC DISINHIBITION

Zhu Z, Baghdoyan H, Lydic R
University of Michigan, Ann Arbor, MI, USA

Introduction: Pain is managed with opioids but side effects include REM sleep disruption (Sleep 28:677, 2005) and altered cholinergic neurotransmission (Anesthesiology 103:779, 2005). Nociception changes across the sleep-wake cycle (J Sleep Res 6:61, 1997) and REM sleep disruption enhances pain perception (Sleep 29: 145, 2006). Cancer of the head and neck is the fifth most common type of cancer (Eur J Cancer Prev 13:139, 2004) and is associated with considerable pain. The PSTN modulates sensory input to the head and neck and the present study is testing the hypothesis that opioids alter ACh release in the PSTN.
Methods: Adult male Wistar rats (n=18) were anesthetized with isoflurane and microdialysis probes were aimed for the PSTN. ACh was measured (pmol/12.5 min) by HPLC during 5 dialysis conditions: 1) Ringer´s (control) followed by Ringer´s containing 2) 1, 3, or 10 μM morphine; 3) 10 μM morphine plus 1 μM naloxone; 4) 10 μM morphine plus 1 μM binaltorphimine (nor-BNI), a Î-opioid receptor antagonist, or 5) 300 μM bicuculline, a $GABA_A$ receptor antagonist.
Results: Dialysis delivery of morphine to the PSTN caused a significant ($F_{(3,86)}$=5.2, p=0.002) concentration dependent increase (21.3%) in ACh release. Coadministration of nor-BNI ($F_{(3,86)}$=10.5, p<0.0001), but not naloxone, with morphine blocked the morphine-induced increase in ACh release. ACh release was significantly ($t_{(28)}$=9.6, p<0.05) increased by bicuculline (108%).
Conclusion: The findings are consistent with the interpretation that morphine increases ACh release in PSTN via GABAergic disinhibition.
Support (optional): NIH grants HL57120, HL40881, MH45361, HL65272 and Department of Anesthesiology.

0006

MICROINJECTION OF THE GABAA RECEPTOR AGONIST MUSCIMOL INTO THE PONTINE RETICULAR NUCLEUS, ORAL PART (PNO) OF C57BL/6J (B6) MOUSE INCREASES WAKEFULNESS AND DECREASES SLEEP

Flint R, Lydic R, Baghdoyan H
University of Michigan, Ann Arbor, MI, USA

Introduction: Preclinical studies have shown that GABAmimetics either increase or decrease sleep, depending upon the site of their administration within the brain. Pontine reticular formation microinjection of $GABA_A$ receptor agonists and antagonists alter sleep and wakefulness in cat (J Neurophysiol 82:2015, 1999) and rat (J Neurophysiol 90:938, 2003). In B6 mouse, PnO microinjection of the $GABA_A$ receptor antagonist bicuculline causes a concentration dependent decrease in wakefulness and increase in REM sleep (Sleep 29:0022, 2006). The present study is testing the hypothesis that microinjection of muscimol into the PnO of B6 mouse increases wakefulness and decreases sleep.
Methods: Adult male B6 mice were implanted with electrodes for recording the electroencephalogram and electromyogram, and with a microinjection guide tube stereotaxically aimed for the PnO. Each mouse received randomized microinjections (50 nL) of muscimol (57.1 ng; 10 mM) and saline (vehicle control) followed by a 4 h recording. States of wakefulness, NREM sleep, and REM sleep were analyzed manually in 10 s bins. The data were evaluated by Wilcoxon matched pairs signed ranks test and a probability value ≤ 0.05 was considered statistically significant.
Results: Microinjection sites were histologically localized to the PnO. Compared to saline, muscimol significantly increased the amount of wakefulness (51%) and decreased the amount of NREM sleep (-98%). REM sleep was eliminated by muscimol. Muscimol significantly decreased the number of episodes of wakefulness (-89%) and NREM sleep (-91%), and significantly increased NREM sleep latency (811%).
Conclusion: Microinjection of muscimol into the PnO of B6 mouse increased wakefulness and decreased sleep. Future studies will determine whether these effects of muscimol on sleep and wakefulness are specific to the PnO, concentration dependent, and blocked by a $GABA_A$ receptor antagonist. Such findings would support the interpretation that $GABA_A$ receptors in the PnO promote wakefulness.
Support (optional): National Institutes of Health grants MH45361, HL65272, HL57120, HL40881, and the Department of Anesthesiology.

0007

EFFECTS OF CONTEXTUAL FEAR EXTINCTION ON SLEEP IN RATS

Wellman L, Holbrook B, Yang L, Tang X, Sanford L
Eastern Virginia Medical School, Norfolk, VA, USA

Introduction: Stressful and traumatic events are often followed by disturbances in sleep which may persist in association with stress-related psychopathology such as anxiety and posttraumatic stress disorder. Exposure therapy, an extinction-like procedure involving repeated presentation of fearful stimuli, may be employed in treatment; however, the relationship between sleep and extinction is not known. In this study, we compared sleep after fear induction and fear extinction in rats.
Methods: Wistar rats (n=24) were implanted with electrodes for recording sleep and, after recovery, assigned to four groups: extinction (EXT), context reexposure without extinction (CR), or two control groups (ECON or CCON). On day 1, EXT and CR underwent shock training involving 20 footshocks (0.8mA, 0.5s duration) over 30 minutes while ECON and CCON rats were allowed 30 minutes free exploration without shock. On day 2, all groups were placed back in the chamber without shock (EXT & ECON for 60 minutes (extinction trial) and CR & CCON for 30 minutes (fear trial)). On day 3, all groups were placed in the chamber without shock for 30 minutes. Sessions were video recorded and scored for freezing. Sleep was recorded for 20 h post-session and scored for NREM, REM, and wakefulness.
Results: Following shock training, both EXT and CR groups exhibited significant reductions in REM in the first 2 h and in NREM during the second h of recording. Following the session on day 2, EXT rats showed significant increases in NREM and REM during the first 2 h of recording while the CR rats continued to show significantly decreased REM. Cessation of freezing indicated that EXT animals had successful fear extinction whereas continued freezing in CR animals indicated a lack of fear extinction.
Conclusion: Contextual fear extinction not only decreases fearful behaviors but also enhances sleep compared to that after fear without extinction.
Support (optional): Supported by NIH research grant MH64827 and MH61716.

0008

GABA LEVELS IN SUBSTANTIA INNOMINATA (SI) OF CAT BASAL FOREBRAIN ARE STATE DEPENDENT

Vanini G, Watson C, Bouchard L, Lydic R, Baghdoyan H
University of Michigan, Ann ARBOR, MI, USA

Introduction: Putatively GABAergic basal forebrain neurons fire selectively during NREM sleep (Brain Res Bull 22:423, 1989), and both $GABA_A$ and $GABA_B$ receptors in the basal forebrain promote NREM sleep (Am J Physiol 281:170, 2001). Cholinergic basal forebrain neurons contribute to cortical activation (Eur J Neurosci 16:2453, 2002), and $GABA_A$ receptors in the basal forebrain inhibit local acetylcholine release (Eur J Neurosci 17:249, 2003). Although basal forebrain GABAergic neurons modulate cortical activation (J Neurosci 20:9252, 2000), no data have quantified state-dependent levels of SI GABA. Therefore, the present study is testing the hypothesis that GABA levels in the SI region of cat basal forebrain vary significantly across states of anesthesia and wakefulness.
Methods: Adult male cats were implanted with electrodes for monitoring arousal state. During each experiment, cats were anesthetized with isoflurane and a microdialysis probe was aimed stereotaxically for the SI and perfused continuously with Ringer´s solution. Upon completion of dialysis sample collection, fluorescent microspheres (0.1 µl) were microinjected into the dialysis site for histological localization. GABA levels (pmol/10 µl) were quantified by HPLC (Neuroscience 144:375, 2007).
Results: To date, dialysis samples (n) have been obtained during anesthesia (n=36), a post-anesthesia NREM sleep-like state (n=11), and post-anesthesia wakefulness (n=16). ANOVA revealed that GABA levels varied significantly as a function of arousal state ($F=7.08$; $d.f.=2,60$; $p<0.01$). Compared to isoflurane anesthesia, GABA levels were 123% greater ($p<0.01$) during the NREM sleep-like state and 65% greater ($p<0.05$) during post-anesthesia wakefulness. Histological localization of dialysis sites is pending.
Conclusion: These results show for the first time that endogenous GABA levels in cat SI are state dependent, and support the interpretation that GABAergic transmission in the SI participates in the modulation of arousal state.
Support (optional): National Institutes of Health grants MH45361, HL57120, HL40881, HL65272, and the Department of Anesthesiology.

0009

LEPTIN INCREASES ANTINOCICEPTIVE RESPONSES IN C57BL/6J-LEPOB (OBESE) MICE FOLLOWING MICROINJECTION OF NEOSTIGMINE INTO THE PONTINE RETICULAR FORMATION (PRF)

Wang W, Baghdoyan H, Lydic R
University of Michigan, Ann Arbor, MI, USA

Introduction: Obese and C57BL/6J (B6) mice differ by a nonsense mutation at one gene, resulting in the inability of obese mice to produce the protein leptin. In obese mice, leptin deficiency alters cholinergic modulation of sleep (J Appl Physiol 98:918, 2005) and contributes to respiratory abnormalities (J Appl Physiol 85:2261, 1998). These respiratory abnormalities are attenuated with leptin replacement (Am J Respir Crit Care Med 159:1477, 1999). Microinjection of neostigmine into the PRF produces significantly less antinociceptive behavior in obese than B6 mice (Soc Neurosci Abstr 248.4, 2006). The present study is testing the hypothesis that leptin replacement in obese mice rescues the antinociceptive response caused by PRF neostigmine.
Methods: Adult male mice (n=9 obese, n=9 B6) were implanted with microinjection guide tubes aimed for the PRF. Four additional obese mice were implanted with PRF microinjectors and ALZET osmotic pumps that continuously delivered mouse recombinant leptin for seven days (30 µg/day). An IITC Hargreaves Paw Withdrawal System was used to measure paw withdrawal latency (PWL) to a thermal stimulus. The PRF was injected with 50 nL of 10 mM neostigmine (151.6 ng) and PWL measurements were taken 10, 20, 30, 60, 90, and 120 min post injection. All data were evaluated by two-way ANOVA and post-hoc multiple comparisons tests.
Results: PWL was expressed as percent maximal antinociceptive effect (%MPE). Obese mice that received leptin lost 16% body weight and showed a %MPE following PRF neostigmine that was 10-fold greater than obese mice without leptin. PRF neostigmine caused a 50% increase in %MPE in B6 mice compared to 2.5% in obese mice that did not receive leptin.
Conclusion: The results support the conclusion that leptin replacement in obese mice can restore the antinociceptive response to PRF neostigmine.
Support (optional): NIH grants HL65272, HL57120, HL40881, MH45361 and the Department of Anesthesiology

0010

INCREASED SLOPE OF SLEEP SLOW-WAVES IN PRE-PUBERTAL CHILDREN COMPARED TO MATURE ADOLESCENTS

Huber R,[1] Jenni O,[2] Riedner B,[1] Tononi G,[1] Carskadon M[3]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) University Children's Hospital Zurich, Zurich, Switzerland, (3) Brown University, Providence, RI, USA

Introduction: A recent hypothesis suggests that slow-wave activity (SWA, 1-4.5 Hz) during sleep reflects synaptic strength (Tononi and Cirelli 2006). Computer simulations show that increased synaptic strength leads to increased synchronization of cortical neurons, which is reflected in increased slope of cortical slow-waves (Hill *et al.*, 2006). This is supported by findings in both rats (Vyazovskiy *et al.*, 2006) and humans (Riedner *et al.*, 2006) in which the slope of slow-waves was increased when sleep pressure was high, i.e. at the beginning of the night, compared to when sleep pressure is low at the end of the night. Here we asked the question, whether the increased SWA level observed in pre-pubertal children compared to mature adolescents (Jenni *et al.*, 2004) is associated with increased synaptic strength as measured by the slope of sleep slow-waves.
Methods: All night sleep recordings were performed for the C3A2 derivation in 8 pre-pubertal children (Tanner 1/2, 11.5±0.3 years) and 7 mature adolescents (Tanner 4/5, 13.9±0.6 years). The EEG was visually scored (30s epochs) for the first 6 cycles, artifact rejected, and bandpass filtered (0.5-4 Hz). Slow-waves were detected as negative signal deflections between two consecutive positive peaks.
Results: SWA showed the well-known homeostatic decline in both groups and was higher in pre-pubertal children compared to mature adolescents. Concurrently, the slope of slow-waves showed a decline throughout the night. In addition, we found a prominent difference in the slope of slow-waves between pre-pubertal children and mature adolescents (pre-pubertal children, 402.2±27.3; mature adolescents, 242.8±20.5 μV/s; $p<0.0001$, unpaired t-test). Even when controlling for the amplitude of slow-waves or the amount of SWA, pre-pubertal children exhibited steeper slope slow-waves than mature adolescents.
Conclusion: The increased slope of slow-waves in pre-pubertal children compared to mature adolescents suggests increased synaptic strength of neurons involved in the generation of sleep slow-waves. Such increased synaptic strength in pre-pubertal children could be due to increased synaptic density and/or increased synaptic efficacy.
Support (optional): EU LSHM-CT-2005-518189 to R.H., NIH Pioneer Award to G.T. and NIMH grant MH52415 to M.A.C.

0011

SLEEP AND WAKEFULNESS-RELATED CHANGES IN GENE EXPRESSION IN THE AVIAN BRAIN

Jones S,[1] Cirelli C,[2] Rattenborg N,[3] Benca R[2]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) University of Wisconsin-Madison, WI, USA, (3) Max Planck Institute, Germany

Introduction: In the rat cerebral cortex, approximately 5% of transcripts are differentially expressed as a function of sleep and wakefulness independent of time of day. Wakefulness-related and sleep-related transcripts belong to distinct functional categories of genes, suggesting that sleep and wakefulness favor different cellular processes. In an effort to determine the extent to which molecular correlates of sleep and waking are conserved across species, we performed a comprehensive microarray analysis of gene expression in the avian brain.
Methods: Using a protocol designed to identify gene expression changes related to behavioral state as opposed to diurnal variation, 18 birds were randomly assigned to one of 3 experimental groups: Sleeping (6 hours), spontaneously wakeful (6 hours) or sleep deprived (6 hours). RNA from the right telenchephalon of 6 birds per experimental group was pooled and hybridized to microarray platforms containing the genomes of two avian species closely related to the sparrow: The chicken (Gallus domesticus) and the Zebra finch Taeniopygia guttata. Biological verification of microarray data was obtained by performing q-PCR on RNA of 12 animals (4 per group) not previously used for microarray analysis.
Results: We found that approximately 2% of transcripts in the avian telencephalon are modulated by sleep and wakefulness. As in rats, wakefulness-related mRNAs code for mitochondrial proteins, heat shock proteins, and proteins involved in synaptic potentiation and glutamatergic transmission. Sleep-related transcripts code for proteins involved in translational processes, cholesterol synthesis and transport, and membrane trafficking and maintenance.
Conclusion: Despite the use of wild-caught birds of mixed age and gender, the molecular correlates of sleep and wakefulness in the avian brain exhibit a remarkable degree of overlap with those transcripts modulated by behavioral state in the rodent cortex. Our data suggests that sleep function may be conserved in phylogenetically distant species.
Support (optional): DAAD10-0021-0041

0012

LONG-TERM EFFECTS OF CUED FEAR CONDITIONING ON REM SLEEP MICROARCHITECTURE AND PHASIC EVENTS IN RATS

Madan V,[1] Brennan F,[2] Ross R,[2] Horbal A,[1] Dunn G,[1] Mann G,[1] Morrison A[1]
(1) University of Pennsylvania, Philadelphia, PA, USA, (2) Philadelphia VA Medical Center, Philadelphia, PA, USA

Introduction: Re-exposure to a fear conditioned cue (CC), 24 hr post-conditioning (short-term effect, Day 1) alters REM sleep (REMS) architecture. To extend our findings, we investigated the disturbances in REMS microarchitecture and its phasic events (myoclonic twitches) two weeks (Day 14) post-conditioning. In addition, we examined the effects of re-exposure to the CC on freezing, a common behavioral index of fear.
Methods: Male Sprague-Dawley rats (n=6) were prepared for polysomnographic recording and habituated to a neutral chamber. A day after baseline (BSL) sleep recording (4 hr), they received five 5-sec tone CC pairings, co-terminating with a 1-sec, 1mA footshock every 30 sec. Rats were placed in the neutral chamber at Day 1 and Day 14 post-conditioning and received 5 tones on each occasion. We videotaped behavior for offline scoring of freezing time, recorded sleep for 4 hr and counted myoclonic twitches to determine the CC effect on phasic REMS activity.
Results: Significant alterations in REMS microarchitecture appeared at Day 14, mainly due to significant decreases in total amount (BSL: 13.36±0.71 min; Day 14: 5.19±2.82 min; $p<0.05$) and number (BSL: 9.17±1.28; Day 14: 3.5±1.99; $p<0.05$) of sequential REMS episodes (occurring at < 3 min intervals). Significant increases in the total amount (> 3 min apart) (BSL: 16.17±1.49 min; Day 14: 27.03±2.74 min; $p<0.001$) and number (BSL: 7.0±0.37; Day 14: 10.67±1.17; $p<0.05$) of single REMS episodes was also evident. Further, significant increase in freezing ($p<0.001$) and myoclonic twitches ($p<0.05$) occurred on Day 14. Changes in REMS measures and muscle twitches correlated significantly with freezing behavior.
Conclusion: Fear-induced alterations in REMS microarchitecture and

associated phasic events suggest an imbalance in REMS regulation. Further, significant effects primarily on Day 14 could be due to memory incubation: a progressive increase in the strength of aversive memory with time.
Support (optional): Supported by RO1-MH072897

0013

THE NUMBER OF INTERLEUKIN-6-IMMUNOREACTIVE CELLS INCREASES IN LAYERS II-III OF THE BARREL FIELD IN RESPONSE TO WHISKER DEFLECTION IN RATS

Guan X, Churchill L, Hall S
Washington State University, Pullman, WA, USA

Introduction: Cytokines, such as interleukin-6 (IL6), are posited to be sleep regulatory substances. Regional sleep intensity, as defined by EEG delta wave power, is dependent upon activity during prior wakefulness. We posit that neuronal activity enhances local production of sleep regulatory cytokines that in turn act locally to enhance EEG delta power. Indeed, cortical TNFá increases in response to whisker stimulation and application of TNFá onto the cortex locally enhances EEG delta power. To analyze the activity-dependence of IL6 we evaluated the number of IL6-immunoreactive (IR) cells within the barrel field after whisker stimulation.
Methods: Five male Sprague-Dawley rats (200-300g) were manually stimulated unilaterally by brushing the longer whiskers for 2 h in the afternoon. After 2 h of stimulation, the rats were perfused with 4% paraformaldehyde and IR cells for the activity marker, fos, and the cytokine, IL6 were analyzed in adjacent sections. Quantitative analysis of 0.14 mm2 within each layer was completed using digital pictures of coronal sections of the somatosensory cortex (SSctx). The number of darkly labeled cells was counted manually by an investigator blind to the experimental conditions.
Results: In SSctx layers II-III and V, large neuron-like cells were stained with IL6-IR in stimulated columns as determined by fos activation. Double-labeling immunofluorescence with IL6 and fos antibodies showed double-labeled cells in layers II-III but not in V. Also double labeling with IL6 and the neuronal marker protein, NeuN, demonstrated that these labeled cells were neurons.
Conclusion: Collectively, these data suggest that afferent activation of a cortical column enhances the level of IL6 protein in pyramidal neurons within layers II-III. These neurons have been implicated in intercolumnar communication. These data support our hypothesis that sleep is activity-dependent and initiated within local networks.
Support (optional): This work was supported by NIH grant No. NS25378 to JM Krueger.

0014

THE EFFECTS OF DOSE ON THE ACTION OF AN ADENYLYL CYCLASE-INHIBITOR TO INCREASE REM SLEEP WHEN INJECTED INTO THE PONTINE RETICULAR FORMATION OF THE RAT

Marks G,[1] Sachs O,[2] Birabil C[2]
(1) University of Texas Southwestern Medical Center and Dallas VA, Dallas, TX, USA, (2) University of Texas Southwestern Medical Center at Dallas, TX, USA

Introduction: Adenylyl cyclase (AC) catalyzes the formation of cAMP, an important intracellular second messenger. Microinjection of the AC-inhibitor, SQ22,536 (60 nl, 0.1 M), into the caudal, nucleus pontis oralis (PnOc) of the rat results in a long-lasting increase in REM sleep. Local injections of an adenosine A1 receptor agonist, through its G-protein coupling, inhibits AC and also increases REM sleep. The dose-response curves of the adenosine agonist to increase REM sleep and inhibit AC in PnOc are both an inverted "U". To explore the nature of this interesting relationship further, we sought to determine the dose-response relationship for increasing REM sleep with the direct inhibitor of AC.
Methods: Long-Evans Hooded rats received multiple unilateral injections (60 nl) in the PnOc at lights-on with three different doses of SQ22,536 (1, 10, 100 mM) and four injections of saline vehicle alone. Standard procedures for electrographic recording and analysis were used to determine wake, NREM and REM sleep in 15 sec epochs for 24 hrs following each injection. Injections were given at least one week apart. Drug effects were assessed by computing the percentage of the control-injection mean for each animal.
Results: SQ22,536 induced a significant increase in REM sleep compared to vehicle control when administered in the 100 mM dose. This increase was observed for 4 and 8 hours post injection. The lower doses failed to produce significant increases in REM sleep. The highest dose increased NREM and decreased wake at 4 hours but not 8 hours.
Conclusion: A dose-response relationship for AC-inhibition demonstrating saturation, rather than an inverted "U", would indicate that the biphasic relationship of adenosinergic and muscarinic agonists to increase REM sleep involves mechanisms before AC in the signal transduction cascade. Higher doses of SQ22,536 are being used to determine if the response saturates.
Support (optional): NIH Grant RO1 MH57434

0015

MOLECULAR EVIDENCE FOR SYNAPTIC POTENTIATION DURING WAKING AND SYNAPTIC DOWNSCALING DURING SLEEP

Pfister-Genskow M,[1] Tononi G,[2] Cirelli C[2]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) Sleep Research Society, Madison, WI, USA

Introduction: We have recently hypothesized that waking is associated with synaptic potentiation, and sleep with synaptic downscaling. In a companion abstract (Vyazovskiy et al), we measured in awake rats the slope of the early cortical evoked potential – an established marker of synaptic strength -, and found that it increases after wakefulness and decreases after sleep. Here we studied whether molecular markers of synaptic potentiation and depression also change between sleep and wakefulness.
Methods: Male adult WKY rats (n=6/group) were killed at 4pm after having spent most of the last 6h asleep (S); at 4pm after 6h of sleep deprivation by exposure to novel objects (SD); or at 4am after having spent most of the last 6h spontaneously awake (W). Protein levels of synaptic glutamatergic GluR-1 and GluR2-containing AMPA receptors, NR2A-containing NMDA receptors, PSD-95, and CamKII were measured by Western blot in cortical synapsoneurosomes.
Results: Both W and SD, compared to S, were characterized by increased levels of total GluR1 (% increase vs. S, SD=53%, W=35%; Mann-Whitney test, p=0.011). CamKII levels also increased in SD-W relative to S (total CamKII, % increase vs. S, SD=27%, W=18%; p<0.05; CamKII phosphorylated at Thr286, SD=65%, W=58%; p<0.05). GluR1 phosphorylated at ser845 was also higher in awake rats (GluR-P845; % increase vs. S, SD=77%, W=50%; p<0.007). SD also showed an increase in GluR-P845/totalGluR1 (SD vs S =48%, p<0.0001). No changes were seen in GluR2, NR2A, and PSD-95 expression.
Conclusion: Wakefulness is associated with markers of cortical synaptic potentiation, including the increased number of synaptic AMPARs containing GluR1 subunits, and the increased expression of phosphorylated and total CamKII. Sleep, instead, is associated with the dephosphorylation of synaptic GluR1 at ser845, an established marker

of synaptic depression. These data provide molecular evidence for synaptic potentiation during wakefulness and synaptic downscaling during sleep.

0016

MOUSE STRAIN DIFFERENCES IN THE EFFECTS OF CORTICOTROPIN RELEASING HORMONE (CRH) ON SLEEP AND ACTIVITY

Sanford L,[1] Yang L,[1] Wellman L,[1] Dong E,[2] Tang X[1]
(1) Eastern Virginia Medical School, Norfolk, VA, USA, (2) Eastern Virginia Medical School, VA, USA

Introduction: CRH plays a major role in CNS responses to stressors and has been implicated in stress-induced alterations in sleep. In the absence of stressors, CRH appears to contribute to the regulation of spontaneous waking and can increase activity. We examined the effects of CRH and astressin (AST), a non-specific CRH antagonist, on sleep and activity in two mouse strains with differential responsiveness to stress to determine whether CRH might also differentially affect undisturbed sleep and activity.
Methods: Less reactive C57BL/6J (B6, n=6) and high reactive BALB/cJ (C, n=6) male mice were implanted with a transmitter for recording sleep and activity via telemetry and with a guide cannula aimed into the lateral ventricle. After recovery from surgery and habituation to handling, ICV microinjections of CRH (L: 0.4, M: 2.0, H: 4.0 microg), AST (L: 1.0, M: 4.0, H: 10.0 microg) or vehicle alone (saline, 0.2 microl) were administered during the fourth h after lights on and sleep was recorded for the subsequent 8 h. Comparisons of total 8 h sleep and activity measures (drug vs. saline) were conducted with paired t-tests.
Results: In B6 mice, REM was significantly decreased after microinjections of CRH_M and CRH_H, and NREM and total sleep were decreased after microinjection of CRH_H. CRH_L and AST did not significantly change sleep, but all three doses of AST reduced activity. In C mice, CRH_M and CRH_H significantly decreased REM, NREM and total sleep, and significantly increased activity. CRH_L and three doses of AST did not significantly alter sleep or activity.
Conclusion: These findings demonstrate that CRH may produce changes in arousal and activity when given to otherwise undisturbed mice. Strain differences in the effects of CRH and AST may be linked to the relative responsiveness of B6 and C mice to stressors and underlying differences in the CRH system.
Support (optional): Supported by NIH research grant MH64827 and MH61716

0017

ROLE OF CORTICOTROPIN RELEASING HORMONE (CRH) IN FOOTSHOCK STRESS-INDUCED ALTERATIONS IN SLEEP

Yang L, Tang X, Wellman L, Sanford L
Eastern Virginia Medical School, Norfolk, VA, USA

Introduction: The central CRH system plays a major role in the stress response and has been implicated in stress-induced alterations in sleep. Uncontrollable footshock (FS) stress can be followed by significant and persisting reductions in REM. To determine the potential role of the CRH system in these reductions, we examined the effects of ICV administered CRH and astressin (AST), a non-specific CRH antagonist, on sleep after FS.
Methods: Male C57BL/6J mice were implanted with transmitters for recording sleep via telemetry and with guide cannulae aimed into the lateral ventricles. After recovery from surgery, the mice received ICV microinjections of CRH (L: 0.4, H: 4,0 microg), AST (L: 1.0, H: 4.0 microg) or vehicle alone (saline, 0.2 microl). They then received 20 FSs (0.2 mA, 2 sec duration, 1 min interstimulus interval). Microinjections and FSs were administered during the fourth h after lights on and sleep was recorded for the following 8 h. Data were analyzed in 4-h blocks. Five days were allowed to elapse between experiments.
Results: Compared to saline, both doses of CRH significantly enhanced the decrease in REM after FS during the second 4-h block [saline: 13.0±2.9; L: 7.6±1.7 and H: 6.4±2.1, $p < 0.05$] and during the total 8-h recording period. No significant differences between saline and CRH were observed for NREM or total sleep after FS. Compared to saline, AST resulted in significant increases in NREM and total sleep after FS during the first 4-h block and in NREM after FS during the total 8-h recording period. Compared to saline, AST did not significantly alter REM after FS.
Conclusion: The results indicate a role for the CRH system in the alterations in sleep that occur in the aftermath of uncontrollable FS stress.
Support (optional): Supported by NIH research grant MH64827 and MH61716.

0018

THE NUMBER OF INTERLEUKIN-1&BETA-IMMUNOREACTIVE CELLS INCREASES IN LAYERS II-III OF THE BARREL FIELD IN RESPONSE TO WHISKER DEFLECTION IN RATS

Guan X, Churchill L, Fix C, Hall S
Washington State University, Pullman, WA, USA

Introduction: Sleep regulatory substances, such as interleukin1&beta (IL1&beta), are likely involved in sleep homeostasis. We hypothesize that neuronal activity enhances local production of IL1&beta and through this mechanism the brain keeps track of time awake. To analyze the activity-dependence of IL1&beta we evaluated the number of IL1&beta-immunoreactive (IR) cells within the barrel field after whisker stimulation.
Methods: Six male Sprague-Dawley rats (200-300g) were manually stimulated unilaterally by brushing the longer whiskers for 2 h in the afternoon. After 2 h of stimulation, the rats were perfused with 4% paraformaldehyde and IR cells for the activity marker, fos, and the cytokine, IL1&beta nwere analyzed using antibodies from Oncogene and R&D Systems, respectively. Quantitative analysis of 0.14 mm2 within each layer was completed using digital pictures of coronal sections of the somatosensory cortex. The number of darkly labeled cells was counted manually by an investigator blind to the experimental conditions.
Results: In layers II-III, large neuron-like cells were stained with IL1&beta -IR in stimulated columns as determined by fos activation. The staining appeared to be localized within a circle of cytoplasm surrounding the nucleus and in the apical dendrites of pyramidal neurons. Double-labeling demonstrated that the neuronal nuclear marker NeuN was colocalized with the neuron-like IL1&beta -IR cells. In the unstimulated columns identified by the absence of fos activation, IL1&beta -IR was mainly localized in astrocyte-like cells within layers I and VI.
Conclusion: Collectively, these data suggest that afferent activation of a cortical column enhances the level of IL1&beta protein in pyramidal neurons within layers II-III. Layers II-III neurons are involved in intercolumnar communication. These data support our hypothesis that sleep is activity-dependent and initiated within local networks.
Support (optional): This work was supported by NIH grant No. NS25378 to JM Krueger.

0019

G PROTEINS IN THE PREFRONTAL CORTEX (PFC) OF SPRAGUE-DAWLEY RAT ARE DIFFERENTIALLY ACTIVATED AS A FUNCTION OF OXYGEN (O2) STATUS AND PFC REGION

Hambrecht V,[1] Vlisides P,[2] Row B,[3] Gozal D,[4] Baghdoyan H,[1] Lydic R[1]
(1) University of Michigan, Ann Arbor, MI, USA, (2) University of Michigan Medical School, MI, USA, (3) Louisville, KY, USA, (4) University of Louisville, Louisville, KY, USA

Introduction: Obstructive sleep apnea, characterized by intermittent upper airway obstruction and hypoxia, can lead to impaired functions regulated by the PFC (J Sleep Res 11:1, 2002) such as attention, affect, learning, and memory. Acetylcholine activates the PFC electroencephalogram (J Neurophysiol 88:3003, 2002) and G protein activation in the PFC is modulated by G protein-coupled muscarinic cholinergic receptors (J Comp Neurol 457:175, 2003). Opioids depress cortical function (Anesthesiology 103:779, 2005) and mu opioid receptors are coupled to G proteins (Neuroreport 9:3025, 1998). The present study is testing the hypotheses that 1) PFC G proteins are activated by the cholinergic agonist carbachol and by the mu opioid agonist DAMGO; and 2) that hypoxia alters agonist activation of G proteins in the PFC.
Methods: For 14 consecutive days, three groups of adult male rats (6/group) were housed under one of three O_2 conditions: (1) intermittent hypoxia (IH) consisting of 10 % O_2 and 21 % O_2 alternating every 90 s for 12 h/day.; (2) sustained hypoxia (SH) as continuous 10 % O_2, and (3) control condition in which rats were housed in room air (RA). The PFC from all 18 rats was serially sectioned and agonist activation of G proteins was quantified in nCi/g using [^{35}S]GTPÁS autoradiography. G protein activation as a function of O_2 status, ligand, and PFC subdivision was compared using t-tests.
Results: Carbachol and DAMGO significantly activated G proteins in the frontal association (FrA; $p < 0.01$) and prelimbic (PrL; $p < 0.001$) regions of the PFC for all three O_2 conditions. Compared to RA, SH increased both carbachol- and DAMGO-stimulated G protein activation in the FrA (carbachol: $p = 0.017$; DAMGO: $p = 0.054$). An additional finding was that of differential G protein activation in different regions of the PFC. Following both IH and SH, G protein activation by DAMGO was significantly greater (IH: $p = 0.0485$; SH: $p = 0.0036$) in the FrA than in the PrL.
Conclusion: These data show for the first time regional differences in G protein activation within subdivisions of the PFC. The finding of hypoxia-induced alterations in PFC G protein activation is consistent with the conclusion that hypoxia causes PFC dysfunction (J Neurosci 21:2442, 2001; Neurosci Lett 305:197, 2001).
Support (optional): NIH grants HL40881, HL57120, HL65272, MH45361, HL65270, HL69932, and the Department of Anesthesiology

0020

REMSD MAY EXTEND THE VISUAL CORTICAL CRITICAL PERIOD BY BLOCKING MATURATION OF INHIBITORY MECHANISMS IN THE MIDDLE LAYER

Shaffery J,[1] Lopez J,[2] Roffwarg H[1]
(1) University of Mississippi Medical Center, Jackson, MS, USA, (2) University of Mississippi Medical Center, MS, USA

Introduction: The increase in inhibitory tone of neurons in the middle layer of visual cortex in early life is thought to underlie a functional plasticity gate that permits production of a developmentally regulated form of long-term potentiation (LTP) in the upper layers after white matter stimulation. Because REM sleep deprivation (REMSD) extends the age until which this form of LTP can be elicited, we wondered whether the inhibitory gate mediates the REMSD effect. Inasmuch as the neurotrophin BDNF can contribute to maturation of inhibition, and REMSD may block its expression, we infused BDNF into one side of visual cortex in REMSD rats and assessed the degree of inhibition in visual cortical layer four bilaterally with paired-pulse stimulation (PPS) protocols.
Methods: Five 35-45 day old Long Evans rats were implanted with sleep recording electrodes as well as a BDNF-filled minipump attached to a saline-loaded cannula. The cannula prevented any neurotrophin delivery during the first 48-hrs of REMSD. During the next 24-hrs of REMSD, BDNF was infused into one hemisphere after which visual cortical slices were prepared for in vitro PPS experiments. A stimulating electrode was set in the WM below layer four and a recording electrode in layer three. After obtaining a stable baseline response at 30-s intervals, PPS´s (20-, 40-, 60- and 80-ms) were presented 30-s apart.
Results: On the non-infused, REMSD-only, side, PPS produced facilitation of the second stimulus of each pair except at 20-ms. BDNF blocked this effect on the opposite side and led to inhibition at all PPS intervals.
Conclusion: Inasmuch as PPS-facilitation is usually observed solely in rats less than 35-days, REMSD appears to have delayed maturation of the inhibitory response to PPS in visual cortex. BDNF may be necessary for maturation of the inhibitory mechanisms in visual cortical layer four as its infusion blocked the REMSD-induced delay of PPS-inhibition.
Support (optional): Supported by: NS31720

0021

STRESSOR CONTROLLABILITY AND FOS EXPRESSION IN STRESS AND REM REGULATORY REGIONS: IMPLICATIONS FOR STRESS-INDUCED ALTERATIONS IN REM

Liu X, Tang X, Sanford L
Eastern Virginia Medical School, Norfolk, VA, USA

Introduction: Uncontrollable stress (e.g., fear conditioning) produces significant reductions in REM that may not be recovered whereas controllable stress (e.g., shuttlebox training) may be followed by significantly increased REM even though the same stressor (footshock) is experienced. We trained mice with inescapable (uncontrollable) and escapable (controllable) footshock and examined Fos expression as a measure of neural activation in brain regions involved in the stress response and in the control of REM to determine whether differential activation of these regions could be a factor in differences in post-stress sleep.
Methods: Mice (C57BL/6J) were trained to escape footshock by moving to a safe chamber in a shuttlebox (n=3). This terminated shock in the escape condition and also terminated shock delivery to yoked-control mice receiving inescapable footshock (n=3). Thus, both groups received identical amounts of footshock. Handling control mice were allowed to freely explore the shuttlebox, but never received footshock (n=2). After training, the mice were returned to their home cage. Training took place on three days (20 trials per day, 0.2 mA, 5.0 sec maximum duration, 1.0 min interstimulus interval). On day three, the animals were sacrificed two h after training and the brains processed for Fos immunohistochemistry. Sections were made through the amygdala, hypothalamic paraventricular nucleus (PVN), laterodorsal tegmental nucleus (LDT), locus coeruleus (LC) and dorsal raphe nucleus (DRN).
Results: Fos expression after inescapable shock was greater than after escapable shock and greater than the handling controls in all regions ($p < .05$). Fos expression after escapable shock was greater than the handling controls in PVN and LDT ($p < .05$), but not in amygdala, LC or DRN.
Conclusion: Controllability reduces stressor-induced neural activity (as

indicated by Fos) in brain regions implicated in the stress response and in the regulation of REM. This reduction may, in part, account for directional differences in REM amounts in the aftermath of uncontrollable and controllable footshock stress.
Support (optional): Supported by NIH research grant MH64827 and MH61716.

0022

ELECTROPHYSIOLOGICAL RECORDINGS FROM GABAERGIC NEURONS IN THE BASAL FOREBRAIN OF KNOCK-IN MICE EXPRESSING GREEN FLUORESCENT PROTEIN UNDER THE CONTROL OF THE GLUTAMIC ACID DECARBOXYLASE 67 PROMOTER

Brown R,[1] Franciosi S,[2] McKenna J,[3] Winston S,[4] Yanagawa Y,[5] Mccarley R[1]
(1) Harvard University, Brockton, MA, USA, (2) Universita di Milano, Milan, Milano, Italy, (3) Brockton, MA, USA, (4) Harvard University, MA, USA, (5) Gunma University Maebashi, Maebashi, Maebashi, Japan

Introduction: Pharmacological, single-unit recording, Fos immunohistochemical and lesion studies have identified the basal forebrain (BF) as a critical region responsible for cortical activation during waking and REM sleep. While considerable data exist concerning cholinergic neurons in this region much less is known regarding GABAergic neurons. Here we use mice expressing green fluorescent protein (GFP) under the control of the glutamic acid decarboxylase promoter (GAD67-GFP knock-in mice) to identify and record from GABAergic BF neurons in order to characterize their intrinsic membrane properties and responses to neurotransmitters involved in sleep-wake control.
Methods: Coronal brain slices were prepared from young (15-22 d) heterozygous GAD67-GFP knock-in animals according to standard techniques. Neurons expressing GFP in the BF (0.50 to -0.10 mm caudal to Bregma) were identified using a Hamamatsu ORCA-AR CCD camera. Whole-cell patch-clamp recordings were made using a Multiclamp 700A amplifier. Drugs were bath-applied.
Results: Recordings were made from 10 small-to-medium sized (long-axis diameter 13-20 μm) GFP-Pos neurons. These neurons could be subdivided into two groups. Group I neurons (n = 6) were spontaneously active, firing at 10 Hz. Their maximal firing rate was 65 Hz. In the presence of tetrodotoxin (TTX, 0.5 μM), their RMP was -69 mV. This group of neurons had a prominent depolarizing sag (Ih, 77 % of peak at the end of a 1 s current pulse to -120 mV). Group II neurons (n = 4) were silent at rest with a RMP of -76 mV. Their maximal firing rate was 62 Hz. In contrast to Group I neurons they lacked Ih. Both groups of neurons were excited (depolarized) by the application of noradrenaline (100 μM).
Conclusion: We have identified the intrinsic membrane properties of two subpopulations of GABAergic BF neurons. Both are likely to be wake-active since they are excited by the wake promoting neurotransmitter noradrenaline.
Support (optional): Supported by NIMH R01 MH062522 and R37 MH039683 (to RWM) and VA

0023

REM-SLEEP AND WAKEFULNESS: FUNCTIONAL RELATIONSHIPS

Gvilia I,[1] Szymusiak R[2]
(1) I. Beritashvili Institute of Physiology, Tbilisi, Georgia, (2) University of California, Los Angeles, CA, USA

Introduction: REM-sleep is homeostatically regulated and the homeostatic pressure for REM-sleep accumulates in its absence, during either nonREM-sleep and/or wakefulness. We hypothesize that REM-pressure accumulates during nonREM-sleep and that wakefulness prevents the build-up of REM-sleep pressure.
Methods: One group of Sprague-Dawley rats (n=4) was REM-sleep deprived (RD) for 2-h by being subjected to brief (2-3 sec) arousing stimuli at the onset of each REM-episode (RD1). A second group of rats (n=4) was REM-deprived for 2-h by being kept awake for 50-60 sec after each REM-entry (RD2). A third group of rats (n=4) was subjected to 2-h RD by being kept awake for 90-120 sec after each REM interruption. A fourth group of rats (n=4) was permitted 2-h spontaneous sleep. After the termination of RD protocols, all rats were permitted 2-h recovery sleep.
Results: Different groups of RD rats exhibited significantly different degrees of REM-sleep homeostatic pressure that was estimated by the number of attempts to enter into REM-sleep during the deprivation protocol. RD1 rats experienced the highest number of REM-attempts within the deprivation period (58.9±2.3). RD2 rats exhibited 21.7±1.7 entries into REM-sleep. RD3 rats had the lowest number of REM entries (9.7±0.33) and this number was not significantly different from that in spontaneously sleeping rats (10.9±0.9). Moreover, RD3 rats exhibited no REM-sleep rebound during the post-deprivation period (15.4±1.1%) compared to control rats (14.9±0.9%), while the other two groups of RD rats exhibited significant increases in the post-deprivation amount of REM-sleep (20.6±0.6% in RD1 and 18.5±1.2% in RD2). Therefore, RD3 did not lead to an elevation of REM-sleep homeostatic pressure compared to spontaneously sleeping rats.
Conclusion: Findings of this study are consistent with the hypothesis that REM-sleep is functionally and homeostatically related to nonREM-sleep rather than to wakefulness. Wakefulness appears to prevent the buildup of REM-sleep homeostatic pressure.

0024

GENOMIC KNOCK-IN MICE WITH ENHANCED GI2 SIGNALING EXHIBIT ALTERED BREATHING DURING RECOVERY FROM ISOFLURANE ANESTHESIA COMPARED TO WILD TYPE MICE

Icaza E,[1] Fu Y,[1] Huang X,[2] Neubig R,[1] Baghdoyan H,[1] Lydic R[1]
(1) University of Michigan, Ann Arbor, MI, USA, (2) Ann Arbor, MI, USA

Introduction: Sleep and anesthesia are different states but exhibit similar traits, such as depressed breathing and altered signal transduction. Anesthetics alter G-protein coupled receptors (GPCRs) in the brain and interact with GPCRs located on airway smooth muscles (Anesthesiology 101:120, 2004). Regulators of G-protein signaling (RGS) proteins bind to $G\alpha_i$ subunits and inhibit signal transduction. Genomic knock-in mice with an RGS-insensitive $G\alpha_{i2}$ G184S allele exhibit enhanced $G\alpha_{i2}$ signaling and provide a novel approach to investigating the role of RGS proteins and signal transduction (Circ Res 98: 659, 2006). The present study is testing the hypothesis that homozygous (GS/GS) and heterozygous (GS/+) mice exhibit altered breathing during recovery from isoflurane anesthesia compared to wild type (WT) mice.

Methods: Mice were administered 3% isoflurane (1 L/min) in a chamber until immobile. Mice then were fitted to an anesthesia mask and maintained at 1.3% isoflurane for 30 min. Anesthesia was discontinued and mice were transferred to a Buxco® plethysmograph chamber where respiratory variables were measured for 1 h. Changes in breathing as a function of anesthesia and genotype were evaluated with ANOVA and Dunnett´s statistic.
Results: Data were obtained from 9 mice (3/genotype) over four anesthesia trials, each separated by one week. Respiratory measures quantified minute ventilation, inspiratory flow rate (ml/sec), and inspiratory time. Minute ventilation and inspiratory flow rate were significantly decreased ($p<0.01$) at 20 and 40 min post anesthesia in GS/GS and GS/+ compared to WT. Duration of inspiration was significantly greater ($p<0.01$) in GS/GS and GS/+ mice than WT mice at 20 min post anesthesia.
Conclusion: During the initial 40 min of recovery from isoflurane anesthesia, respiratory depression in GS/GS and GS/+ is greater than in WT mice.
Support (optional): NIH Grants HL65272, GM39561, HL57120, HL40881, MH45361, and the Department of Anesthesiology

0025

ELECTROPHYSIOLOGICAL RECORDINGS FROM GABAERGIC NEURONS IN THE LATERAL PONTINE TEGMENTUM (LPT) REGION OF KNOCK-IN MICE EXPRESSING GREEN FLUORESCENT PROTEIN UNDER THE CONTROL OF THE GLUTAMIC ACID DECARBOXYLASE 67 PROMOTER

Brown R,[1] Winston S,[1] Yanagawa Y,[2] McCarley R[3]
(1) Harvard University, Brockton, MA, USA, (2) Gunma University Maebashi, Maebashi, Maebashi, Japan, (3) VAMC and Havard Medical School, Brockton, MA, USA

Introduction: Recent experiments combining Fos immunohistochemistry as a marker of neuronal activation and anatomical tracing techniques have identified a population of GABAergic neurons in the lateral pontine tegmentum (LPT) as playing a critical role in the control of muscle tone during sleep (especially rapid-eye-movement (REM) sleep). Here we use mice expressing green fluorescent protein (GFP) under the control of the glutamic acid decarboxylase promoter (GAD67-GFP knock-in mice) to identify and record from GABAergic neurons in the LPT in order to characterize their intrinsic membrane properties and responses to neurotransmitters involved in sleep-wake control.
Methods: Coronal brain slices were prepared from young (10-16 d) heterozygous GAD67-GFP knock-in animals according to standard techniques. Neurons expressing GFP in the LPT region (-4.60 to -5.02 mm caudal to Bregma) were identified using a Hamamatsu ORCA-AR CCD camera. Whole-cell patch-clamp recordings were made using a Multiclamp 700A amplifier. Drugs were bath-applied.
Results: Whole-cell current-clamp recordings were made from 13 small-to-medium sized (13-20 µm) GFP-Pos neurons in the LPT region. All neurons had a modest depolarizing sag. At the offset of hyperpolarizing current steps, 8 neurons responded with a single action potential. These neurons were excited by the cholinergic receptor agonist carbachol (10 µM, 8.1 ± 1.9 mV, n = 4). One neuron tested with Ox A (500 nM) and one tested with Ox B were excited. Three neurons responded at the offset of hyperpolarizing current pulses with a burst of action potentials. These neurons were hyperpolarized by carbachol (-4.5 ± 1.2 mV, n =3).
Conclusion: We propose that carbachol-inhibited GABA neurons are those neurons previously identified as REM-off neurons projecting to and inhibiting REM-on (and muscle-atonia on) neurons in the subcoeruleus (sublaterodorsal) region during waking. In contrast, carbachol-excited GABA neurons are likely to be involved in turning off other neurons (e.g. aminergic neurons) during REM sleep.
Support (optional): Supported by NIMH R01 MH062522 and R37 MH039683 (to RWM) and VA

0026

THE ROLE OF THE DOPAMINERGIC PATHWAY IN REGULATING SLEEP-WAKE PATTERNS IN A MODEL OF PARKINSON´S DISEASE IN RATS

Lima M,[1] Andersen M,[2] Reksidler A,[3] Vital M,[3] Tufik S[2]
(1) Universidade Federal de São Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Universidade Federal de São Paulo, São Paulo, Sao Paulo, Brazil, (3) Universidade Federal do Paraná, Curitiba, PR, Brazil

Introduction: In the present study, we examined the sleep-wake patterns and tyrosine hydroxylase (TH) expression profile in rats surgically lesioned with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) into the substantia nigra pars compacta (SNpc).
Methods: After 48h baseline recording, rats were submitted to an intranigral MPTP infusion through cannulas previously implanted surgically. Immediately after performing the infusions, the sleep-wake patterns were evaluated during 5 days. After the end of the electrophysiological experiment, rats were transcardially perfused for brain fixation allowing TH-immunohistochemistry examination to determine the neuronal loss in the SNpc. Another set of animals were operated and underwent the very same infusion procedure in order to investigate the TH protein expression in the SNpc. Sham groups followed the same procedures but were infused with sterile saline 0.9%.
Results: The data indicated that a 50% dopaminergic neuronal loss restricted to the SNpc, inflicted by MPTP, was able to decrease the latency to the onset of sleep during the 5 days of recording in both light and dark periods. Moreover, an increase in the latency to paradoxical sleep was observed on day 1. The MPTP group also presented more pronounced sleep efficiency during 4 days of recording, and a consequent reduction in the percentage of wakening on the same days. The percentage of slow wave sleep (SWS) was increased in the MPTP group on days 2 and 3 only in the dark period. Nevertheless, percentage of paradoxical sleep was found to be diminished during days 1 and 2 for light and dark periods and day 3 for light period only. On day 4, paradoxical sleep presented an increase in both periods. Complementarily, TH expression was reduced in the MPTP group compared to sham only on day 1.
Conclusion: These data provide novel evidence that sleep-wake patterns are directly regulated by the dopaminergic nigrostriatal pathway in this model of Parkinson´s disease.
Support (optional): AFIP, FAPESP, CEPID, CAPES

0027

EFFECTS OF SLEEP DEPRIVATION ON TYROSINE HYDROXYLASE EXPRESSION AND DOPAMINE-RELATED BEHAVIORS IN TWO MODELS OF PARKINSONS DISEASE

Lima M,[1] Andersen M,[2] Reksidler A,[3] Vital M,[4] Tufik S[2]
(1) Universidade Federal de Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Universidade Federal de São Paulo, São Paulo, Sao Paulo, Brazil, (3) Universidade Federal do Paraná, Curitiba, Brazil, (4) Universidade Federal do Paraná, Curitiba, PR, Brazil

Introduction: In the present study, we examined the effects of sleep deprivation in two mice models of Parkinson's disease (PD) induced by reserpine+.αMT (.α methyl-p-tyrosine) and rotenone. We verified the

tyrosine hydroxylase (TH) protein expression profile in the substantia nigra (SN) and striatum and dopamine-related behaviors.
Methods: C57BL/6 mice were distributed into three groups: control, reserpine (1mg/kg ip)+.αMT (250mg/kg ip) and rotenone (5mg/kg ip). After the groups were sleep-deprived (SD) for 24h one set of animals (n=5/group) were behaviorally observed in the open-field, catalepsy and grasping tests. Another set of animals (n=5/group) were decapitated for dissection of the SN and striatum for western blotting analyses. The remaining groups of mice were allowed sleep rebound for 24h and one set of mice was behaviorally tested afterwards. The remaining groups (n=5/group) were decapitated for dissection of the SN and striatum and further western blotting analyses.
Results: Data indicated that TH expression in the SN was reduced only in the rotenone mice of non-sleep deprived groups. SD added a synergic effect on TH expression depletion, which was found to be reduced in control, reserpine+.αMT and rotenone groups. A similar profile was encountered in the striatum. Despite the rebound, TH expression still diminished in reserpine+.αMT and rotenone groups in comparison to control in SN and striatum. Open-field revealed marked impairment of locomotion parameters for reserpine+.αMT group but SD reversed that. A similar effect was observed in the grasping test. Catalepsy test demonstrated that SD did not reverse the dopaminergic impairment, which returned to baseline only after rebound.
Conclusion: This study suggests that SD regulates TH expression in addition to its influence on dopaminergic supersensitivity.
Support (optional): AFIP, FAPESP, CEPID, CAPES

0028

DEVELOPMENTAL CHANGES IN CONNEXIN 36 MRNA EXPRESSION AND PROTEIN LEVELS IN THE SUBCOERULEUS NUCLEUS

Charlesworth A,[1] Yates C,[2] Ye M,[3] Zhou Y,[4] Garcia-Rill E[3]
(1) Univ. Arkansas for Medical Sci., Little Rock, AR, USA, (2) University of Arkansas for Medical Sci., Little Rock, AR, USA, (3) University of Arkansas for Medical Sciences, Little Rock, AR, USA, (4) University of California, Irvine, Irvine, CA, USA

Introduction: REM sleep in man decreases from ~8 hours in the newborn to ~1 hour in the adult, and this decrease occurs from birth until the end of puberty. In schizophrenia, anxiety disorders and depression, increased REM sleep drive is a major, incapacitating symptom. We hypothesize that this effect is a regression to a previous developmental state. We investigated the expression of the gap junction protein Connexin-36 (Cx 36) in the mesopontine tegmentum and more specifically, the SubCoeruleus (SubC) nucleus of the rat, which is involved in the control of REM sleep.
Methods: The mesopontine tegmentum was dissected from rats at different ages, spanning the developmental decrease in REM sleep. To investigate SubC specifically, samples of SubC tissue was punched from 400 um brainstem slices. Rat Cx 36 (Gja9) mRNA expression was assessed by real-time quantitative RT-PCR, normalized to rat housekeeping genes Enolase, Gapdh and Hprt. Cx 36 protein levels were determined by western blot along with actin as a loading control.
Results: In the mesopontine tegmentum, Cx 36 mRNA expression levels in the adult were about 1/3 of those at day 7, with a similar developmental decrease in Cx 36 protein levels in the adult. SubC Cx 36 protein levels at 30 days, the end of the developmental decrease in REM sleep in the rat, were about 1/3 of those at day 10.
Conclusion: These data show that there is an age-dependent decrease in Cx 36 mRNA expression and protein levels in the mesopontine tegmentum and specifically in the SubC paralleling the decrease in REM sleep. This suggests that the decrease in REM sleep could be due to a decrease in gap junction gene expression, which results in lower electrical coupling between the neurons of the SubC. This could implicate gap junction gene mis-expression in REM sleep disorders.
Support (optional): USPHS grants NS20246 and NS20146.

0029

MODAFINIL INCREASES THE AMPLITUDE OF THE SLEEP STATE-DEPENDENT P13 MIDLATENCY AUDITORY EVOKED POTENTIAL IN THE RAT

Wallace Huitt T, Skinner R, Mennemeier M, Garcia-Rill E
University of Arkansas Medical Sciences, Little Rock, AR, USA

Introduction: Modafinil (MOD) is a stimulant that affects sleep-wake states and appears to be effective in the treatment of Narcolepsy. The pedunculopontine nucleus (PPN) is known to be active during waking and REM sleep. The P13 auditory evoked potential is thought to be a measure of PPN output and is the rodent equivalent of the human P50 potential. The P13 potential is sleep state-dependent, blocked with scopolamine, and habituates to stimuli presented at rates >2 Hz. The amplitude of the P13 potential can be considered a measure of level of arousal. The present study was undertaken to determine the effects of injections of MOD into the PPN on the manifestation of the P13 potential.
Methods: The vertex recorded P13 potential was studied in adult male (n=8) Sprague-Dawley rats implanted with recording plugs and microinjection cannulae bilaterally as previously described. Following control recordings, saline or MOD (200μM) was microinjected (0.2μl) into the PPN. Recordings were performed before and at 3, 5, 10, 15, 25, 35, 45 and 55 min post injection.
Results: MOD increased the amplitude of the P13 potential, while saline had no effect. Significant (Two way repeated measures ANOVA, df=8, F=2.22) increases in amplitude were observed at 10 min ($p<0.05$), 25 min ($p<0.01$) and 45 min ($p<0.05$) following MOD injection compared to within group control recordings, although numerical increases were observed at 5, 15 and 35 min. Significant (df=15 F=3.59) increases in amplitude were observed at 25 min ($p<0.01$) and 35 min ($p<0.05$) following MOD injection compared to saline injection, although numerical increases were observed at 10 and 15 min.
Conclusion: These results demonstrate that the amplitude of the P13 potential is increased by MOD injection into the PPN, and that specific receptors in the PPN may be activated by MOD to increase the level of arousal.
Support (optional): USPHS grants: RR020146, and NS020246

0030

ELECTRICAL COUPLING IN WHOLE CELL RECORDED SUBCOERULEUS NEURONS

Heister D, Hayar A, Garcia-Rill E
Center for Translational Neuroscience, Little Rock, AR, USA

Introduction: The Subcoeruleus (SubC) is thought to generate P-waves, paroxysmal discharges during rapid eye movement (REM) sleep, in the rat. Injections of carbachol (CAR) into the SubC are known to induce REM sleep. We previously reported the presence of spikelets in SubC neurons. The present results suggest that electrical coupling in at least some SubC cells may modulate the function of this nucleus.
Methods: We performed patch-clamp recordings from SubC neurons in brain slices from 8-12 day old rats.
Results: Whole cell patch-clamp recordings revealed that CAR may have an excitatory effect on gap junctions as shown by the induction of a theta rhythm (4-8 Hz) with spikelets, a physiological marker for the presence of gap junctions, in 25% (8/32) of SubC cells. These events

persisted in the presence of the synaptic blockers CNQX, APV and gabazine but were inhibited by the gap junction blocker carbenoxolone (CBX). The use of CBX also led to significant decreases in oscillatory power in these neurons. Of the cells responding to CAR with increased oscillatory activity, 18 had LTS currents, 24 had Ia currents and 20 had Ih currents. Immunocytochemical labeling for GABA revealed that some of these neurons were GABAergic, suggesting that gap junctions are localized specifically to at least some inhibitory networks within the SubC.
Conclusion: The present results show that CAR had a direct effect on some GABAergic SubC neurons. Furthermore, the existence of intracellularly connected cells and physiologically recorded spikelets are signature indications for the presence of gap junctions. This study suggests the presence of electrotonic coupling in at least some SubC neurons, which may be induced to oscillate by CAR. The generation of synchronized, electrically coupled bursts of activity by the SubC may be one potential mechanism behind PGO waves and the induction of REM sleep.
Support (optional): USPHS grants: DC06356, DC07123, RR020146, and NS020246.

0031

IMPAIRED GABAERGIC AND GLYCINERGIC NEUROTRANSMISSION INDUCES REM-SLEEP BEHAVIOUR DISORDER (RBD) IN TRANSGENIC MICE

Brooks P,[1] Tse G,[2] Peever J[3]
(1) University of Toronto, Toronto, Ontario, Canada, (2) University of Toronto, Ontario, Canada, (3) Toronto, Ontario, Canada

Introduction: Chronic RBD is a neurological disorder that is characterized by excessive phasic muscle activity in REM sleep, which often leads to disturbed sleep and physical injury. It is also a harbinger of neurodegenerative disorders, with 80-90% of RBD patients eventually developing Parkinson´s disease or other synucleinopathies. Although its cause is unknown, RBD is effectively treated with the benzodiazepine clonazepam (a $GABA_A$ agonist). This suggests that dysregulation of the endogenous inhibitory processes that normally suppress phasic muscle activation in REM sleep may underlie the exaggerated motor activity in RBD. *We therefore hypothesize that transgenic mice with impaired $GABA_A$ and glycine receptor transmission would have excessive motor activity in REM sleep and therefore exhibit an RBD phenotype.*
Methods: To test this hypothesis, we used a transgenic mouse model in which both GABAergic and glycinergic neurotransmission is severely down-regulated (Becker *et al.*, J. Neurosci, 22:2505-12, 2002). To characterize levels of somatic muscle activity, we recorded both EEG and neck EMG activity across the sleep-wake cycle in freely-behaving transgenic (Tg, n=4) and wild-type mice (Wt, n=4).
Results: While Tg mice have normal sleep-wake architecture, they have abnormal motor activity during sleep, and particularly in REM sleep. Using both videography and EEG/EMG activity, we observed that all Tg mice exhibited a clear RBD phenotype. They presented with overt periods of vigorous limb movements and jerks. Compared to Wt mice, Tg had a 217% (2-way RM ANOVA; P=0.016) increase in muscle activity during REM sleep. Although basal levels of muscle activity were similar in Tg and Wt mice during both waking and NREM sleep, all Tg mice had regular myoclonic twitches in NREM sleep.
Conclusion: We conclude that: 1) GABAergic and glycinergic processes regulate motor suppression in both REM and NREM sleep; and, 2) impaired inhibitory neurotransmission may underlie RBD.
Support (optional): This research was supported by grants from the Canadian Institutes of Health Research and the National Science and Engineering Research Council of Canada.

0032

PURINERGIC TRANSMISSION BY P2X RECEPTORS AND ENTDP3 IN HYPOCRETIN AND SENSORY NEURONS IN ZEBRAFISH

Appelbaum L, Skariah G, Mourrain P, Mignot E
Stanford University, Palo Alto, CA, USA

Introduction: The hypocretin/orexin (HCRT/ORX) excitatory neuropeptides are expressed in a small population of lateral hypothalamic cells in mammals and fish. In humans, loss of these cells causes the sleep disorder narcolepsy. Identification of genes expressed in these cells may shed new light on the regulation of sleep and the pathophysiology of narcolepsy.
Methods: In this study, we have used in situ hybridization in zebrafish embryos to identify receptors and enzymes regulating ATP-mediated transmission in hypocretin cells.
Results: We isolated the zebrafish homolog of ecto-nucleoside triphosphate diphosphohydrolase (ENTDP3), an extracellular enzyme known to hydrolyze ATP, and found it expressed in HCRT cells, as previously reported in mammals. This enzyme was also expressed in the trigeminal nuclei area and in primary sensory neurons, also called Rohon-Beard, in the spinal cord. We next studied the expression of all known purinergic receptor (p2x) genes and found a strikingly similar pattern of expression to entpd3 for multiple members of this family. Specifically, p2x2, p2x3.1, p2x3.2, and p2x8 were expressed in the trigeminal area and subsets of Rohon-Beard spinal cord neurons. In contrast to mammals, p2x2 was not expressed in hypocretin cells. Rather, p2x8 was expressed in lateral hypothalamic cells.
Conclusion: The conservation of expression of these genes in HCRT cells and sensory neurons across vertebrates suggest an important role for ATP mediated transmission in the regulation of sleep and the processing of sensory inputs.
Support (optional): HHMI, McKnight and NS23724

0033

PONTINE-WAVE (P-WAVE) GENERATOR ACTIVATION-DEPENDENT MEMORY PROCESSING INVOLVES PROTEIN KINASE A (PKA) ACTIVATION IN THE CA3 SUBFIELD OF DORSAL HIPPOCAMPUS

Vetrivelan R, Traore M, Datta S
Boston University, Boston, MA, USA

Introduction: During post-training rapid eye movement (REM) sleep, activation of P-wave generating cells are critical for the consolidation of two-way active avoidance (TWAA) memory processing. More recently, we have shown that this P-wave generator activation-dependent memory processing requires intact CA3 subfield of the dorsal hippocampus (CA3-DH). In the present study, we have examined the role of CA3-DH PKA activation in the TWAA memory processing in freely moving rats.
Methods: Ten adult male Sprague-Dawley rats were chronically implanted with sleep-wake recording electrodes and bilateral guide tubes for microinjections into the CA3-DH. After postoperative recovery, rats were exposed to shuttle box context (thirty minutes) and baseline sleep-wave activities were recorded between 10 AM and 4 PM for two consecutive days. One day after final baseline recording session, rats were placed in the shuttle box and subjected to a session of 30 TWAA learning trials. Immediately after training trials, rats were microinjected bilaterally with either KT-5720 (2.0 mol in 200 nl/site), a specific inhibitor of cAMP-dependent PKA (cAMP-PKA) activation, or control saline (200 nl/site) into the CA3-DH. After microinjections, rats

were recorded for sleep-wake activities for six-hours (between 10 AM and 4 PM). Twenty-four hours after the training session, rats were tested for TWAA memory.
Results: The sleep-wake data revealed that compared to after control saline, KT-5720 microinjections into the CA3-DH did not produce any significant changes in the wakefulness, slow-wave sleep, or REM sleep. Microinjection of KT-5720 caused significant changes in the activity patterns of DH. In the test trials of TWAA learning, however, KT-5720 microinjected rats showed a significant deficit in the retention of TWAA memory.
Conclusion: These findings suggest that the time-dependent activation of cAMP-PKA in the CA3-DH is an important step for the consolidation and/or retention of TWAA memory. These results also indicated that the cAMP-PKA system in the CA3-DH might not be involved in the regulation of sleep-wake behavior.
Support (optional): This research was supported by NIH grants NS34004 and MH59839.

0034

PEDUNCULOPONTINE TEGMENTAL (PPT) CAMP-DEPENDENT PKA (CAMP-PKA) ACTIVATION BLOCKS THE EFFECTS OF GABA-B RECEPTOR-MEDIATED SUPPRESSION OF REM SLEEP IN FREELY MOVING RATS

Traore M, MacLean R, Vetrivelan R, Datta S
Boston University, Boston, MA, USA

Introduction: Neurotransmitter-mediated excitation and inhibition of PPT cells are important processes for regulation of REM sleep. Our recent studies have demonstrated that the activation of GABA-B receptors within the cholinergic cell compartment of the PPT suppresses REM sleep by inhibiting REM-on cells. Since GABA-B receptor-mediated physiological actions involve inhibition of adenylyl cyclase, an important enzyme for intracellular cAMP synthesis, we hypothesized activation of the PPT intracellular cAMP-PKA would attenuate the GABA-B receptor activation-mediated suppression of REM sleep.
Methods: Twenty-eight adult male Sprague-Dawley rats were chronically implanted with sleep-wake recording electrodes and guide tubes for microinjections into the PPT. Prior to the final recording session, half of those rats (n=14) received unilateral microinjection of control saline (100 nl) and half received unilateral microinjection of SpCAMPS (1.5 nmol in 100 nl; cAMP-PKA activator) into the PPT. Fifteen minutes after the first microinjection, half of the SpCAMPS (n=7 rats) and half of the saline-microinjected sites were microinjected with Baclofen (1.5 nmol in 100 nl, GABA-B receptor specific agonist). The other halves of each group were microinjected with saline. Following microinjections, sleep-wake activities were measured for 6-hours (10 AM to 4 PM).
Results: The results demonstrated that SpCAMPS + saline treated rats spent significantly more time in REM sleep ($p<0.001$), than saline + saline treated rats. REM sleep was eliminated for the first three hours in rats that received saline + Baclofen microinjections. When the Baclofen microinjection site was pretreated with SpCAMPS, the REM sleep suppressing effect of Baclofen disappeared.
Conclusion: These findings suggest that the PPT GABA-B receptor activation-mediated suppression of REM sleep may be mediated through the inhibition of the cAMP-PKA signal transduction pathway. These results also suggest that activation of cAMP-PKA in the PPT promotes REM sleep.
Support (optional): This research was supported by NIH grants MH59839 and NS34004.

0035

CARBACHOL INDUCES SYNCHRONIZATION OF IPSCS AT THETA FREQUENCY IN WHOLE-CELL RECORDED SUBCOERULEUS NEURONS.

Hayar A,[1] Heister D,[2] Garcia-Rill E[3]
(1) Univ. Arkansas for Medical Sci., Little Rock, AR, USA, (2) University of Arkansas for Medical Sciences, Little Rock, AR, USA, (3) University of Arkansas, Little Rock, AR, USA

Introduction: Descending cholinergic projections from the pedunculopontine nucleus modulate electrical activity in the SubCoeruleus (SubC), which has been implicated in the control of REM sleep. The SubC includes a heterogeneous population of neurons that might be differentially modulated by cholinergic activation.
Methods: We performed extracellular and patch-clamp recordings from SubC neurons in brain slices from 8-12 day old rats.
Results: In extracellular recordings, carbachol decreased the frequency or inhibited the firing of 5 of 5 SubC cells. In 3 of these 5 cells, the inhibition was followed by increased firing, suggesting a biphasic effect. In whole-cell voltage-clamp recordings (holding potential -50 mV), carbachol induced an outward current in 7 of 7 SubC cells. The outward current reached a peak in ~30 sec from the onset of the response, and then decreased in amplitude and was followed by a small inward current in 2 cells. This suggests either a rapid desensitization of the cholinergic receptors or opposing outward and inward currents induced by carbachol. The outward current induced by carbachol persisted in the presence of CNQX, APV and gabazine in 2 of 2 cells, suggesting a direct effect. Carbachol alone or in the presence of a muscarinic M2 receptor antagonist, induced the appearance of IPSCs or increased the frequency of baseline IPSCs in 7 of 9 SubC cells. The IPSCs evoked by carbachol occurred at theta frequency (4-8 Hz) and were blocked either by gabazine or by a combination of gabazine and strychnine, suggesting that they might be mediated by GABAergic and glycinergic receptors. The presence of doublet IPSCs during application of carbachol suggests that multiple GABAergic SubC cells fired synchronously and may be electrically coupled.
Conclusion: We suggest that cholinergic activation of inhibitory SubC interneurons might be responsible for synchronizing SubC neuronal activity and inducing theta rhythm.
Support (optional): USPHS grants: DC06356, DC07123, RR020146, and NS020246.

0036

DEVELOPMENT OF CHOLINERGIC RESPONSES IN PARAFASCICULAR (PF) NEURONS.

Ye M,[1] Wilkes S,[2] Garcia-Rill E[3]
(1) University of Arkansas for Medical Sciences, Little Rock, AR, USA, (2) Univ. Arkansas for Medical Sci., Little Rock, AR, USA, (3) University of Arkansas, Little Rock, AR, USA

Introduction: The Pf receives cholinergic input from the pedunculopontine nucleus (PPN), which is active during waking and REM sleep. There is a developmental decrease in REM sleep in humans between birth and puberty, and between 10 and 30 days in the rat. This study determined if the cholinergic input to Pf changes during the developmental decrease in REM sleep in the rat.
Methods: Intracellular recordings were performed in Pf neurons in 12-21 day rat brainstem slices in artificial CSF, and their responses to the mixed cholinergic agonist carbachol (CAR) determined.
Results: Previous developmental studies showed that there are two types of Pf cells (based on AHP characteristics) that differ in morphology and physiology from thalamic relay neurons, including the

frequency of low frequency of LTS cells (19%), although they are still developing throughout the developmental decrease in REM sleep. We tested 79 Pf neurons for responses to CAR (50uM) and found that 57% were hyperpolarized, 33% were depolarized and 10% had no response. In 40 of these cells, we tested CAR in the presence of tetrodotoxin (TTX, 30uM) and determined that they showed the same response to CAR (26/40, 65% hyperpolarized, 14/4, 35% depolarized), suggesting direct postsynaptic effects. No statistical difference in the degree of hyperpolarization or depolarization was observed over age in this sample, although there was a trend towards decreasing depolarization and increasing hyperpolarization.
Conclusion: The mixed cholinergic agonist CAR had excitatory or inhibitory effects directly on Pf neurons, although the effect did not change dramatically during the developmental decrease in REM sleep.
Support (optional): USPHS grants: RR020146, and NS020246.

0037

WAKE/SLEEP AND OREXIN CHANGES IN RATS EXPOSED TO MATERNAL DEPRIVATION

Feng P,[1] Vurbic D,[1] Wu Z,[1] Strohl K[2]
(1) Case Western Reserve University, Cleveland, OH, USA, (2) Division of Pulmonary, Critical Care and Sleep Medicine, Case Western Reserve University, Cleveland, OH, USA

Introduction: Stress modulates the HPA axis and wake/sleep regulation and suggests that chronic stress by neonatal maternal deprivation might result in adult abnormal wake/sleep regulation and alterations within the orexinergic system. We studied wake/sleep states, brain level of orexins, orexin receptors and corticotropin-releasing hormone (CRH) in adult rats neonatally subjected to maternal deprivation (MD) or control procedure.
Methods: Forty-six male rat pups were neonatally subjected to ten days of either MD or control procedure from postnatal day 4. Eleven MD and twelve control rats were implanted with EEG and EMG electrodes at three months of age for polysomnographic recording and recorded for 48 hours after ten days of post-surgical recovery and adaptation. These rats and additional rats that did not undergo surgery were sacrificed for ELISA, radioimmunoassay and western blot measurement of orexins, orexin receptors and CRH in multiple brain regions.
Results: Neonatal MD induced a significant increase of total wake (580 min in MD rat vs. 478 min in control rat) and decrease of total sleep (857 min in the MD rat vs. 961 min in the control rat) during the light period, which corresponds to human night time. The increase of wakefulness specifically includes a large and significant increase of quiet wake (363 min in the MD vs. 250 min in the control rat) during the light period and a small but significant decrease in active wake (624 min in the MD vs. 759 min in the control rat) in the dark period. At the molecular level, MD leads to significantly increased hypothalamic CRH and orexin A (11 pg/mg in the MD rat vs. 5 pg/mg in the control rat), and frontal cortical orexin 1 receptors (OX1R) (relative O.D. for the MD rat was 1.2 vs. 0.9 for the control rat). However, hippocampal orexin B was significantly reduced in the MD rat.
Conclusion: Neonatal MD produced adult increased total wake time during light period and increased orexin A, OX1R, but not orexin B. These data suggest that the adult MD rat had partial features of insomnia.
Support (optional): Work is supported by NASARD Young Investigator Award, NIH MH 069854 and Louis Stokes Cleveland VA Medical Center

0038

A QUANTITATIVE MEASURE OF ANXIETY: AN IMPORTANT INDICATOR TO STUDY THE EFFECTS OF STRESS ON SLEEP-WAKE BEHAVIOR

MacLean R, Traore M, Datta S
Boston University, Boston, MA, USA

Introduction: Disturbed sleep is a common subjective complaint among individuals diagnosed with anxiety disorders. In rodents, exposure to inescapable shock (IS) has been shown to decrease REM sleep, escapable shock (ES) increases REM sleep and re-exposure to a fear conditioned (FC) context decreases REM sleep. Although differences in sleep-wake architecture are noted, the correlation to level of anxiety is assumed or absent. Utilizing the elevated plus maze (EPM) after exposure to ES, IS or FC, we are comparing an objective measure of anxiety and resulting differences in sleep architecture. We intend to elucidate the degree to which specific shock paradigms are anxiogenic and create a comprehensive link between specific variations in sleep architecture and higher levels of anxiety.
Methods: Male Wistar rats were implanted with EEG, EMG and hippocampal theta electrodes. After recovery and recording of baseline sleep, rats were exposed to one of five manipulations: ES, IS, FC, or control (CES or CIS; utilizing either chamber with no shock exposure). Immediately after experimental manipulation, EPM was employed to measure anxiety and polygraphic signs of sleep-wake were recorded for 6h.
Results: Preliminary results of ES and IS reveal variation in anxiety level within each of the shock manipulations. These differences not only shed light on the amount of anxiety resulting from each manipulation, but also changes in the sleep-wake cycle that could be correlated with heightened anxiety level. Additionally, the effects of specific levels on anxiety on the expression of various proteins in the medial prefrontal cortex, amygdala and hippocampus will be evaluated at the 6h time interval.
Conclusion: This paradigm promises to establish a method of analyzing the effect of stress on specific changes in sleep architecture using a quantitative measure of anxiety level. This connection could elucidate new diagnostic and assessment criteria for anxiety disorders.
Support (optional): This research was supported by NIH grants NS34004 and MH59839.

0039

GLUCOSE MICROINJECTED INTO THE PONTINE RETICULAR FORMATION (PRF) OF ANESTHETIZED C57BL/6J (B6) MOUSE DECREASES PRF ACETYLCHOLINE (ACH) RELEASE

Puro A, Baghdoyan H, Lydic R
University of Michigan, Ann Arbor, MI, USA

Introduction: Hyperglycemia attenuates morphine-induced REM sleep inhibition (Neurobiol Learn Mem 64:33, 1995) and alters morphine requirement for pain (Acta Anaesthesiol Scand 48:619, 2004; Anesthesiology 99:1409, 2003) but the brain regions and neurotransmitter systems underlying these effects of hyperglycemia are not understood. The finding in rat that intraperitoneal (i.p.) glucose administration attenuates morphine-induced REM sleep inhibition was speculated to result from a morphine-induced increase in PRF ACh release (Neurobiol Learn Mem 64:33, 1995). The logic of such an inference is consistent with the fact that PRF ACh release increases during REM sleep (Anesthesiology 103:1268, 2005). The present study is testing the hypothesis that increasing systemic and PRF glucose levels increase PRF ACh release.

Methods: Adult male B6 mice (n=3) were anesthetized with isoflurane and a microdialysis probe was placed in the PRF. ACh (pmol/12.5 min) was measured by HPLC during dialysis with Ringer´s before and after i.p. injection of 100 mg/kg glucose. Within 10 min of i.p. glucose, hyperglycemic rats have extracellular brain glucose concentrations of 4.5 mM (J. Neurosci. 14:5068, 1994). Therefore, additional mice (n=3) were anesthetized and a combination microdialysis and microinjection probe was used to dialyze the PRF and measure ACh before and after PRF microinjection (50 nL) of 4.5 mM glucose.
Results: For 75 min following i.p. glucose (100 mg/kg) administration, B6 mice revealed no significant change in PRF ACh release. Microinjecting 4.5 mM glucose directly into the PRF caused a significant ($p<0.05$) decrease (-13%) in PRF ACh release measured for 75 min after increasing PRF glucose content.
Conclusion: Glucose does not increase ACh release in PRF of B6 mouse. Previous studies in B6 mouse show that the PRF mediates supraspinal, cholinergic antinociception (Sleep 29: Abst 0012, 2006) and the present results are consistent with evidence that hyperglycemia can attenuate the antinociceptive action of morphine (Anesthesiology 99:1409, 2003).
Support (optional): NIH grants HL65272, HL57120, HL40881, MH45361, and the Department of Anesthesiology

0040

APNEA-INDUCED POTENTIATION OF THE HIPPOCAMPAL FEPSP IS ASSOCIATED WITH A REDUCTION IN THE PAIRED-PULSE PLASTICITY OF CA1 NEURONS

Fung S,[1] Xi M,[1] Yamuy J,[1] Morales F,[1] Chase M[2]
(1) Websciences International, Los Angeles, CA, USA, (2) University of California, Los Angeles, Los Angeles, CA, USA

Introduction: Chronic hypoxia and sleep apnea result in cognitive impairments that are thought to involve cellular damage to the CA1 region of the hippocampus. Because paired-pulse facilitation promotes cognitive functions, we hypothesize that apnea may affect the short-term plasticity of CA1 neurons due to the enhanced presynaptic release of the excitatory transmitter glutamate. Accordingly, the present study was designed to determine the acute effects of apnea on the paired-pulse ratio of the CA1 monosynaptic field potentials (fEPSPs).
Methods: Adult guinea pigs were anesthetized with chloralose and immobilized with Flaxedil. Double-pulse (0.2 ms, inter-pulse intervals 30-50 ms, repetition rate 1/s) cathodal stimulation of hippocampal CA3´s Schaffer collaterals evoked fEPSPs that were recorded extracellularly from the dendritic field of CA1. Apnea was induced by ventilatory arrest to desaturate oxyhemoglobin to 50% SpO_2; recovery to >95% SpO_2 occurred upon re-ventilation. Changes in the fEPSPs of CA1 were examined during pre-apneic and post-apneic conditions.
Results: Single episodes of apnea resulted in the potentiation of the initial fEPSP; this effect was greatest at one minute after the termination of apnea. The mean amplitude (1.7 mV±0.1) of the post-apneic fEPSP was significantly larger ($p < 0.005$) compared with the pre-apneic control (1.2 mV±0.1). These changes were accompanied by a significant decrease ($p < 0.005$) in the paired-pulse ratio during the post-apneic period (1.17±0.06) compared with the pre-apneic period (1.42±0.05).
Conclusion: The present results indicate that apnea-induced potentiation of the hippocampal CA1 fEPSP is accompanied by a decrease in the paired-pulse ratio; these data suggest that there is an increase in the release of an excitatory transmitter, such as glutamate, at CA1 synapses during periods of apnea. We hypothesize that the synaptic changes that occur chronically in sleep apnea patients contribute to the excitotoxicity of CA1 neurons that, in turn, impairs various hippocampal functions.
Support (optional): This research was supported by NIH grants MH69372 and HL60296.

0041

CORTICOTROPIN-RELEASING FACTOR (CRF) REGULATION OF NEONATAL REM SLEEP

Liu X,[1] Vurbic D,[2] Fan H,[1] Wang S,[1] Feng P[2]
(1) Medical College of Zhengzhou University, Zhengzhou, Henan Province, China, (2) Case Western Reserve University, Cleveland, OH, USA

Introduction: Rodents and humans have much more REM sleep neonatal period than in adulthood. REM sleep regulation in this period remains to be understood. Current evidence suggests that corticotropin-releasing factor (CRF) may play a role in promoting neonatal REM sleep. In the following study, we investigated the effect of NBI 27914 (NBI), a CRF R1 receptor antagonist, on sleep/wake states, brain levels of ACTH and acetylcholine (ACh) in two-week old rats.
Methods: EEG and EMG electrodes were implanted in 40 male rats at postnatal (PN) day 13 and recorded for 12 hours PSG on the next day. After the first 6 hours, 8 rats were injected with one of the following: vehicle, NBI 12.5 mg/kg, NBI 25 mg/kg, 50 mg/kg and atropine. Additional 20 rats were killed 2 hours after injection with either NBI or vehicle on PN 14 without surgery. ACTH and ACh were quantified by radioimmunoassay and fluorometric assay in multiple brain regions.
Results: Compared with the baseline, REM sleep was significantly decreased in groups treated with all doses of NBI but not with DMSO/saline. The reduction of REM sleep was dose related and was replaced primarily by NREM sleep. The highest dose of NBI also induced an increase of wakefulness. NBI induced no change of ACTH but a small and significant decrease of ACh in the medulla (7.3 pg/mg for the NBI27914 group vs. 8.2 pg/mg for the control group). In addition, atropine also suppressed REM sleep significantly. However, this REM reduction was compensated for by wakefulness but not NREM sleep.
Conclusion: Our data for the first time discovered that blockage of CRF R1 receptor deprives neonatal REM sleep. The data suggest that CRF promotes REM sleep during the neonatal period in contrast to promoting wakefulness in adulthood. The mechanism for CRF in enhancing REM sleep may be associated with but not similar to the cholinergic mechanism.
Support (optional): Work was supported by Award of Program for Innovative Scientist in Medical Science of Henan Province, Department of Health, Henan Province, China, NIMH RO1 MH 069854 and Cleveland VA Research Service

0042

CLOMIPRAMINE SUPPRESSES ACTIVE WAKE, REM SLEEP AND EXPRESSION OF OREXINERGIC MRNA

Li D,[1] Hu Y,[2] Fan H,[1] Wang S,[1] Feng P[2]
(1) Medical College of Zhengzhou University, Zhengzhou, Henan Province, China, (2) Case Western Reserve University, Cleveland, OH, USA

Introduction: Orexins, including orexin A and orexin B, promote wake and suppress sleep. Chronic administration of clomipramine (CLI), a multiple aminergic neurotransmitter reuptake inhibitor and an antidepressant, in neonatal rats produced a long lasting decrease of REM sleep and decrease of orexins levels in multiple brain regions. However, the acute effect of CLI on wake/sleep states and orexin expression in adult rats is not known. We report the acute effect of CLI

on wake/sleep percent and orexinergic gene expression in rat.
Methods: Twenty-three adult male rats were divided into two groups. Electrodes for both EEG and EMG recording were surgically implanted for sleep. After seven to nine days post surgical recovery, three days of polysomnographic recording were conducted. From the third day of recording, rats were injected (i.p.) every 12 hours with either saline or CLI and were killed by decapitation two hours after the third injection. Brain tissue from the frontal cortex, hippocampus and hypothalamus were collected for RT-PCR. mRNA of preproorexin, orexin 1 receptors (OX1R) and orexin 2 receptors (OX2R) were semi-quantified.
Results: 1. The CLI group had significantly less REM sleep (5.5% in CLI vs. 9.3% in baseline and vs. 9.4% in rat treated with saline) compared with either their own baseline day or compared with the same day of the saline group. The CLI group also had longer REM latency (652 min) compared with the saline group (399 min). 2. The CLI group had significantly less active wake (25.4%) and more quiet wake (16.9%) when compared to the saline group (27.6% for active wake and (14.7% for quiet wake). No differences were found in total sleep and slow wave sleep. 3. The expression of both prepro-orexin mRNA and OX2R mRNA were significantly decreased in the CLI group in the frontal cortex, hippocampus and hypothalamus. No significant differences were found in OX1R mRNA expression between saline and CLI group.
Conclusion: CLI treatment significantly suppressed active wake, increased quiet wake and deprived REM sleep. Simultaneously, CLI suppressed the expression of prepro-orexin mRNA and OX2R mRNA but not OX1R mRNA.
Support (optional): Work was supported by Award of Program for Innovative Scientist in Medical Science of Henan Province, Department of Health, Henan Province, China, NIMH RO1 MH 069854 and Cleveland VA Research Service

0043

TNF-ALPHA MEDIATES SLEEP ALTERATION IN PROTEASOME INHIBITOR, MG-132, -INDUCED PARKINSONISM RATS

Chang F,[1] Yi P,[2] Lu C[1]
(1) National Taiwan University, Taipei, Taiwan, (2) Jen-Teh Junior College of Medicine, Nursing and Management, Mioali, Taiwan

Introduction: Recently the pathogenesis of Parkinson´s disease (PD) has been focused on the microglia activation and the increased secretion of cytokines. A body of clinical evidence suggests that sleep is altered in PD patients; however there is a lack of basic cellular mechanisms. This study is designed to elucidate the effect of TNF-alpha in a proteasome inhibitor, MG-132, -induced Parkinsonism rat.
Methods: Male Sprague-Dawley rats were surgically implanted with EEG electrodes and microinjection cannulae directly into substantia nigra (SNpc). Rats were allowed a minimum of one-week recovery period, and kept on a 12:12h Light:Dark cycle at 23 ± 1 °C. Locomotion was recorded by infrared motion detector. After recovery, 24-h baseline recording and pyrogen-free saline (PFS)-treated recording were obtained as control. An ubiquitin-proteasome system inhibitor, MG-132, was injected directly into SNpc to cause degeneration of dopaminergic neurons and subsequently induced Parkinsonism. Sleep was recorded from the 7th day after MG-132-treatment. Three doses of TNF receptor fragment (TNFRF; 1.0, 12.5 and 25.0 µg/2µl) were administered in the subsequent days. Rotation induced by apomorphine (0.25 mg/kg, s.c.) and decreased locomotion activity were used to confirm the Parkinsonism induced by MG-132.
Results: Slow wave sleep (SWS) increased from 17.8 ± 1.2 % obtained after control to 23.8 ± 1.5 % during the dark period, but decreased from 53.6 ± 1.5 % to 46.0 ± 1.5 % during the light period at the 7-day after MG-132 microinjection. Rapid eye movement sleep (REMS) was not consistently altered in both dark and light periods after MG-132 treatment. TNFRF dose-dependently blocked MG-132-induced SWS alterations during both the dark and light periods. TNFRF did not change MG-132-induced decrease in locomotion. Neither MG-132 nor TNFRF alters slow wave activity during SWS.
Conclusion: These results suggest that TNF-alpha mediates the slow-wave sleep alteration induced by proteasome inhibitor, MG-132.

0044

HYPOCRETINERGIC FIBERS AND RECEPTORS IN THE INFERIOR COLLICULUS

Torterolo P,[1] Vanini G,[2] Zhang J,[3] Sampogna S,[3] Chase M[3]
(1) Facultad de Medicina, Universidad de la República, Montevideo, Uruguay, (2) Universidad de la República, Montevideo, Uruguay, (3) Webscience International, Los Angeles, CA, USA

Introduction: Hypocretin-containing neurons, which are localized in the postero-lateral hypothalamus, project throughout the central nervous system. These neurons are involved in mediating a number of behaviors that occur in conjunction with emotional and motivational states.
The inferior colliculus (IC) is an integrative nucleus in the mesencephalon wherein ascending as well as descending auditory information is processed. This nucleus is involved in the analysis of sound frequencies and intensity as well as in sound-source localization. In addition, IC nitric oxide (NO) plays a role in electrocortical arousal evoked by acoustic stimulation, and GABAergic neurons in the IC have been postulated to exert a tonic control on the neural substrates involved in the expression of defensive behaviors.
The present study represents the first in a series of experiments that are designed to determine the role of the hypocretinergic system in controlling auditory functions. Our initial objective was to determine the presence of hypocretinergic fibers and receptors in the IC.
Methods: Four adult guinea pigs were prepared in order to carry out single/double immunhistochemical explorations with primary antibodies against hypocretin-1, hypocretin-2, and hypocretin-receptor-1. Antibodies against GABA and NO-synthase were also employed in conjunction with antibodies against hypocretin-receptors and peptides. Antigen-antibody reactions were revealed and the data were analyzed by standard methodologies.
Results: Hypocretinergic fibers were observed throughout the auditory pathway; however the IC was the most highly innervated site. Hypocretin-containing fibers as well as neurons containing hypocretin receptor-1 were present in the external, dorsal and central subnuclei. GABAergic neurons in the IC contained the hypocretin-receptor-1, however, the majority of nitrergic neurons did not express this receptor.
Conclusion: These data demonstrate that the hypothalamus, through a descending hypocretinergic pathway, innervates specific areas of the IC, which, we hypothesize, are involved in auditory functions that are expressed during various emotional and motivational states.
Support (optional): TWAS grant for P.T.

0045

STRESS ALTERED-SLEEP: A ROLE FOR SEROTONIN/HYPOCRETIN INTERACTIONS?

Rachalski A,[1] Alexandre C,[2] Hamon M,[2] Adrien J,[2] Fabre V[1]
(1) UMR 677 INSERM/UPMC, Paris, France, (2) UMR 677 INSERM/UPMC, France

Introduction: Several factors are known to influence sleep homeostasis. Thus, restraint stress (RS) is followed by a REM sleep rebound in which serotonin (5-HT) participates. Hypocretin (hcrt), a hypothalamic

neuropeptide, might interact with 5-HT in this response. Indeed, hcrt activates numerous structures involved in sleep regulation such as Raphe Nuclei (RN), inhibits REM sleep, and contributes to stress response. Conversely, 5-HT neurons inhibit the hypocretinergic system.

Here, we evaluated the consequences of RS on hcrt neurotransmission, and of hcrt impairment on stress-induced sleep modifications in wild-type mice and in mice lacking the 5-HT transporter (5-HTT-/-), that exhibit altered serotonergic tone and increased REM sleep amounts at baseline.
Methods: In situ hybridization, immunocytochemistry and radioimmunoassay approaches were used to assess the activity of hypocretinergic neurons under basal conditions and after RS (90 minutes) in 5-HTT-/- compared to 5-HTT+/+ mice (CD1 background). In addition, the effects of specific hypocretinergic receptor 1 (hcrtR1) blockade by SB-334867 (30 mg/kg, i.p.) on sleep were assessed by polysomnographic recordings in wild-type and mutant mice.
Results: Under basal conditions, hcrt1 peptide levels in RN were higher in 5-HTT-/- mutants than in wild-type mice (+46%), while preprohypocretin mRNA contents did not differ.
RS activated hypocretinergic neurons, as indicated by a higher density of hypocretin/c-fos immunopositive neurons in stressed animals. In 5-HTT-/- mice, RS further increased RN hcrt1 levels (+26%) but induced no sleep rebound. Acute administration of SB-334867 only marginally affected sleep in unstressed mice. However, a robust stress-increased REM sleep rebound was restored in 5-HTT-/- mice that had been pretreated with this hcrtR1 antagonist.
Conclusion: Altogether, our data support the existence of functional interactions between hypocretinergic and serotonergic systems at baseline and after RS. The effects of such interactions on REM sleep rebound are revealed in mice with altered serotonergic tone.

0046

5-HT1A RECEPTORS IN THE VENTRAL PART OF THE LATERODORSAL TEGMENTUM ARE INVOLVED IN THE PONTINE CIRCUITRY REGULATING REM SLEEP IN MICE.

Bonnavion P,[1] Fabre V,[2] Hamon M,[2] Adrien J[2]
(1) UMR 677 INSERM/UPMC, Paris, France, (2) UMR 677 INSERM/UPMC, France

Introduction: Serotoninergic influences from the pontine tegmentum participate in REM sleep regulation, yet, the mechanisms remain poorly understood. Our study aims at identifying the brainstem neuronal targets of serotonin involved in REM sleep control in the mouse. We focused on the laterodorsal tegmentum (LDTg) and surrounding structures, and investigated whether activation of 5-HT1A receptors (5-HT1AR) in these areas alters REM sleep, and which are the phenotypes of neurons expressing these receptors and involved in these effects.
Methods: Adult male C57Bl6 mice were implanted with electrodes for sleep monitoring and a guide tube for microinjections into the ventral part of the LDTg (LDTgV). After recovery, mice received unilateral microinjections (50 nl) of 8-OH-DPAT (250 pg), a 5-HT1A agonist, or saline, and sleep was recorded during 6h thereafter. The specific action at 5-HT1AR was assessed by pre-treatment with the 5-HT1A antagonist, WAY100635 (0.5 mg/kg, ip).
The distribution of 5-HT1AR encoding mRNA was visualized by in situ hybridization, and neuronal phenotypes were characterized by immunohistochemistry and/or in situ hybridization.
Results: Microinjection of 8-OH-PAT into the LDTgV (n=7) induced during 3 hours a 60 % decrease in the number of REM sleep episodes ($p<0.01$) and a 40 % increase in their duration ($p<0.05$), with no change in wake or non-REM sleep. These effects were prevented by pre-treatment with WAY100635, indicating their mediation by 5-HT1AR. Cells expressing 5-HT1AR in the LDTg are exclusively localized in the ventral part of the structure. Double labeling experiments showed that these cells are mainly GABAergic neurons and only rarely cholinergic cells. We are currently investigating the glutamatergic phenotype in this area.
Conclusion: These data suggest that, in mice, the specific activation of 5-HT1AR in the LDTgV, mainly on GABAergic neurons exerts an inhibitory influence on REM sleep initiation but promotes REM sleep maintenance.

0047

HYPO AND HYPERFUNCTIONING OF BRAIN MUSCARINIC CHOLINERGIC SYSTEM (MCHS) AND CHANGES OF PARADOXICAL SLEEP (PS) IN THESE CONDITIONS

Nachkebia N,[1] Chkhartishvili E,[2] Nachkebia A,[2] Chijavadze E,[3] Babiloze M,[2] Dzadzamia S,[2] Oniani N[4]
(1) I Beritashvili Institute Of Physiology, Tbilisi, Georgia, (2) Georgia, (3) I Beritashvili Institute Of Physiology, Georgia, (4) I.Beritashvili Institute of Physiology, Tbilisi, Georgia, Georgia

Introduction: Today, direct relation of MChS to basic mechanisms of PS has no doubt. But the question whether MChS represents only triggering mechanism for PS or it is also responsible for its course/maintainence remains unclear. Accordingly we were interested, what are the PS changes during hyper- or hypofunctioning of MChS.
Methods: On cats (n=5) metallic electrodes were implanted under Nembutal anesthesia. EEG registration lasting 12 hr daily started after animals´ recovery. Muscarinic antagonists (MAs), atropine, scopolamine, were injected intraperitoneally at three doses, three times, with two day interval.
Results: Bearing in mind the pharmacokinetic of MAs, EEG registration periods were divided in two parts: 1. from the injection of MAs to the appearance of the first PS episode, MChS hypofunctioning period; 2. from the first PS to the end of EEG registration, MChS hyperfunctioning period. During MChS hypofunctioning PS deprives completely, PS latency lengthens sharply. After partial restoration of MChS functioning firstly appears the attempts of entering in PS, revealing in the onsets of muscular atonia, but it lasts several sec and than animals crouched and awaked. Such attempts are very frequent in postinjectional 4-4.5 hr period. The first PS episode develops only after partial recovery of hippocampal theta rhythm. Along with cholinorecepors releasing from MAs occupation, PS incidence and total amount increases. Effects are more pronounced during repeated administration of MA.

In recovery period, after complete removal of MAs, develops MChS hyperfunctioning which exhibited in the significant enhancement of ponto-geniculo-occipital waves, REMs and hippocampal theta rhythm frequency. In this period PS incidence rises much more but the length of PS episodes is again shorter than in baseline because they are interrupted by enhanced emotional tension.
Conclusion: The level of MChS functioning is essential both for the triggering and for the course/maintainence of PS.

0048

INFLUENCE OF HYPO AND HYPERGLYCEMIA ON THE STRUCTURE OF SLEEP-WAKING CYCLE

Chijavadze E,[1] Babilodze M,[2] Chkhartishvili E,[2] Mchedlize O,[2] Nachkebia N,[1] Mgaloblishvili-Nemsadze M,[3] Oniani N[4]
(1) I Beritashvili Institute Of Physiology, Tbilisi, Georgia, (2) Georgia, (3) I.Beritashvili Institute of Physiology, Dept. Neurobiology of Sleep and Wakefulness Cycle, Tbilisi, Georgia, (4) I.Beritashvili Institute of

Physiology, Tbilisi, Georgia

Introduction: Glucose is a major source of energetic supply for the brain. It is known that the metabolism level changes in different phases of sleep-waking cycle (SWC). In this respect study of an influence of artificially induced hyper- and hypoglycemia on SWC should be considered highly interesting.
Methods: The work was made in adult Wistar rats. Hyperglycemia was induced by intraperitoneal administration of glucose or protamine sulphate and hypoglicemia - by humulin L. Level of blood glucose (BG) was measured in control conditions and on the background of above drugs´ administration, once in every 3 hours throughout a day. The EEG recordings of SWC continued 12 hours following a drug administration.
Results: Hyperglicemia prolonged total duration of the paradoxical sleep (PS) and decreased light slow wave sleep, while the amount of waking and deep slow wave sleep (DSWS), within 12 hr SWC, not changed. Analysis of daily SWC has shown that the highest content of PS during hyperglicemia occurred twice. These "peaks" coincided with increased levels of BG. In the other periods of SWC, distribution of the SWC phases was even. On the background of hyperglicemia the number of attempts of PS onsets increased significantly and coincided with maximal concentration of BG. As to SWC of hypoglicemic animals, it did not differ significantly from that of normoglicemyc animals.
The latency of first PS in hyperglycemic animals was significantly attenuated, while in hypoglicemic animals duration of first PS latency did not change significantly. Besides, hyperglicemia induced increased number of separate EEG awakenings significantly decreased during DSWS and did not occur in PS altogether.
Conclusion: The results obtained certify that alteration of BG level influences SWC in general, and PS – in particular; this may be due to altered excitability of CNS and first of all to increased excitability of the W system.

0049

THREE NOVEL WAVEFORMS EXHIBIT STATE-DEPENDENT ACTIVITY BEFORE THE DEVELOPMENTAL EMERGENCE OF DELTA WAVES IN THE INFANT RAT CORTEX.

Seelke A,[1] Blumberg M[2]
(1) Iowa City, IA, USA, (2) University of Iowa, Iowa City, IA, USA

Introduction: Sleep states are commonly identified by examining changes in the electroencephalogram (EEG). It has long been believed that the development of state-dependent neocortical activity is marked by the emergence of delta waves at postnatal day 11 (P11). Here we describe three waveforms, slow action transients (SATs), cortical sharp waves (CSWs) and gamma bursts (GBs) that exhibit state-dependent activity before delta waves emerge.
Methods: In experiment 1, EEG, EMG, and behavior were recorded from freely moving P9, 11, and 13 subjects. In experiment 2, P5, 7, 9, 11, and 13 subjects were fitted with a custom-made o-clamp and their heads were fixed within the stereotaxic apparatus where they cycled between periods of sleep and wakefulness. Cortical local field potential (LFP) activity was recorded using 16-channel laminar silicon electrodes as well as DC-coupled Ag/AgCl electrodes.
Results: As described elsewhere, delta activity was first seen at P11. We found evidence of infraslow activity in the form of SATs that were present before the onset of delta activity. The low-frequency, high-amplitude SATs were most prevalent at P9 and decreased in prevalence with increasing age. We also found two waveforms that were present in the cortex as early as P5: CSWs and GBs. CSWs exhibited a low rate of occurrence at P5, peaked at P9 and then decreased until P13; GBs also exhibited a low rate of occurrence at P5, but then increased steadily until P13. Furthermore, CSWs and GBs were present throughout the cortex, but only exhibited phase reversals in frontal and parietal lobes, demonstrating that these waveforms were endogenously generated. Finally, SATs, CSWs, and GBs all exhibited state-dependency well before the onset of delta waves.
Conclusion: At least three waveforms (SATs, CSWs, and GBs) were present and exhibited organized state-dependent activity by P5, well before the onset of delta activity in the infant rat neocortex.
Support (optional): NIMH 50701 and 66424

0050

BRAIN RESPONSES PREDICT IMPACT OF SLEEP LOSS ON ATTENTION

Millis B, Molfese D, Warren C, Pratt N, Waford R
University of Louisville, Louisville, KY, USA

Introduction: The P300 component of the human brain wave is associated with attention control in an oddball paradigm. When an infrequent tone is presented, a larger, positive ERP component occurs 300ms after the onset (P300) (Kray, Eppinger, & Mecklinger, 2005; Holcomb, Ackerman, & Dykman, 1985, 1986). Few studies examine P300 latency and amplitude variations in non-clinical pediatric populations. Given that past studies (Dahl, 1996) suggest that sleep deprived children have difficulty with focused attention, we explored whether the P300 response in sleep-restricted children would be smaller and slower than in children with normal sleep patterns.
Methods: The current study investigated executive attention by combining behavioral and P300 waveform information from children 4 to 8 years of age who experienced a minor sleep reduction from their baseline amount of sleep for seven consecutive nights. Behavioral attention information was collected using the NEPSY Visual Attention subtest. ERPs were then recorded after one week of baseline sleep and after a second week of 1 hour sleep restriction using a Geodesic Sensor Net with 128 Ag/AgCl electrodes during the oddball paradigm. One hundred trials of frequent (70%) and target (30%) tones were counterbalanced between 1000 and 1500 Hz. Actigraphy recordings verified sleep times during both weeks.
Results: A stepwise multiple regression model was developed using the ERP component scores obtained at week 1 as the independent variables and the NEPSY Visual Attention scores obtained at week 2 as the dependent variable. The ERPs accounted for 44% of the total variance in predicting NEPSY Visual Attention scores after the children´s sleep was reduced for one week, R square = .44, $F(2,21) = 8.25$, $p<.002$.
Conclusion: These data are interpreted to suggest that neural based risk factors can signal the cognitive resilience of individuals in handling subsequent sleep loss.

0051

SLEEP AND RESPONSES TO SLEEP DEPRIVATION OF MICE LACKING BOTH INTERLEUKIN-1 RECEPTOR 1 AND TUMOR NECROSIS FACTOR- RECEPTOR 1

Baracchi F, Opp M
University of Michigan, Ann Arbor, MI, USA

Introduction: Data demonstrate that interleukin-1, (IL-1) and tumor necrosis factor-α (TNF) are involved in the regulation of NREMS. Mice lacking the IL-1 type 1 receptor (IL-1R1 KO) spend less time in NREMS during the light period, whereas mice lacking the p55 receptor for TNF (TNFR1 KO) spend less time in NREMS during the dark period. These observations suggest that IL-1 and TNF may contribute to NREMS regulation at different times of the day. To investigate further

the roles of the IL-1 and TNF systems in sleep regulation we characterized sleep in IL-1R1 and TNFR1 double KO mice (IL-1R1/TNFR1 KO).
Methods: Male mice (30-40g, n=6 / strain; Jackson Laboratories) were surgically instrumented with EEG electrodes and with a thermistor to measure brain temperature. After recovery and adaptation to the recording apparatus, 48 h undisturbed baseline recordings were obtained. Mice were then subjected to 6 h sleep deprivation by gentle handling at light onset.
Results: Relative to control mice (B6129SF2/J), the IL-1R1/TNFR1 KO mice spent less time in NREMS during the last 8-h of the dark period and less time in REMS during the first half of the light period. After sleep deprivation, control mice exhibited a transient NREMS rebound and a prolonged REMS rebound, whereas there was no increase in NREMS or REMS duration in the IL-1R1/TNFR1 KO mice.
Conclusion: This study demonstrates that the lack of both IL-1R1 and TNFR1 results in a sleep phenotype that differs from expected on the basis of sleep of mice lacking only one of these cytokine receptors. In addition, these results provide addition evidence that these cytokine systems contribute to alterations in sleep that follow prolonged wakefulness. Additional studies are required to ascertain whether the sleep phenotype of these animals is due to interactions between the two cytokine systems, or to compensatory mechanisms specific for this genotype.
Support (optional): National Institutes of Health: HL080972; GM067189. The Department of Anesthesiology of the University of Michigan Medical School.

0052

ASSOCIATION BETWEEN APNEA-HYPOPNEA INDEX AND BRAIN ACTIVATION IN OBSTRUCTIVE SLEEP APNEA DURING A SHORT-TERM ATTENTION TASK

Patel M,[1] Drummond S,[2] McKenna B,[2] Ancoli-Israel S,[2] Ayalon L[2]
(1) University of California San Diego, San Diego, CA, USA, (2) University of California, San Diego, San Diego, CA, USA

Introduction: An association between Obstructive Sleep Apnea (OSA) severity and cognition in various domains has been reported, however very little is known about the cerebral substrates underlying these changes. Here we assessed the association between apnea hypopnea index (AHI), reaction time, and brain activation (measured by FMRI) during a short-term attention task.
Methods: Fourteen OSA patients (1F; age = 45.6 +/- 3.13, BMI = 30.6 +/- 1.52, AHI = 32.1 +/- 5.43) underwent PSG and an FMRI scan the next morning. During FMRI, subjects performed a Go-Nogo Task, and the `Go´ trials were used to index short-term attentional processing. A regression was done to assess the relationship between AHI and brain activation during the `Go´ part of the task. Correlation assessed the relationship between AHI and reaction time.
Results: Increasing AHI was associated with decreased activation during the 'Go' trials in the right anterior cingulate (Broadman´s Area (BA) 32/24), inferior frontal gyrus, right cuneus, lingual gyrus, BA 17 visual cortex, right inferior frontal gyrus (BA 46 and 10), and left inferior frontal gyrus (BA 45). Increased activation was found in the right inferior parietal lobule/BA 40. AHI correlated with `Go´ reaction time mean ($r = .85$, $p < .01$) so that patients with high AHI had longer reaction times.
Conclusion: Increased disease severity in sleep apnea was associated with decreased brain activation in task-related brain areas during the `Go´ part of the Go-Nogo task and slowed reaction times. These data are consistent with previous findings that attention, motor functions, and reaction times are impaired in OSA patients, and extend them to show that both performance and cerebral activation is impaired during short-term attention tasks in moderate-severe sleep apnea patients.
Support (optional): NIH M01 RR00827, NIMH 5 T32 MH18399, NIA AG08415

0053

SPONTANEOUS SLEEP AND RESPONSE TO SLEEP DEPRIVATION IN GHRELIN KNOCKOUT MICE

Szentirmai E,[1] Kapas L,[2] Sun Y,[3] Smith R,[3] Krueger J[4]
(1) Washington State University, Pullman, WA, USA, (2) Fordham University, Bronx, NY, USA, (3) Baylor College of Medicine, Houston, TX, USA, (4) Pullman, WA, USA

Introduction: Previous experiments in our laboratory revealed that intracerebroventricular and intrahypothalamic injections of ghrelin induce wakefulness in rats. To further investigate the possible roles of ghrelin in the regulation of arousal, we studied the spontaneous sleep and sleep deprivation-induced sleep responses in ghrelin knockout (KO) and wild-type (WT) mice.
Methods: Spontaneous sleep-wake activity was recorded in male ghrelin KO (n =10) and WT (n =12) mice for 2 days. On the third day, mice were sleep deprived by gentle handling for the last 6 hours of the light period and recovery sleep was recorded from the beginning of the dark period for 23 hours.
Results: Ghrelin WT and KO mice had similar diurnal rhythms of sleep with more NREMS and REMS during the light period than at night. The amounts of sleep and wakefulness did not differ significantly between the two groups. During the light period ghrelin KO mice had significantly more wake and NREMS episodes (105.4 ± 4.7 and 104.9 ± 4.7, respectively) than WT mice (85.6 ± 5.1 and 85.6 ± 5). The average duration of NREMS episodes was significantly shorter in ghrelin KO (4.2 ± 0.4 min) than in WT mice (5.4 ± 0.4 min). Sleep deprivation induced rebound increase in NREMS and REMS in both WT and KO mice, with no significant difference between the two groups.
Conclusion: Ghrelin KO mice exhibit normal amount of spontaneous sleep, which is more fragmented during the light period, and they are capable of mounting normal homeostatic sleep responses to sleep deprivation. These findings are similar to those that were observed in orexin KO mice. The results are in line with the hypothesis that hypothalamic circuits formed by ghrelin, orexin and neuropeptide Y neurons play a role in regulating vigilance.
Support (optional): NIH (USA) grant No. NS27250

0054

PARENTAL HISTORY OF ALCOHOLISM AND SLEEP EEG IN 9- AND 10-YEAR-OLD BOYS

Tarokh L,[1] Van Reen E,[1] Carskadon M[2]
(1) Brown University, Providence, RI, USA, (2) Providence, RI, USA

Introduction: A parental history of alcoholism (PH+) is the single strongest predictor of subsequent alcoholism. One physiological characteristic of PH+ individuals is increased alpha power in the resting awake EEG. The aim of the present study is to determine if these physiological differences are state specific (i.e., limited to waking EEG) or state independent markers of this increased vulnerability for alcoholism. To this end, we examine frequency spectra of sleeping EEG in alcohol naïve parental history positive (PH+) and negative (PH-) boys.
Methods: Fourteen Tanner stage 1 and 2 boys (mean age=9.2y, SD=.6y) were classified as either PH+ (n=5) or PH- (n=9) based on DSM-IV criteria applied to structured interviews (CDIS-IV). Standard sleep recordings were run in lab for two nights; adaptation and baseline.

Sleep data from the baseline night were visually scored in 30-second epochs using standard criteria. EEG (C3/A2, C4/A1, O2/A1, O1/A2) power spectra were calculated for each 30-second epoch and averaged separately for NREM and REM sleep.
Results: Greater spectral power was observed during NREM and REM in the lower alpha band (7-10 Hz) for the PH+ group. These differences reached statistical significance ($p < .05$) in electrodes over central regions during REM and NREM; differences over occipital regions were statistically significant ($p < .05$) for REM sleep only. Additionally, the PH+ group exhibited diminished power in the beta band (18-27 Hz) during NREM sleep over central and occipital regions.
Conclusion: The observed differences support the hypothesis that elevated power in the alpha band is a state-independent physiological marker of parental history of alcoholism. The NREM sleep difference in the beta frequency band is a novel finding and may reflect a sleep-specific signature of parental history of alcoholism. Future cross-sectional and longitudinal analyses will examine sleep EEG as a function of adolescent maturation.
Support (optional): This research was supported by AA13252 (to MAC) and AA07459-21 (to LT)

0055

FOS EXPRESSION IN PONTINE NORADRENERGIC CELL GROUPS NEGATIVELY CORRELATES WITH THE DURATION OF CARBACHOL-INDUCED REM SLEEP-LIKE STATE IN URETHANE-ANESTHETIZED RATS

Rukhadze I, Fenik V, Branconi J, Kubin L
Department of Animal Biology and Ctr. for Sleep and Respiratory Neurobiology, University of Pennsylvania, Philadelphia, PA, USA

Introduction: Noradrenergic (NE) neurons of the locus coeurelus (LC) and A5 group are silenced during REM sleep (REMS) and REMS-like state elicited in urethane-anesthetized rats by pontine microinjections of carbachol. Withdrawal of noradrenergic excitation contributes to REMS-related depression of activity in hypoglossal (XII) motoneurons that innervate the genioglossus, an important upper airway dilator (Fenik *et al.*, 2005). However, NE excitatory drive to XII motoneurons may originate in NE cell groups of yet unknown patterns of activity across the sleep-wake cycle (Rukhadze & Kubin, 2007). Our goal was to assess REMS-related changes in NE cell activity using Fos immunohistochemistry and an anesthetized rat model in which dorsomedial pontine microinjections of carbachol can repeatedly elicit multiple REMS-like episodes.
Methods: In 16 urethane-anesthetized, paralyzed, vagotomized and artificially ventilated rats, we recorded the cortical EEG, hippocampal and XII nerve activity. Rats received different numbers of pontine carbachol (10 mM, 10 nl) or saline injections that yielded REMS-like episodes that over a 3 h period prior to sacrifice had a total duration of up to 63 min. Brainstem sections were immunohistochemically processed for Fos and tyrosine hydroxylase (TH), a marker for catecholaminergic neurons. TH-positive cells with and without Fos were counted in A1/C1, A5, A7 and sub-coeruleus (SubC) regions.
Results: The percentage of TH+Fos cells relative to all TH cells was on each side negatively correlated with the cumulative duration of REMS-like state for the A7 ($R=0.78$, $P<0.001$; slope=-0.55 %/min) and A5 ($R=0.63$, $P<0.01$; slope=-0.38 %/min) groups, and contralaterally to carbachol injections for SubC neurons ($R=0.52$, $P<0.05$; slope=-0.30 %/min); for A1/C1 cells, a similar trend was not significant. The correlation with the total volume of carbachol injected was not significant.
Conclusion: Our results suggest that A7 cells, like those in A5 and LC, decrease their activity during REMS.
Support (optional): HL-47600.

0056

MICROINJECTIONS OF 2-ADRENERGIC AGONIST, CLONIDINE, INTO THE NORADRENERGIC A7 CELL REGION REDUCE HYPOGLOSSAL (XII) NERVE ACTIVITY IN URETHANE-ANESTHETIZED RATS

Fenik V, Rukhadze I, Branconi J, Kubin L
Department of Animal Biology and Ctr. for Sleep & Respiratory Neurobiology, University of Pennsylvania, Philadelphia, PA, USA

Introduction: Antagonism of α1-adrenergic receptors located in the XII nucleus region reduces XII nerve activity and attenuates its depression subsequently produced during REM sleep-like state elicited by pontine carbachol in urethane-anesthetized rats (Fenik *et al.*, Am. J. Resp. Crit. Care Med., 2005). Thus, there is evidence that a withdrawal of noradrenergic excitation may be a major cause of REM sleep-related suppression of activity in XII motoneurons, which in obstructive sleep apnea patients serve as important upper airway dilators. Since the wake-related noradrenergic excitation of XII motoneurons may originate in several pontomedulary catecholaminergic regions (Rukhadze & Kubin, J. Chem. Neuroanat., 2007), we used microinjections of clonidine, an agonist that inhibits noradrenergic neurons, to test whether silencing of neurons in the pontine A7 group reduces XII nerve activity.
Methods: In 8 urethane-anesthetized, paralyzed, vagotomized and artificially ventilated rats, we recorded XII nerve activity, cortical EEG and hippocampal activity and sequentially microinjected clonidine (0.75 mM, 20-40 nl) into A7 groups of both sides.
Results: Of the 16 injections performed, 7 were placed 100 μm or less from the nearest cells of the A7 group, as determined by immunohistochemistry. With a latency of 76 s ± 21 (SE), each of these injection elicited a long-lasting (over 15 min) decrease of XII nerve activity (mean: 27.9% ± 2.2 of the pre-clonidine level, $p<0.01$). The decreases were associated with only a short (4.2 min ± 1.2) increase of arterial blood pressure and no changes in cortical or hippocampal activity. The remaining 9 injections were placed 200-800 μm away from the A7 group and were either ineffective (8), or resulted in XII nerve depression accompanied by changes in electrocortical signals (1).
Conclusion: A7 cells provide noradrenergic excitatory drive to XII motoneurons that may be withdrawn during REM sleep, thus contributing to depression of upper airway motor tone.
Support (optional): HL47600.

0057

SLEEP RESPONSES TO GHRELIN, LEPTIN AND CHOLECYSTOKININ IN GHRELIN KNOCKOUT MICE

Szentirmai E,[1] Kapas L,[2] Sun Y,[3] Smith R,[3] Krueger J[4]
(1) Washington State University, Pullman, WA, USA, (2) Fordham University, Bronx, NY, USA, (3) Baylor College of Medicine, Houston, TX, USA, (4) Pullman, WA, USA

Introduction: Our laboratory previously showed that central injection of ghrelin promotes wakefulness in rats. In addition to playing a role in the regulation of vigilance, ghrelin is also implicated in feeding acting together with other peripheral and central peptides. These signals are also capable of altering sleep. The aim of the present experiment was to study whether the absence of ghrelin affects sleep responses to systemic administration of different feeding-regulatory peptides.
Methods: Ghrelin knockout (KO) and wild-type (WT) mice were implanted with EEG and EMG electrodes. Groups of mice (n = 7-13) received intraperitoneal injections of isotonic NaCl (10 ml/kg) or ghrelin (400 μg/kg), or cholecystokinin (CCK) (50 μg/kg), or leptin (100 μg/kg

or 1000 µg/kg) 5-10 min before dark onset and in separate experiments ghrelin (400 µg/kg) before light onset. Sleep was recorded for 12 hours after the injections.
Results: Systemic injection of 400 µg/kg ghrelin did not have any effect on the sleep of WT mice. In ghrelin KO mice, ghrelin significantly increased the amount of NREMS in the first hour after dark and light onset injections (by 43 % and 72 %, respectively). CCK induced similar significant NREMS increase in ghrelin KO and WT mice in the first 3 hours after injection (59 % and 38 %, respectively). The small dose of leptin failed to induce any changes in sleep. The high dose of leptin significantly increased the time in NREMS in ghrelin KO and WT mice (72 % in KO and 70 % in WT) in the first hour after injection.
Conclusion: The lack of ghrelin does not affect the somnogenic effects of systemic administration of leptin and CCK, while it affects the sleep responses to exogenous ghrelin. It is possible that the different response to ghrelin observed in ghrelin KO mice may be due to their altered sensitivity to ghrelin.
Support (optional): NIH (USA) grant No. NS27250

0058

FMRI CAN DIFFERENTIATE EARLY AND LATE STAGE 1 SLEEP

Picchioni D,[1] Fukunaga M,[2] Carr W,[3] Braun A,[2] Balkin T,[1] Duyn J,[2] Horovitz S[2]
(1) Walter Reed Army Institute of Research, Silver Spring, MD, USA, (2) National Institutes of Health, Bethesda, MD, USA, (3) Naval Medical Research Center, Silver Spring, MD, USA

Introduction: Sleep onset is a complex neural process that involves both increases and decreases in brain activity and this process cannot be properly characterized by a single sleep stage. We examined the possibility that fMRI would identify differences in brain activity between epochs of stage 1 immediately following wake and immediately preceding stage 2.
Methods: Data for this research were obtained from four participants during 60-minute daytime scanning sessions without any prior sleep deprivation. EEG data were obtained using MRI-compatible equipment. Sleep was scored using standard criteria. Periods of interest were identified that began with at least one 30s-epoch of wake, were followed by at least 60s of continuous stage 1, and ended with at least one 30s-epoch of stage 2. Three fMRI contrasts were performed. The first (EARLY1) and last (LATE1) 30 seconds of stage 1 sleep were independently contrasted with time points obtained during WAKE. The results of these two contrasts were then contrasted with each other [i.e., (LATE1 - WAKE) - (EARLY1 - WAKE)] so the final output reported below represents the difference in activity between EARLY1 and LATE1 but as compared to WAKE.
Results: There was increased activity in the hippocampus bilaterally--with stronger activation on the left. There was decreased activity in the precuneus bilaterally. There was increased activity in the precentral gyrus bilaterally. There was decreased activity in the left inferior frontal gyrus.
Conclusion: These results support the idea that there are a variety of changes in brain activity--including increases--during sleep onset. These changes can be detected using fMRI and potentially used to differentiate stages of sleep that would otherwise be grouped together based on standard EEG criteria.
Support (optional): DP is supported by the National Academy of Sciences-National Research Council Postdoctoral Research Associateship Program.

0059

MEASUREMENT OF THE PROPENSITY TO SLEEP BY MEANS OF A MODIFIED RODENT MULTIPLE SLEEP LATENCY TEST

McKenna J,[1] Cordeira J,[2] Tartar J,[2] Ward C,[2] McCoy J,[3] Lee E,[4] Thakkar M,[2] McCarley R,[2] Strecker R[2]
(1) Boston VA Healthcare/Harvard Medical School, Brockton, MA, USA, (2) Boston VA Healthcare/Harvard Medical School, MA, USA, (3) University of Southern Mississippi, MS, USA, (4) Bio-Pharmaceutical, SK Corporation, MA, South Korea

Introduction: A novel rodent multiple sleep latency test (rMSLT) was developed that contained features of both the clinical MSLT and published animal studies, in order to measure the propensity to fall asleep. Rats were exposed to six hours of sleep deprivation (SD) or interruption (SI), employing automated devices, and sleepiness was evaluated following treatments.
Methods: The rMSLT included six sleep latency trials conducted within a three hour period, either at the end of the light, or beginning of the dark period. On a separate day, uninterrupted rebound sleep was examined after SD or SI.
Results: Six hours of SD or SI decreased sleep latencies compared to control time-of-day matched baseline sleep latencies: a) The mean sleep latency after 6h of SD that ended in the light period was 1 min, 14 s compared to baseline sleep latencies of 7 min, 59s; b) 6h SD ending in the dark period was 6 min 50 s compared to baseline of 13 min, 10 s; c) 6 h SI ending in the light period, was 4 min 31 s compared to baseline was 7 min, 22 s; d) 6 h SI ending in the dark period was 5 min 43 s compared to baseline of 13 min, 35 s. Average NREM episode durations and average delta power in NREM during uninterrupted recovery following SD or SI were also examined.
Conclusion: The propensity to fall asleep following SD or SI was evident in our measurement with both the rMSLT and polysomnographic analysis of the recovery period. As well, we were able to demonstrate a sleep-loss induced elevation in the homeostatic sleep drive at a time of day usually difficult to evaluate due to behavioral arousal pressure (at the beginning of the dark period).
Support (optional): VA Service Awards to RES and RWM; NIMH (39683), NHLBI (HL060292); NHLBI (HL07901) to JT; and NHLBI (HL07901) and NIMH (MH070156) to JTM

0060

ELECTROPHYSIOLOGICAL EVIDENCE FOR SYNAPTIC POTENTIATION DURING WAKING AND SYNAPTIC DOWNSCALING DURING SLEEP

Vyazovskiy V,[1] Faraguna U,[2] Cirelli C,[1] Tononi G[3]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) 1-Scuola Superiore Sant'Anna; 2-University of Wisconsin-Madison, Madison, WI, USA, (3) University of Wisconsin, Madison, WI, USA

Introduction: We have recently hypothesized that waking is associated with synaptic potentiation and sleep with synaptic downscaling. In support of this hypothesis, in a companion abstract (Pfister-Genskow et al) we showed that molecular markers of synaptic potentiation and depression change between sleep and wakefulness. In the present study we investigated whether the slope of the early cortical evoked potential, induced by electrical stimulation of the cerebral cortex in awake rats, increases after wakefulness and decreases after sleep.
Methods: Male adult WKY rats (n=7-15/group) were used. Intracortical local field potentials (LFP) recordings were obtained with bipolar concentric electrodes from the left frontal cortex while the right frontal cortex was stimulated (pulses 0.1 ms duration). Evoked responses were

collected during quiet immobile wakefulness i) after spontaneous or enforced waking during the dark period; ii) after undisturbed sleep during the light period; iii) after 4 h sleep deprivation starting at light onset (SD). LFPs and the EMG were continuously recorded to quantify vigilance states and slow wave activity in NREM sleep.
Results: We measured the slope of the first negative component of the transcallosal evoked responses (latency to the peak 4.3 ms ± 0.4, mean ±SEM). The slope of this component was high after spontaneous waking period at light onset, and decreased during ensuing sleep. SD prevented this decrease, and even resulted in higher values of the slope, compared to pre-SD levels. Consistently, the slope was high after 12 h of enforced waking during the dark period, and showed a pronounced decrease following recovery sleep.
Conclusion: As predicted by the synaptic homeostasis hypothesis, an established indicator of synaptic strength - the slope of the early monosynaptic cortical evoked potential - increased after wakefulness and decreased after sleep. The data provide electrophysiological evidence for synaptic potentiation during waking and synaptic downscaling during sleep.
Support (optional): NIH Director´s Pioneer award to GT, Swiss National Science Foundation grant PBZHB-106264 to VVV.

0061

DIFFERENTIAL EFFECTS OF GABOXADOL AND ZOLPIDEM ON NEURONAL FIRING OF OREXIN SENSITIVE NEURONS IN THE RAT DORSAL RAPHE NUCLEUS

Li Y,[1] Uhegbu E,[1] Hutson P,[1] Renger J,[2] Kraus R[1]
(1) Merck & Co., West Point, PA, USA, (2) Merck Research Laboratories, West Point, PA, USA

Introduction: Zolpidem enhances synaptic GABA-ergic neurotransmission by potentiating an inhibitory chloride conductance through $GABA_A$ receptors expressed in the postsynaptic junction, thereby causing sedative-hypnotic effects. Gaboxadol, a selective extrasynaptic $GABA_A$ receptor agonist, acts on a unique &delta-containing $GABA_A$ receptor subtype located exclusively outside the synapse. In an attempt to functionally differentiate Gaboxadol from Zolpidem we have studied the effects of both drugs on the orexin neuronal system in the rat brain. Orexinergic neurons localized within the hypothalamus synthesize orexin-A and –B. These neuropeptides bind with high affinity to orexin1 and orexin2 GPCRs expressed in multiple regions of the brain, such as the serotoninergic dorsal raphe nucleus (DRN), involved in the regulation of sleep and wakefulness.
Methods: Extracellular single unit recordings were performed from the dorsal raphe nucleus at 32ºC to study changes in basal neuronal firing and orexin-A induced firing mediated by Zolpidem and Gaboxadol. Coronal slices from 20-30 days old Sprague Dawley rats were used. Recording region was visualized using a differential interference contrast microscope and an infrared video system.
Results: We found that both drugs inhibited basal and orexin-A induced firing dose-dependently at clinically relevant µm concentrations. In contrast to Zolpidem, Gaboxadol caused complete inhibition of firing at 10 µm without inducing desensitization. Concomitant application of Gaboxadol and Zolpidem potentiated the effects of both drugs resulting in complete cessation of basal and orexin induced firing at 3 µm suggesting synergistic interaction of the drugs.
Conclusion: We conclude that Gaboxadol can be discriminated from benzodiazepine site ligands such as Zolpidem based on effects on neuronal firing in a functional rat brain slice assay.
Support (optional): This work was supported by Merck & Co.

0062

SLEEP DEPRIVATION INCREASES TNF PROTEIN (26 KDA) LEVELS IN THE CORTEX

Taishi P,[1] Churchill L,[1] Krueger J[2]
(1) Washington State University, Pullman, WA, USA, (2) Pullman, WA, USA

Introduction: Tumor necrosis factor α (TNFα) is a key element in the brain cytokine network and is involved in non-rapid eye movement sleep (NREMS) regulation. TNFα is synthesized as a transmembrane 26 kDa protein that is cleaved to the soluble 17 kDa peptide. Central administration of TNF siRNA is effective at reducing both TNF mRNA and TNF immunoreactivity in the rat cortex. Since sleep deprivation (SD) increases brain TNF&alphamRNA levels, we determined if the transmembrane TNF&alpha(26 kDa) protein responded to 6 h of SD in the cortex using Western blots.
Methods: Male Sprague-Dawley rats (280 – 350 g) were randomly divided into SD (n = 8) and control (n = 8) groups. Rats were kept on a 12:12 light:dark cycle, and SD began at light onset by gentle handling. At the end of the 6 hr period, the cortex was quickly dissected and frozen. Total protein was extracted by homogenizing the tissue in radio-immunoprecipitation assay buffer with proteinase inhibitors. Cortical protein (50 µg) was resolved by SDS-PAGE, transferred to nitrocellulose membrane, and incubated overnight with a specific primary polyclonal goat antibody to rat TNFα. Then the membrane was incubated with HRP-labeled donkey antigoat-IgG secondary antibody, treated with Western blotting detection reagents, and exposed to Kodak film.
Results: There was a strong TNF-immunoreactive band at 26 kDa; this band was specifically blocked with rat recombinant TNF. The 26 kDa TNF protein showed a significant increase after SD compared with the control group ($p < 0.05$).
Conclusion: These results suggest that the transmembrane TNF protein up-regulates after SD in the cortex. Results are consistent with the hypothesis that increases in TNFα mRNA during the wake state produce increases in the transmembrane protein, which may then be hydrolyzed and released to promote NREMS.
Support (optional): NIH (USA) NS 25378 and NS 31453.

0063

EFFECTS OF SLEEP RESTRICTION ON SPEECH DISCRIMINATION IN CHILDREN

Waford R, Pratt N, Warren C, Millis B, Molfese D
University of Louisville, Louisville, KY, USA

Introduction: Research examining the impact of sleep in school-age children suggests that even mild sleep loss produces marked deficits in cognitive development and functioning (Gozal, 2005; Kheirandish & Gozal, 2006). The present study investigated the degree of recovery in cognitive functioning following a week of one-hour sleep restriction.
Methods: We recorded event-related potentials (ERPs) as a measure of neurocognitive development (Molfese & Molfese, 2004, Lyytinen, 2005). ERPs were recorded from 6 and 7 year old children (N = 32) while they listened to the following computer generated speech syllables, /ba/, /da/, /ga/. A 128- electrode high-density array was used.
Results: Analyses indicated differences in speech processing across all portions of the brainwave. These effects were qualified by an interaction that illustrated an early difference in right hemisphere processing of /da/ (20 ms - 212 ms) between children in control and restricted sleep conditions, $F(1,30)=5.173$, $p<.05$. Furthermore, this effect was not present during the baseline week or recovery week, clearly resulting from the week of sleep restriction.

Conclusion: It appears that children during sleep restriction altered their initial stages of speech perception. The speech sound /da/, while phonetically distinct, is acoustically very similar to /ba/. Sleep loss could disrupt the acoustic perception of /da/, causing it to be phonetically coded incorrectly. Such changes in perception could contribute to disruptions in cognitive and linguistic functioning, skills necessary for reading and language development and comprehension.

0064

INTERMITTENT AND SUSTAINED HYPOXIA DIFFERENTIALLY REGULATE CELL DEATH: ROLE OF PKA

Gozal E,[1] Miller C,[2] Sachleben L,[1] Dematteis M,[3] Rane M[4]
(1) Department of Pediatrics, Louisville, KY, USA, (2) Department of Physiology and Biophysics, Louisville, KY, USA, (3) HP2 Laboratory, La Tronche, France, (4) Department of Medicine, Louisville, KY, USA

Introduction: Sleep apnea is associated with cerebrovascular morbidity involving intermittent hypoxia (IH). We previously used PC12-cells as an in vitro model of neurons and showed that mild IH induced caspase-dependent cell death, while mild sustained hypoxia (SH) was less deleterious. Moreover, we uncovered a role for PKA activity in regulating cellular metabolism and oxidative stress response to hypoxia that may contribute to the differential effect of IH versus SH. To identify signaling pathways underlying differential neuronal susceptibility to IH and SH, we examined metabolic and signaling responses of wild type (WT) and PKA-deficient (123.7) PC12-cells exposed to severe IH or SH.
Methods: WT and 123.7 cells were exposed to IH (cyclic 0.1-21% O2) or SH (continuous 0.1% O2) up to 48h. Cell viability was assessed by Trypan Blue exclusion and MTT assay. Metabolic status was studied by determination of ATP levels and AMP-kinase (AMPK) activation. Immunoblotting of p38 MAPK and SAPK-JNK phosphorylation assessed the activation of stress-induced kinases.
Results: In WT-cells, SH-induced cell death started at 24h and progressively increased at 48h while cell death was delayed at 48h with IH. In contrast, 123.7-cells tolerated both SH and IH. AMPK-activation, suggesting ATP depletion, occurred in WT cells at 24h SH but not IH, and correlated with decreased ATP levels and cell death, while remaining unchanged in 123.7-cells. p54-SAPK-JNK phosphorylation increased in WT-cells at 48h SH, while moderately increasing with IH and remaining unchanged in 123.7 cells. p38 MAPK phosphorylation remained unchanged in both cell types.
Conclusion: These data suggest that PKA regulates cell metabolic response to hypoxia and hypoxia-induced stress kinases activation that may underlie differential susceptibility to IH and SH. Modulation of hypoxia-induced PKA signaling may therefore provide novel therapeutic strategies for diseases associated with hypoxia.
Support (optional): NIH-HL-074296, 2 P20 RR015576, R56AI059165

0065

SLEEP DEPRIVATION IMPAIRS SEARCH FOR RARE TARGETS

Santhi N,[1] Horowitz T,[2] Wolfe J,[2] Czeisler C[3]
(1) Brigham and Women's Hospital/Harvard Medical School, Boston, MA, USA, (2) Brigham and Women's Hospital/Harvard Medical School, MA, USA, (3) Brigham and Women's Hospital / Harvard Medical School, Boston, MA, USA

Introduction: Many socially critical visual search tasks in fields such as airport baggage screening and radiology involve search for infrequently occurring or low prevalence targets. Low target prevalence by itself leads to increased miss errors; this is the prevalence effect. Many of these critical jobs are also performed at night. Our goal was to examine if sleep deprivation modulates the prevalence effect in visual search.
Methods: Thirty-one healthy subjects participated in a 36 h constant routine. A visual search task was administered every two hours. Subjects reported whether a target (block 2) was present in set of simultaneously presented distractors (block 5s). We varied set size (number of items: 10, 20, 30, or 40) and target prevalence (high: 50% vs. low: 10%). We measured search rate (slope of the RT x set size function) and sensitivity (d' an accuracy index: normalized hits - false alarms).
Results: We obtained three important results. First, there was a prevalence effect: d' was lower in the low prevalence condition ($F\ 1, 3858 = 111.52$, $p < .001$). Second, sleep deprivation induced a speed/accuracy trade-off: search rate sped up with time awake ($F\ 1,34 = 8.83$, $p < .01$), but errors increased (d' declined: $F\ 1,29 = 30.59$, $p < .001$), indicating decision stage impairments. Third, most critically, this trade-off occurred earlier in the low prevalence condition. After 24 hrs awake, there was a significant decrease in d´ in the low prevalence condition (2.58 +/- .05 – 2.34 +/- .05; $p < .01$) but not in the high prevalence condition (2.88 +/- .05 – 2.83 +/- .05; $p > .05$). Similarly, the change in RT slope after 24 hrs awake was greater at low prevalence the (22 +/- 3 – 16 +/- 3 ms/item) than at high prevalence (23 +/- 3 – 21 +/- 3 ms/item).
Conclusion: These results suggest that safety and performance in socially critical low target prevalence search tasks may be especially vulnerable to the detrimental effects of sleep deprivation.
Support (optional): National Heart Lung and Blood Institute (R01; HL52992) to CAC, General Clinical Research Center Program of the National Center for Research Resources (M01 RR02635) to BWH GCRC, and a Fellowship in Sleep, Circadian and Respiratory Neurobiology from the National Heart Lung and Blood Institute (T32 HL07901) to NS.

0066

THE DECREASE OF SLEEP SLOW WAVE SLOPES WITH DECREASING SLEEP PRESSURE LEADS TO A REDISTRIBUTION OF EEG POWER WITHIN THE SWA BAND TOWARDS LOWER FREQUENCIES

Vyazovskiy V,[1] Cirelli C,[1] Tononi G[2]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) University of Wisconsin, Madison, WI, USA

Introduction: Slow-wave activity during NREM sleep (SWA, 0.5-4.0Hz) increases after waking and decreases during sleep. The homeostatic decline of SWA is, however, slower for frequencies <1Hz, and why this is the case is unclear. Here, were used empirical and simulated local field potential (LFPs) signals to investigate whether the changes in slow wave parameters may account for the different time course of <1Hz and >1Hz SWA.
Methods: Male adult WKY rats (n=15) were used. Individual slow waves were detected in the intracortical bipolar recordings, and their amplitudes and the slopes (mean first derivative of the first and second segment) were determined for high (first 3h of the light period) and low (last 3h) sleep pressure. In the simulated LFP signal the proportion of high/low-amplitude slow waves was 6/7 and 1/7 for the high and low sleep pressure respectively, and in the latter the slopes were ~33% lower compared to the high sleep pressure signal.
Results: In vivo, LFP under low sleep pressure was characterized by i) decreased SWA, ii) rare occurrence of high-amplitude slow waves, iii) overall decrease in slow wave slopes and iv) a shift of the spectral peak towards lower frequencies (<1Hz). Consistently, simulated LFP under low sleep pressure was also characterized by decreased SWA and by a shift of the spectral peak towards lower frequencies (<1Hz). Further

simulations revealed that the decreased incidence of high-amplitude slow waves was primarily responsible for the decrease in absolute power in the SWA range, while the reduced slopes of slow waves resulted in the increase in the low frequency power at the expense of higher frequencies.
Conclusion: The slower homeostatic decline of <1Hz SWA unlikely reflects a distinct neurophysiological process, but rather results from a redistribution of power density within the SWA band due to the concomitant changes in the slope of the slow waves.
Support (optional): NIH Director´s Pioneer award to GT, Swiss National Science Foundation grant PBZHB-106264 to VVV

0067

CHRONIC RECORDING OF SLEEP-DEPENDENT CORTICAL PLASTICITY: A LONGITUDINAL STUDY IN THE FREELY-MOVING CAT

Jha S,[1] Steinmetz N,[1] Coleman T,[1] Frank M[2]
(1) University of Pennsylvania, Philadelphia, PA, USA, (2) Philadelphia, PA, USA

Introduction: During a critical period of development, monocular deprivation (MD) induces a rapid remodeling of synaptic weights in visual cortex (V1) towards the open eye; a phenomenon called ocular dominance plasticity (ODP). We have shown recently that sleep enhances ODP via an activity-dependent process. To better isolate the role of sleep in ODP, we recorded V1 neurons in critical period cats in sleep-wakefulness before, during and after MD.
Methods: Critical period cats (MD and non-MD control groups) were prepared for polysomnography and micro-wire recordings. In the MD group (n=6, 41sites), multi-unit activity across sleep/wake was recorded before (baseline), during and after a 6-hr right eye MD. The non-MD cats (n=3, 16sites) were treated identically except that no MD was performed. Changes in OD at each site were assessed by calculating a left-eye/right-eye firing-rate ratio in alert cats at the beginning and end of each period.
Results: Six-hr MD caused a shift in OD towards the non-deprived eye, which further increased after 6 hours of sleep (baseline vs post-MD, $p<0.05$; post-MD vs post-MD sleep, $p<0.0001$(paired t-test)). These changes did not occur in neurons from control cats. We find that ODP occurs in two stages: depression of deprived-eye (DE) responses during wakefulness and subsequent potentiation of non-DE responses after sleep. This latter process was associated with increased neuronal firing during NREMS and REMS and a decrease in EEG slow-wave activity (SWA). The degree of non-DE potentiation after sleep correlated with overall shifts in OD ($r=0.88$, $p<0.001$). Additionally, we found correlations between changes in ODP and increases in post-MD NREMS firing-rate ($r=0.37$, $p<0.02$), and post-MD changes in SWA ($r=-0.57$, $p<0.01$).
Conclusion: Our findings show that sleep and wakefulness are both required for experience-dependent plasticity, but engage distinct cellular mechanisms. They also demonstrate that synaptic plasticity in-vivo is associated with highly specific changes in neuronal activity during sleep.
Support (optional): Supported by NIH RO1 MH 067568 and ASMF 30-CA-05

0068

CHARACTERIZATION OF EEG DURING RESPONSE LAPSES TO STIMULI IN THE CHOICE VISUAL PERCEPTION TASK

Sing H, Hall S, Russo M, Kautz M, Thorne D, Redmond D
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: Direct synchrony of EEG with stimuli and response intervals provide accurate assessments of the alertness/drowsiness state of the individual at each stimulus during cognitive testing. .
Methods: EEG sampled at 1000 Hz was collected from C3, C4 placements during performance on the Choice Visual Perception Task (CVPT). Nineteen test sessions were administered to 13 volunteers over a 4 day resident study which included a 40 hr continuous wakefulness period. The CVPT device is arc shaped with 11 light emitting diodes (LED) embedded at 15º intervals from the arc´s center extending to 75º on each side. Randomly lit single or double LEDs of 250ms duration provide the stimulus with response of a key press. A non-response exceeding 3sec is recoreded as a lapse. 150 stimuli are presented in each session with random interstimuli intervals between 5 and 16.5secs. A separate digital channel in direct synchrony with the EEG channels, records each stimulus and response. A high frequency band (HF,) 201-500 Hz and a low frequency band (LF), 1-15 Hz are delineated from spectral analysis and their relative proportions to the total spectral energy are calculated.
Results: Individual performance on the CVPT varied. One SD rresilient volunteer had mean accuracy of 97.8% for the 19 sessions and 32 lapses (out of 2850 stimuli). At the other extreme, a volunteer had mean accuracy of 58.8% and 1110 lapses. Other volunteers performed between these extremes. EEG of the SD resilient volunteer during stimuli and response intervals showed HF consistently greater than LF. These proportions were reversed for the non-resilient volunteer during testing.
Conclusion: Observations of EEG in direct synchrony with the S/R interval in a vigilance task can not only reveal the alertness state of the individual at that moment, but may also portend increasing drowsiness, possibly leading to sleep onset.

0069

THYROTROPIN-RELEASING HORMONE DIRECTLY EXCITES HYPOCRETIN/OREXIN NEURONS IN THE MOUSE HYPOTHALAMUS

Hara J,[1] Xie S,[1] Sakurai T,[2] Kilduff T[1]
(1) SRI International, Menlo Park, CA, USA, (2) University of Tsukuba, Tsukuba, Ibaraki, Japan

Introduction: Thyrotropin-releasing hormone (TRH) is a tripeptide hormone that stimulates the release of thyroid-stimulating hormone and prolactin from the anterior pituitary. TRH is synthesized in multiple brain areas, including the dorsomedial hypothalamus, a nucleus known to project to the lateral hypothalamic area in which the hypocretin (Hcrt) cells are located. TRH is known to be excitatory in brain areas such as the thalamus. TRH receptor 1 (TRH-R1) is predominantly expressed in the hypothalamus, whereas TRH-R2 is present broadly throughout the brain. TRH and TRH analogs are known to reduce cataplexy in the narcoleptic dog. To determine whether TRH directly affects the Hcrt system, we investigated the neurophysiological effects of TRH on defined Hcrt neurons.
Methods: Hypothalamic slices (250 M) were prepared from neonatal transgenic mice in which the enhanced green fluorescent protein (EGFP) was linked to the Hcrt promoter. Slices were perfused (2 ml/min) with physiological solution containing (mM): NaCl 135, KCl 5, CaCl2 1, MgCl2 1, NaHCO3 25, glucose 10. Whole-cell recordings

were made using an Axopatch 1D amplifier.
Results: In current-clamp mode, TRH (0.03 – 1 μM) produced excitatory effects in a concentration-dependent manner (32/34 cells), manifested as membrane depolarization, decreased input resistance and increased firing rate. The excitatory effects persisted in the presence of 0.5 M tetrodotoxin (n=5). In voltage-clamp mode, TRH (100 nM) increased the frequency of spontaneous excitatory postsynaptic currents (EPSCs) by 15% and reduced the amplitude of EPSCs by 24% (n=3) without affecting IPSCs.
Conclusion: These results indicate that TRH directly and consistently excites Hcrt neurons and that TRH may differentially modulate excitatory and inhibitory inputs to Hcrt neurons. The direct interaction between the TRH and Hcrt systems provides an excitatory pathway to tune Hcrt neuronal activity that may have implications for the control of wakefulness and suppression of cataplexy and REM sleep.
Support (optional): Supported by NIH R01 MH61755, R01 AG020584 and R43MH072162.

0070

LEARNING A VISUAL SKILL FOLLOWING ACOUSTIC EEG SLOW-WAVE ACTIVITY SUPPRESSION IN SLEEP

Aeschbach D,[1] Cutler A,[2] Ronda J[3]
(1) Brigham and Women's Hospital/Harvard Medical School, Boston, MA, USA, (2) Brigham and Women's Hospital, MA, USA, (3) Brigham and Women's Hospital/Harvard Medical School, MA, USA

Introduction: Slow-wave activity (SWA; power density in the 0.75-4.5 Hz range) in the sleep EEG is a marker of sleep homeostasis that may be linked to neuronal plasticity and benefit sleep-dependent learning. However, while a relationship between SWA and learning has been derived from correlation studies, we have recently found learning of a motor skill to be unaffected by acoustic SWA suppression in sleep after training. Here we used the same SWA suppression paradigm to test the effect on learning a visual skill.
Methods: 20 healthy subjects participated in a single-blind parallel group protocol that included an adaptation night, a baseline night (BL), an experimental night (EX; with or without SWA suppression), and a recovery night (RC). Time in bed was 8 h except for EX during which it was 4 h. In 11 subjects (age 18-29 y; 7 F), SWA was suppressed with acoustic tones (45-100 dBA), and in 9 subjects (age 18-30 y; 6 F) no tones were presented (control). Subjects trained on a visual texture discrimination task (TDT) following BL in session 1, and were tested 24 h later following EX in session 2, and again following RC in session 3. In each session, subjects´ discrimination skill was tested at progressively shorter stimulus onset asynchronies (i.e. interval between onset of target and masking stimuli) to determine the discrimination threshold. Learning was defined as the decrease in the discrimination threshold in session 2 and 3 compared to the training session.
Results: In EX, SWA was reduced to 67% in the suppression group compared to BL, but remained close to BL levels (99%) in the control group (p=0.002 between groups, unpaired t-test). REM sleep amount did not differ between groups. The decrease in the discrimination threshold, i.e. the learning effect, was smaller in the suppression group than in the control group both following EX (4 vs. 25 ms; p=0.02, Wilcoxon), and following RC (25 vs. 52 ms; p=0.04). SWA in EX correlated with the decrease in the discrimination threshold following EX (r=0.77, p=0.0003, Spearman), and following RC (r=0.52, p=0.03).
Conclusion: Visual skill learning appears to depend on processes underlying SWA in the non-REM sleep.
Support (optional): NARSAD, Milton Fund of Harvard University, and NCRR-GCRC-M01-RR02635 to Brigham and Women´s Hospital.

0071

AN INTEGRATED EEG/EMG/GLUCOSE SYSTEM FOR MICE AND RATS

Johnson D,[1] Harmon H,[1] Naylor E,[2] Gabbert S,[1] Aillon D,[1] Johnson D,[1] Wilson G,[3] Turek F[4]
(1) Pinnacle Technology, Inc., Lawrence, KS, USA, (2) Northwestern University, Chicago, IL, USA, (3) University of Kansas, Lawrence, KS, USA, (4) Northwestern University, Evanston, IL, USA

Introduction: Glucose is the primary energy source in the brain, and glucose levels vary in specific brain regions with respect to their activity. The ability to measure glucose from specific brain areas in vivo while simultaneously recording sleep/wake in rodents would provide a powerful new tool to researchers to better examine the function of specific sites within the brain during the sleep process and to leverage the advantages conferred by using rat and mouse models for research,
Methods: Pinnacle developed a prototype turnkey EEG/EMG system with an integrated glucose biosensor for rats and mice. A tethered EEG/EMG/Biosensor system was designed for mice and a wireless EEG/EMG/Biosensor system was designed for rats.
Results: Glucose levels within the cerebral cortex of the mouse were measured concurrently with EEG and EMG waveforms. The data clearly show an increase of extracellular glucose during the waking period and a decrease during sleep. Interestingly, extracellular glucose does not immediately rise upon waking but rather takes 15-20 minutes before increasing. When all epochs of sleep were compared over the entire 20-hour recording period, the average glucose levels during all waking epochs was significantly higher (ANOVA; df=2, F=16.9, p<0.001) than during either NREM or REM sleep epochs. Previous researchers demonstrated this phenomenon in mice; however, in those experiments glucose levels were determined post-mortem using enzymatic assays.
Conclusion: The ability to better monitor glucose regulation in animals subjected to long-duration sleep deprivation—paradigms which are difficult and expensive to accomplish in humans—will help to elucidate some of the ties between the metabolic system and sleep. The system being developed is also compatible with other biosensors (lactate, glutamate, ATP, etc.). These tools will enable other lines of research that are currently not possible in freely, moving awake rodents.
Support (optional): NIH 1R43MH076318-01

0072

RESPECTIVE ROLE OF HISTAMINE AND OREXIN NEURONS IN SLEEP-WAKE CONTROL

Anaclet C,[1] Parmentier R,[1] Guidon G,[1] Buda C,[1] Sastre J,[1] Haas H,[2] Lin J[3]
(1) INSERM-U628, Lyon, France, (2) AE (Europe), Germany, (3) INSERM-U628, Claude Bernard University, Lyon, France, Lyon, France

Introduction: The posterior hypothalamus is classically recognized for its importance in maintaining waking. Our previous studies suggest that this role is mediated, in part, by the widespread projecting histamine(HA)-neurons. The identification of orexin cells adjacent to HA-neurons and their diffuse projections strengthens the idea that multiple neuronal populations are involved in the hypothalamic control of sleep-wake states. This study was designed to determine the respective role of HA and orexin neurons in wake regulation using histidine-decarboxylase(HDC, HA-synthesizing enzyme) and orexin knockout(KO) mice.
Methods: Male adult HDC-(n=9) and orexin-KO mice(n=15) and their wild-type(WT) genotypes were simultaneously investigated using multidisciplinary approaches: polygraphic sleep-wake recording, analysis of cortical EEG power spectral density, HDC and orexin gene

identification with PCR, HA and orexin immunohistochemistry, pharmacological administration and behavioral tests.
Results: HDC-KO and orexin-KO mice share some phenotypes, such as mild obesity and an increase in paradoxical sleep(PS), but are distinct in terms of the following phenotypes: 1) The PS increase in HDC-KO mice was seen during the light-period, whereas that in orexin-KO mice occurred during darkness; 2) Only HDC-KO mice showed a deficit of waking around lights-off, accompanied by an impaired EEG; 2) Both WT and orexin-KO mice were able to respond to a new environment with increased waking, whereas HDC-KO mice fell asleep and showed signs of somnolence faced with various behavioral stimuli; 3) orexin-KO, but not their littermate WT or HDC-KO mice, displayed signs of narcolepsy and failed to respond to a motor challenge (wheel test) with increased waking and locomotion.
Conclusion: We hypothesized that HA and orexin neurons might exert a synergistic/complementary control during waking: the amine being mainly responsible for its qualitative aspects, cortical EEG arousal and cognitive activities; whereas the neuropeptide more involved in its behavioral aspects (e.g., locomotion, food intake) and emotional reactions.
Support (optional): Supported by INSERM-U628 and European contract (No QLRT-2001-00826)

0073

TOPOGRAPHY OF SLEEP SPINDLES MAPPED WITH 256-CHANNEL ELECTROENCEPHALOGRAPHY

Torassa T,[1] Quiring J,[2] Luu P,[3] Tucker D[3]
(1) Electrical Geodesics, Inc., Eugene, OR, USA, (2) Electrical Geodesics, Inc, OR, USA, (3) Electrical Geodesics, Inc., OR, USA

Introduction: Sleep spindles appear to represent an oscillation circuit between the thalamocortical (TC) cells and thalamic reticular nucleus (TRN) cells that, in conjunction, modulate the activity of the TC cells during the sleep cycle. The role of the cortex is a key issue in understanding this circuitry. Important clues to this path may be the vertex midline distribution of sleep spindles, and the frequent emergence of spindles from sharp waves and K-complexes that also show a vertex midline distribution. We present topographical mapping of sleep spindles in normal subjects with the goal of understanding this important transition process in normal and pathological states of brain activity.
Methods: 256-channel EEG was recorded for a sample of 10 adults while sleeping. The data were digitally filtered 11-16 Hz bandpass. Sleep spindles were identified by the following criteria: a) the presence of 10-14 Hz activity within a 1 second interval; and b) within this time period, 4 peaks must have an amplitude of 20mv or more. These spindles were then mapped into topographical 2D maps.
Results: We found that there was variability within spindles reflecting sequential activation of multiple cortical regions. We also found that between subjects there was a wide variety of spindle topographies. Source estimation of individual spindles revealed predominant limbic engagement, with posterior cingulate common in most subjects.
Conclusion: We believe that sleep spindles may not always be initiated in the same way. There may be a reciprocal relationship between the connections of the cortex and the thalamus that may play a role in the spindle topographical distributions.
Support (optional): none

0074

SLOW WAVE ACTIVITY IS LOWER IN YOUNG HEALTHY AFRICAN AMERICANS AS COMPARED TO CAUCASIANS

Tasali E,[1] Leproult R,[2] Spiegel K,[3] Holmback U,[2] Whitmore H,[2] Van Cauter E[2]
(1) The University of Chicago, Chicago, IL, USA, (2) University of Chicago, Chicago, IL, USA, (3) Universite Libre de Bruxelles, Bruxelles, Belgium

Introduction: Recent epidemiologic evidence suggests race and gender disparities in the duration and quality of sleep as assessed by actigraphy. Slow wave activity (SWA) is a stable trait dependent marker of the intensity of NREM sleep. Our previous findings have shown that experimental suppression of SWA without change in total sleep time is associated with decreased insulin sensitivity in healthy young adults. In the present study, we examined the ethnic differences in SWA in young healthy African Americans, a population at high risk for insulin resistance, as compared to Caucasians individually matched for age, gender and body mass index (BMI).
Methods: Overnight polysomnographic data were obtained from 12 African Americans (mean ± SEM: age= 27.1±1.3 years; BMI=22.6 ±0.7 kg/m2, 4 women) and 12 Caucasians (age=27.2±1.3 years; BMI=22.5±0.6 kg/m2, 4 women). Subjects had no sleep complaints. Sleep disorders were ruled out by screening polysomnography. Spectral analysis was performed on the central EEG lead (C4-A1) by fast Fourier transform in the delta frequency (0.5-4.0 Hz) band. SWA levels were derived from the mean NREM (stages 2, 3 and 4) absolute delta power during the first 6 hours of the recording after sleep onset.
Results: African Americans had markedly lower SWA as compared to Caucasians (803 ± 92 μV2 vs 1201 ± 127 μV2; p = 0.03).
Conclusion: The current findings provide evidence for ethnic differences in the intensity of NREM sleep. Lower levels of SWA in African Americans could be related to their reported poor sleep quality and higher risk for insulin resistance.

0075

PARADOXICAL SLEEP AND RESTORATIVE FUNCTION OF CEREBRAL TISSUE

Kovalzon V,[1] Evdokimenko A,[2] Rusakova I,[3] Rutskova E,[4] Dorokhov V,[3] Loginov V,[5] Fesenko G[3]
(1) Severtsov Institute of Ecology/Evolution, Russian Academy of Sciences, Moscow, Russia, (2) Faculty of Fundamental Medicine, Moscow Lomonosov State University, Moscow, Russia, (3) Russia, (4) Institute of Higher Nervous Activity/Neurophysiology, Academy of Sciences, Russia, (5) Lab of Psychophysiology, Modern Humanitarian Academy, Moscow, Russia

Introduction: The effect of several stress influences which induce enlarged and unspecific damage of cerebral tissue, on subsequent sleep have been studied in rats preliminary implanted (under chloral-hydrate anaesthesia, 0.4 g/kg i.p.) with conventional electrodes for polysomnography and maintained in separate chambers under artificial 12:12 LD condition.
Methods: Four different experimental models were used, one chronic and 3 acute: (i) general rostral cerebral ischemia induced by a permanent occlusion of one common carotid artery; (ii) hypoxic hypoxy; (iii) hypoglycemia; (iv) “penicillinium” epilepsy. 24 hr continuous polysomnographic recording followed carotid occlusion and lasted up to 45th day. Acute influences were followed by only partial polygraphic observation of sleep through a 3-hr daily “window”, 09-12AM.
Results: In all the models significant increase (up to 20% of the

recording time against 9% of baseline level) of PS percentage during the "light" period was found which reached its maximum within 1-5 days since the stress influence. The following dynamics have been found to be dependent upon the character of stimuli used. In a case of acute influences, PS percentage returned the baseline level within 5-6 days. In a case of chronic influence, the PS percentage returned to baseline level in 40-45 days since the day of occlusion.
Conclusion: Sharp increase of PS percentage following stress stimuli which induce cerebral tissue damage could be regarded in favor of the hypothesis of the increase in neural tissue restitution processes during PS periods.
Support (optional): The study is supported by the Program of the Presidium of Russian Academy of Sciences "Fundamental Sciences – to the Medicine", and the Russian Humanitarian Science Foundation (04-06-00242a).

0076

TIME COURSE OF INDUCIBLE NITRIC OXIDE SYNTHASE EXPRESSION DURING SLEEP DEPRIVATION IN THE CHOLINERGIC BASAL FOREBRAIN AND CORTEX

Kalinchuk A,[1] Porkka-Heiskanen T,[2] McCarley R,[3] Basheer R[1]
(1) Harvard University, West Roxbury, MA, USA, (2) University of Helsinki, Helsinki, Finland, (3) Harvard University, Brockton, MA, USA

Introduction: Short-term sleep deprivation (SD) (3h in rodents) has been shown to result in selective increases in extracellular adenosine (AD) and, more recently, in inducible nitric oxide (iNOS)-mediated nitric oxide (NO) production in the cholinergic basal forebrain (CBF) (Kalinchuk *et al.*, Eur J Neurosci, 2006). Both AD and NO increases in CBF increase homeostatic sleep response. In the CBF, inhibition of iNOS prevents SD-induced increase in AD suggesting iNOS-mediated NO production precedes AD increase (Kalinchuk *et al.*, J Neurochem, 2006). SD-induced increase in AD was also observed in cortex (Porkka-Heiskanen *et al.*, Neurosci, 2000), albeit to a lesser extent suggesting iNOS-mediated NO production during SD might be triggered also in cortical areas during longer-term SD. In order to investigate the time course of iNOS induction in the CBF and cortical areas that receive projections from CBF we examined iNOS mRNA and protein changes following SD of varying durations.
Methods: Male rats (n=4) were sleep-deprived for 3h, 6h and 12h and sacrificed with their time-matching undisturbed controls. Brain tissue samples were collected from the CBF and the target cortices (prefrontal and frontal). Changes in iNOS mRNA and iNOS protein were measured by real time polymerase chain reaction (RT-PCR) and Western blot, respectively.
Results: RT-PCR revealed increase in iNOS mRNA level after 3h but not after 6h SD in the CBF and after 6h SD in cortex. iNOS protein was significantly increased in the CBF after 3h SD and stabilized at the same level after 6h and 12h SD. Similar to mRNA in the cortex iNOS protein was increased only after 6h and 12h SD but not after 3h.
Conclusion: We conclude that SD-induced iNOS-mediated NO production follows a specific temporal and spatial pattern with the CBF being the first to respond to SD followed by changes in its projection cortical areas.
Support (optional): VA Medical Research Award; NIMH R37 MH039683; Academy of Finland.

0077

ALTERED SLEEP PATTERN IN A MOUSE MODEL OF GEFS+

Papale L,[1] Martin M,[2] Andersen M,[1] Perry J,[3] Keating G,[4] Decker M,[4] Tufik S,[1] Escayg A[4]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Emory University, GA, USA, (3) Univ Fed Sao Paulo, Sao Paulo, Brazil, (4) Emory University, Atlanta, GA, USA

Introduction: SCN1A is one of the four voltage-gated sodium channels that are primarily expressed in the central nervous system. Mutations in SCN1A underlie several subtypes of human epilepsy including Generalized Epilepsy with Febrile Seizures Plus (GEFS+) and Severe Myoclonic Epilepsy of Infancy (SMEI). To examine the functional consequences of SCN1A dysfunction, we generated a mouse model of GEFS+ by introducing an identified human SCN1A mutation into the orthologous mouse gene. Since intermittent hypoxia (IH), such as that encountered with repetitive apnea in premature infants is associated with neonatal seizures, we examined the GEFS+ mice for alterations in seizure activity and sleep architecture following neonatal hypoxia and sleep deprivation.
Methods: GEFS+ mice and wildtype littermates were subjected to IH (20 seconds of 10% O2 and 40 seconds of compressed air for 6 hours/day) from postnatal day 7 to postnatal day 12. After a 24-hour baseline sleep recording, the adult mice were subjected to 6 hours of sleep deprivation by gentle handling followed by 24 hours of additional sleep recording.
Results: A higher incidence of visible spontaneous seizures and reduced REM sleep was observed in adult GEFS+ mice following neonatal IH. Reduced REM sleep was also observed after sleep deprivation.
Conclusion: These results suggest that the effects of hypoxia on seizure activity and sleep architecture may be exacerbated in the presence of a preexisting sodium channel mutation. These results may also shed light on the sleep fragmentation observed in patients with epilepsy.
Support (optional): Papale (FAPESP), Decker (HL72722), Tufik (AFIP, CEPID, CNPq), Escayg (NS046484).

0078

ANATOMICAL STRESS MEASURES ARE NOT CORRELATED WITH REDUCTIONS IN SIZE OF LOCUS COERULEUS NEURONS FOUND AFTER REM SLEEP DEPRIVATION

Shaffery J,[1] Allard J,[2] Manaye K,[3] Roffwarg H[1]
(1) University of Mississippi Medical Center, Jackson, MS, USA, (2) National Institutes of Health (NIH), MD, USA, (3) Howard University College of Medicine, Washington, DC, USA

Introduction: Although NE production in cortex is initially increased by pedestal-method REM sleep deprivation (REMSD), microdialysis studies have shown that NE production decreases after a few days. In this study, using the automated, gentle cage-shaking system that selectively and efficiently enforces REMSD, we determined REMSD effects on number of locus coeruleus (LC) cells expressing tyrosine hydroxyalse immunoreactivity (TH-ir), TH being the rate-limiting enzyme for NE production. In addition, we assessed several anatomical indices of stress, including thymus, adrenal, spleen, and whole-body weight.
Methods: Nine kittens (postnatal days, PN42-49) from two litters were randomly assigned to either control or REMSD conditions. Another group (n=9) remained with the mother (Normal). The automated system selectively and substantially reduced REMS continuously for seven days. Control animals experienced an equal number of shakes, but outside of REMS, primarily during waking. After seven days, animals were sacrificed and the LC was serially sectioned throughout its

entirety. The fractionator stereological method was used to estimate number of LC cells in every kitten. The thymus, adrenals and spleen were dissected, stored in formalin and weighed later.
Results: The number of TH-ir cells in LC differed across groups ($F(2,10) = 5.1$, $p = 0.028$). Though TH-ir cell estimates were highest numerically in the control group, they were significantly greater than only the REMSD kittens (Bonferroni t-test, $p<0.05$). Body weight, thymus and spleen were different between groups (One-Way ANOVA´s, $p<0.05$). Though they did not differ from each other, both control and REMSD kittens showed greater stress levels than normals on these measures ($p<0.05$).
Conclusion: The TH-ir cell number difference between control and REMSD is not accounted for by a corresponding change in any of the stress indices. The relatively larger number of TH-ir cells found in the controls nevertheless may have resulted from their greater number of shakings in the Wake state.
Support (optional): Supported by: NS31720 and NS39407-03S1.

0079

LEARNING TO REACH LOCALLY INCREASES SLOW WAVE ACTIVITY (SWA) IN RAT MOTOR CORTEX

Hanlon E,[1] Faraguna U,[2] Vyazovskiy V,[1] Tononi G,[3] Cirelli C[1]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) Scuola Superiore Sant'Anna, Madison, WI, USA, (3) University of Wisconsin, Madison, WI, USA

Introduction: We hypothesized that SWA homeostasis is linked to synaptic potentiation associated with learning during wakefulness. In humans, we found that a motor learning task engaging a specific cortical region leads to a local increase in sleep SWA that is correlated with improved performance post-sleep. Here we tested how motor learning affects SWA in rats. We used a pellet reaching task known to induce synaptic potentiation in the trained motor cortex but not in other cortical areas.
Methods: Male Long Evans rats were implanted for polysomnographic recordings (local field potentials, frontal, parietal, occipital) and kept in a 12:12 light:dark cycle (lights on at 10am). Continuous video-recordings were performed to confirm behavioral states. Visual scoring of sleep stages and EEG power spectral analysis was based on 4-sec epochs. After surgery and habituation to sucrose pellets (baseline, B), animals were trained (10-11am) to reach with their preferred paw through a small hole in the front of the reaching chamber to retrieve a single sucrose pellet. After training (T), rats were allowed uninterrupted sleep, and were retested on subsequent days (PT1-PT2).
Results: All rats (n=11) learned the task during the first training day, and showed smaller (PT1) or no further improvement (PT2) in performance afterwards. SWA increased (T vs B) in motor but not in parietal cortex. The SWA increase was maximal in the low range (0.75-2.5Hz), peaked in the first hour of sleep, returned to baseline after ~5h, and was smaller or not present in PT1-PT2. Some rats (5/11) showed a post-sleep enhancement in performance (at the beginning of PT1 they were better than at the end of T), which was associated with an SWA asymmetry (trained>untrained motor cortex). The other rats showed no post-sleep enhancement and no SWA asymmetry.
Conclusion: As in humans, motor learning in rats produced a local (motor but not parietal) and reversible increase in SWA. Moreover, a post-sleep enhancement in performance was associated with SWA asymmetry between trained and untrained motor cortex. Finally, SWA returned to baseline when rats performed the task without further improvement, suggesting that plasticity, rather than use, drives SWA changes.

0080

EFFECTS OF INTRACORTICAL MICROINJECTIONS OF NICOTINIC AGONISTS ON SLEEP REGULATION

Faraguna U,[1] Vyazovskiy V,[2] Douglas C,[3] Tononi G,[4] Cirelli C[2]
(1) 1-Scuola Superiore Sant'Anna 2-University of Wisconsin, Madison, Madison, WI, USA, (2) University of Wisconsin-Madison, Madison, WI, USA, (3) University of Wisconsin-Madison, WI, USA, (4) University of Wisconsin, Madison, WI, USA

Introduction: The systemic administration of nicotine affects sleep in both humans and animals, most consistently by increasing sleep latency and decreasing NREM and REM duration. Nicotine also affects spontaneous and evoked cortical activity, but its direct effects on sleep regulation in the cerebral cortex are unclear. Here we studied sleep and its homeostatic regulation after microinjections of several nicotinic agonists in the rat frontal cortex.
Methods: Male WKY rats (7-8 week old) were implanted chronically for polysomnographic recordings [local field potentials (LFPs, frontal and parietal) and the EMG], and kept in a 12:12 light:dark cycle (lights on at 10am). Continuous video-recordings were performed to confirm behavioral states. Visual scoring of sleep stages and EEG power spectral analysis was based on 4-sec epochs. Intracortical microinjections in the frontal cortex (0.5ul/min, up to 5ul) or intraperitoneal (ip) injections of nicotinic agents or vehicle were performed between 10.30 and 11.30 am (nicotine, n=5; epibatidine, n=10; A85380, n=3; UB-165, n=2; ABT-418, n=2; epiboxidine, n=2).
Results: Local cortical microinjections of nicotine, A85380, and epiboxidine produced an immediate and dose-dependent (up to 7 hours) increase in polysomnographically and behaviorally-defined waking, while injections of ABT-418 and UB-165 had no effect. The pharmacologically-induced waking was associated with an EEG pattern undistinguishable from that of spontaneous waking, and was followed by an increase in sleep duration, no signs of sleep fragmentation, and reduced or no immediate SWA rebound. Prolonged wakefulness (up to 9 hours) was also observed after both local and ip injections of epibatidine (10mM, n=6), which however also caused an immediate short-lasting (~20sec) generalized seizure, and was followed by fragmented sleep (with shorter sleep episodes and more brief awakenings).
Conclusion: Intracortical administration of nicotinic agents suppresses sleep and blunts the immediate SWA rebound. The future use of highly selective agents may clarify whether these effects are mediated by alpha4beta2 and/or alpha7 nicotinic receptors.
Support (optional): Supported by NIH Director´s Pioneer Award to GT.

0081

CONSEQUENCES OF NEONATAL REM SLEEP DEPRIVATION

Morrissey M,[1] Yamada K,[2] Gru A,[3] De Erausquin G,[2] Duntley S[4]
(1) Washington University, Saint Louis Missouri, Saint Louis, MO, USA, (2) Washington University in St. Louis, St. Louis, MO, USA, (3) Washington University, MO, USA, (4) Washington University in St. Louis, Saint Louis, MO, USA

Introduction: Rapid eye movement (REM) sleep deprivation is associated with neurocognitive impairment, probably due to the importance of REMS in memory and learning consolidation. In infants and young rodents Active Sleep (AS, similar to REMS) comprises up to 60% of sleep. The consequences of neonatal AS deprivation are not fully understood. Our studies demonstrate that clomipramine and clonidine induced AS deprivation between P10-14 increases hippocampal dentate granule cell neurogenesis and is accompanied by reduced brain mass, when assessed at P35. Our central hypothesis is that there is a critical time window in the neonatal period when synaptic

circuitry is established between brain regions regulating AS and brain regions responsible for learning, and that AS suppression by illness or drug exposure during this critical time window results in synaptic dysfunction.
Methods: Animals were injected twice daily from P10 – P15 with clonidine or clomipramine (with respective saline controls). All animals received BrdU with the injections. The animals were sacrificed at P35 for histological assessment of BrdU labeled cells in the dentate gyrus of the hippocampus.
Results: Clomipramine (11 exp, 10 ctrl) produced an increase in BrdU positive cells ($t(1,19) = 4.568$, $p < .001$) when measured at P35. In addition, clonidine (5 exp, 4 ctrl) had a similar effect ($t(1,7) = -3.599$, $p < .009$).
Conclusion: Pharmacological AS deprivation produces long-lasting effects on the hippocampus. These findings suggest AS may play a critical role in CNS development, and that disruption of AS early in development may have long lasting consequences on the CNS.

0082

CORTICAL ACETYLCHOLINE RELEASE IS LATERALIZED DURING ASYMMETRICAL SLOW WAVE SLEEP IN NORTHERN FUR SEALS

Lapierre J,[1] Kosenko P,[2] Lyamin O,[3] Siegel J,[1] Mukhametov L[2]
(1) University of California, Los Angeles, North Hills, CA, USA, (2) Utrish Dolphinarium Ltd., Moscow, Russia, (3) North Hills, CA, USA

Introduction: Northern fur seals are unique in that they exhibit both unihemispheric slow wave sleep (USWS), as seen in cetaceans, and bilateral slow wave sleep (BSWS) as seen in all terrestrial mammals. Sleep is predominately bilateral on land but asymmetrical in water. This phenomenon provides us with the opportunity to determine which of the many physiological changes seen bilaterally in terrestrial mammals are linked to the EEG defined sleep state, and which may be related to the behavioral quiescence and sensory input reduction that typically accompanies sleep. The aim of this study was to examine bilaterally the pattern of cortical acetylcholine (ACh) release across the sleep-wake cycle in northern fur seals.
Methods: Cortical ACh release was measured bilaterally in four male northern fur seals (Callorhinus ursinus) (20-25 kg, 2-3 yrs) using in vivo microdialysis, in combination with, polygraph recordings of electroencephalogram (EEG), electrooculogram (EOG), and neck electromyogram (EMG). ACh levels were determined using high-performance liquid chromatography coupled with electrochemical detection.
Results: Consistent with previous findings for terrestrial mammals, ACh release was state-dependent. ACh levels increased by approximately 200% during quite wakefulness (QW) and by 275% during active wakefulness (AW) when compared to BSWS as baseline. During rapid eye movement (REM) sleep, ACh release was similar to that observed during QW. During these states, ACh was synchronously released from both hemispheres ($R2 = 0.71$). However, during episodes of interhemispheric EEG asymmetry (i.e. asymmetrical slow wave sleep (ASWS)), ACh release was lateralized with maximal release in the hemisphere displaying low voltage activity. Furthermore, slow wave EEG spectral power (1-4 Hz) and cortical ACh release in the same hemisphere were negatively correlated.
Conclusion: Cortical acetylcholine release is lateralized during asymmetrical slow wave sleep in northern fur seals.
Support (optional): DARPA, NSF, and Utrish Dolphinarium Ltd.

0083

SELECTIVE SEROTONIN REUPTAKE INHIBITORS REDUCE EYE MOVEMENTS BUT AUTONOMIC REM SLEEP REMAINS INTACT

Bar A,[1] Suraiya S,[2] Pillar G[2]
(1) Technion – Israel Institute of Technology, Haifa, Israel, (2) Technion- Israel Institute of Technology, Haifa, Israel

Introduction: The standard Polysomnographic definition of Rapid Eye Movements (REM) sleep is based predominantly on EEG, EOG and EMG signals. Recently, detection of REM sleep based on changes in the autonomic nervous system activation has been reported. Selective serotonin reuptake inhibitors (SSRIs) are known to suppress REM sleep when scored in standard Polysomnography, whereas, their effect on the "Autonomic REM sleep" is unknown. We hypothesized that the "Autonomic REM sleep" compared to "polysomnographic REM" is affected differently by SSRIs.
Methods: We prospectively recruited adult patients who were chronically treated with SSRIs. The control group patients were chosen retrospectively from the sleep lab database, after case-to-case matching of gender, age and BMI. None of the controls was on SSRIs or CNS active medications. All patients had a standard PSG with a simultaneous Watch_PAT100 (WP100) recording. The WP100 detects REM sleep via the Peripheral Arterial Tone (PAT) signal, which reflects changes in the autonomic nervous system activation. The WP studies were automatically analyzed by the device's software. The PSG studies were scores for sleep stages according to the R&K criteria by a scorer who was blinded to the WP results.
Results: Eleven patients were recruited so far (10 males), aged 53±13 years, BMI=30.6±6.2 kg/m2. The control group consists of 11 subjects (10 males), aged 54±12 years, BMI=31.0±5.9 kg/m2. PSG-REM sleep was significantly shorter than the WP100-REM sleep in the study group (12.4±5.1% versus 17.8±8.3%, respectively, P<0.05, unpaired t-test, 1-tail), but not in the control group (17.6±4.0% versus 16.1±5.1%, respectively, non significant).
Conclusion: We concluded that the effect of SSRIs on REM sleep is differential. The "Autonomic REM sleep" is either unaffected or affected to a lesser extent than the classical polysomnographic REM features (predominantly eye movements).

0084

BNDF AFFECTS THE HOMEOSTATIC REGULATION OF SLEEP

Faraguna U,[1] Vyazovskiy V,[2] Douglas C,[2] Nelson A,[2] Tononi G,[3] Cirelli C[4]
(1) 1-University of Wisconsin-Madison; 2-Scuola Superiore Sant'Anna, Pisa, Italy, Madison, WI, USA, (2) University of Wisconsin-Madison, WI, USA, (3) University of Wisconsin, Madison, WI, USA, (4) University of Wisconsin-Madison, Madison, WI, USA

Introduction: Slow wave activity (SWA; 0.5-4.0Hz) during NREM sleep increases as a function of waking duration. We have proposed that synaptic potentiation occurring during waking may be responsible for such increase. Consistent with this hypothesis, we recently showed that the cortical expression of BDNF, a molecule known to induce synaptic potentiation, is positively correlated with the amount of exploratory behavior during wakefulness, and with the SWA response during subsequent sleep. Here we tested whether BDNF plays a causal role in sleep homeostasis.
Methods: Male WKY rats (7-8 week old) were implanted chronically for polysomnographic recordings and kept in a 12:12 light:dark cycle (lights on at 10am). Local field potentials (LFPs) were recorded from the left and right frontal and parietal cortical areas using bipolar electrodes. Intracortical microinjections were performed in frontal cortex (0.5 ul/min, up to 5 ul, 10.30-11.30am), and rats were kept awake by gentle handling for 20 min (BDNF, n=7) or 3 hrs (K252a, n=6; anti-BDNF, n=4). Sleep stages were scored visually (4-sec epochs). EEG power spectra (0.25-20 Hz) were computed and normalized relative to baseline to permit interhemispheric comparison.
Results: Cortical unilateral microinjections of BDNF (0.1 ug/ul) induced an increase of SWA in the injected hemisphere relative to the contralateral one. The interhemispheric asymmetry was specific for NREM sleep, and was absent after vehicle injections. By contrast, microinjections of a polyclonal anti-BDNF antibody (0.5 ug/ul) or K252a (40uM), an inhibitor of BDNF TrkB receptors, led to a decrease in SWA in the injected site relative to the contralateral hemisphere. In all cases the induced asymmetry was reversible within 9 hrs after the injection.
Conclusion: SWA on the injected hemisphere was higher, relative to the non-injected hemisphere, after BDNF injections, and lower after injections of BDNF blockers. This suggests that BDNF may be causally involved in sleep homeostasis.
Support (optional): Supported by NIH Director´s Pioneer Award to GT.

0085

CLINICAL CORRELATES OF INCREASED DELTA SLEEP

Phillips N, Watson N, Kapur V
University of Washington, Seattle, WA, USA

Introduction: Stage 3-4 (delta) sleep is an anabolic state, marked by increases in growth hormone and rejuvenation of immune, nervous, muscular, and skeletal systems. Studies have emphasized its importance for cognitive processing and memory consolidation. To our knowledge detailed patient characteristics associated with increased delta sleep have not been described. We sought to identify clinical characteristics associated with increased delta sleep in a general sleep clinic population. We hypothesized that patients with neurological disorders, sleep restriction, or hypoventilation would demonstrate increased delta sleep. Medication effects were also hypothesized.
Methods: We performed a case-control study of increased delta sleep, defined as > 25% of total sleep time on polysomnography, in 109 adult sleep clinic patients (56 cases, 53 controls) matched for age, sex, and date of polysomnography. Neurological diagnoses, current medications, subjective pre-study sleep duration, polysomnographic variables, and room air arterial blood gas levels were ascertained via chart review when available. The Wilcoxon rank sum test (Mann-Whitney) was used for continuous variables, and the chi square test was used for categorical variables.
Results: Increased delta sleep was associated with Down syndrome (p=0.01) and elevated carbon dioxide levels (p=0.05), but not neurological disorders as a whole (p=0.13). Cases slept significantly less during the study night compared to controls (median 329 vs. 375 minutes, $p < 0.01$). Other significant differences in polysomnographic variables between cases and controls were observed. Increased delta was associated with zolpidem use on the study night ($p < 0.05$).
Conclusion: In our unselected clinical sample, we found that Down syndrome, elevated carbon dioxide levels, decreased total sleep time during polysomnography, and zolpidem use were associated with increased delta sleep.

0086

IS THERE A RELATIONSHIP BETWEEN THE <1HZ CORTICAL SLOW OSCILLATION AND THE ABILITY TO EVOKE A K-COMPLEX IN THE HUMAN EEG?

Nicholas C,[1] Trinder J,[1] Kim Y,[1] Colrain I[2]
(1) University of Melbourne, Parkville, Victoria, Australia, (2) SRI International, Menlo Park, CA, USA

Introduction: The animal model of the K-complex postulates that the K-complex is the EEG manifestation of the depolarizing phase of the <1Hz cortical slow oscillation. Whilst studies have investigated this in human EEG, none have tested for relationships between the oscillation and evoked K-complex occurrence. Several studies have shown an increase in K-complex activity as Non-REM sleep progresses, possibly due to an increase in the power of the slow oscillation with progression into slow wave sleep. The present study investigates this relationship, using the voltage of low pass filtered EEG as an indicator of the position of the <1Hz oscillation.
Methods: Data were collected from 10 healthy young men on three nights. During one night, approximately 700 tones were presented with a random ISI (20-35sec) during sleep, irrespective of sleep stage. Direct Current EEG was recorded using Neuroscan amplifiers and software. Evoked K-complexes were identified. Ten-second EEG segments prior to tone presentation were low pass filtered at 1.5Hz. Non-REM sleep stage and EEG voltage at time of tone presentation (filter phase shift corrected) were used to predict the occurrence of an evoked K-complex, within each subject, using logistic regression.
Results: Non-REM sleep stage significantly predicted K-complex elicitation in 9 of 10 subjects (Group: *p<.001*). Voltage at time of tone presentation and the voltage by stage interaction only proved to be significant predictors in 3 subjects (Voltage Group: *ns,* Voltage by stage Group: *p<.05*). When stage 2 data were assessed in isolation, voltage only predicted K-complex elicitation in 1 subject (Group: *ns*).
Conclusion: The observation that Non-REM sleep stage predicts the likelihood of evoking a K-complex supports earlier findings that K-complexes were more likely to occur as the cortex progresses through Non-REM sleep. The remaining results, suggest that although the slow oscillation and K-complexes co-vary across sleep, the slow oscillation may not modulate evoked K-complex production in humans.
Support (optional): AA14201

0087

GHRH INCREASES CYTOPLASMIC CALCIUM LEVELS IN CULTURED CORTICAL NEURONS

Liao F,[1] De A,[1] Urza M,[1] Krueger J[2]
(1) Washington State University, Pullman, WA, USA, (2) Pullman, WA, USA

Introduction: Growth hormone releasing hormone (GHRH) promotes non-rapid eye movement sleep (NREMS) in mice, rats, rabbits and humans. Previous studies on GHRH sleep regulatory mechanisms mainly focused on hypothalamic GHRHergic neurons. Recently, we found that the expression of GHRH receptors in the cortex is associated with the usage and the functional state of the cortical columns, thereby suggesting that cortical GHRH may influence EEG delta power during NREMS. The cellular action of GHRH on cortical neurons is poorly understood. Because GHRH enhances Ca2+ in hypothalamic neurons, in the present study, we challenged primary cortical cell cultures with GHRH and measured the cytosolic Ca2+ levels in these neurons.
Methods: Primary cortical neuron cultures were prepared from fetuses of 18-19-day gestation. The neurons were used in experiments 10–13 days after isolation. Neurons were challenged with 100 nM GHRH and cytosolic Ca2+ levels were measured with Fura-2 by ratio imaging (De *et al.*, 2002). Immunocytochemistry was performed to determine the expression of GHRH-receptors.
Results: GHRH-receptor-immunoreactivity was detected in cultured primary cortical cells. When initially exposed to 100 nM GHRH, 8.2% (145 out of 1762) of the neurons in culture increased their Ca2+ levels. When these GHRH-responsive neurons were exposed to a second challenge of GHRH, 30.3% (44 out of 145) of them responded again (results from 36 coverslips from 7 isolations).
Conclusion: Results suggest that GHRH acts on cortical neurons by increasing their cytosolic Ca2+ concentration. This finding will be useful to explore the role of GHRH in the process of cortical column state determination.
Support (optional): This work is supported by funding from NIH Grant # NS27250

0088

THE EFFECT OF AGE ON NASOPHARYNGEAL CROSS-SECTIONAL AREA

Omran A,[1] Mansour K,[1] Badr S,[2] Rowley J[1]
(1) Wayne State University, Detroit, MI, USA, (2) Detroit, MI, USA

Introduction: Sleep-disordered breathing is more prevalent in the elderly. It is unclear if age-related changes in upper airway mechanics are a contributing factor. We hypothesized that nasopharyngeal cross-sectional area (CSA) is smaller in the elderly compared to non-elderly.
Methods: Compared 10 pairs (6 female, 4 male) of subjects matched for BMI. Elderly group had mean age 64.5±5.4 yrs; non-elderly, 28.2±5.9 yrs. A computational fluid dynamics model based upon upper airway flow and time of breathing cycle was used to measure nasopharyngeal CSA. CSA was measured at the beginning of inspiration (CSA-I) and at peak inspiratory flow (CSA-PK) for 10 breaths during wakefulness and NREM sleep for each subject. Paired t-tests were used to compare the groups.
Results: There was no difference in BMI (elderly 26.5±5.4 kg/m^2 v. nonelderly, 26.0±5.0 kg/m^2, p=ns); body surface area (BSA) was larger in the non-elderly group (elderly, 1.74±0.21 m^2 v. nonelderly, 1.85±0.23 m^2, p=0.006). During wakefulness, CSA-I (elderly, 158.4±28.4 mm^2 v. nonelderly, 201.6±51.8 mm^2, p=0.002) and CSA-PK (elderly, 147.7±30.1 mm^2 v. nonelderly, 186.7±49.6 mm^2, p=0.002) were smaller in the elderly. During NREM sleep, CSA-I (elderly, 60.2±10.7 mm^2 v. nonelderly, 96.6±33.9 mm^2, p=0.009) and CSA-PK (elderly, 52.9±11.7 mm^{22} v. nonelderly, 84.5±34.8 mm^2, p=0.012) were smaller in the elderly. After correction for BSA, CSA-I (elderly, 33.0±6.1 mm^2 v. nonelderly, 51.6±22.1 mm^2, p=0.008) and CSA-PK (elderly, 30.6±5.7 mm^2 v. nonelderly, 44.2±21.1 mm^2, p=0.008) during NREM sleep (but not wakefulness) remained significantly smaller in the non-elderly group.
Conclusion: 1. Nasopharyngeal CSA is smaller in elderly subjects compared to non-elderly subjects matched for gender and BMI. 2. After correction for the difference in BSA between groups, inspiratory CSA during NREM sleep, but not wakefulness, is smaller in the elderly. 3. A smaller CSA during inspiration during NREM sleep may predispose the elderly to airway collapse and contribute to increased prevalence of sleep-disordered breathing.
Support (optional): NHLBI/VAMC

0089

SLEEP RESTRICTION REDUCES HEART RATE VARIABILITY

Banks S, Bergamo C, Dinges D
University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: Heart rate variability (HRV) derived from the electrocardiogram (ECG) is a measurement of naturally occurring, beat-to-beat changes in heart rate. A reduction in HRV has been associated with hypertension and is a predictor of mortality after an acute myocardial infarction. This study investigated the effect of five nights of sleep restriction on HRV.
Methods: Preliminary analyses were conducted on N=39 subjects (age range 21-45yr; 23 females) participating in a laboratory-controlled chronic sleep restriction protocol. Subjects underwent 2 nights of baseline sleep (B1 & B2; 10h TIB) followed by 5 nights of sleep restriction (SR5; 4h TIB). ECG was recorded continuously using Rozinn RZ153 Plus Digital Holter monitors (sample rate 180/sec, frequency response 0.05Hz-60Hz). A 30 minute (10:00-10:30h) sample of ECG on B2 and SR5 were used for initial analysis. Subjects were seated at computer consoles completing neurocognitive tasks during ECG recording. ECG data were binned into 5 minute windows and then averaged across the 30 minute sample. Both heart rate (HR) and HRV were calculated.
Results: There was a statistically significant decrease in HRV after 5 nights of sleep restriction (p=0.05) while HR was increased (p=0.04).
Conclusion: These preliminary data suggest that 5 nights of chronic sleep restriction to 4h TIB has a negative effect on cardiac activity. If this finding is sustained by a larger cohort it may support a path by which short sleep duration may be associated with an elevated risk of cardiovascular disease and mortality. Increasing sleep TIB after sleep restriction is currently being assessed for the recuperative value of recovery sleep relative to HRV.
Support (optional): Supported by NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute, and NIH grant NR 009281 and RR00040.

0090

EFFECT OF NEUROMUSCULAR ACTIVITY ON UPPER AIRWAY MECHANICS DURING SLEEP.

Sankri-Tarbichi A,[1] Rowley J,[1] Badr S[2]
(1) Wayne State University, Detroit, MI, USA, (2) Detroit, MI, USA

Introduction: Upper airway compliance is related to both neuromuscular activity and non-neuromuscular factors. Mechanical ventilation suppresses central ventilatory motor output, leading to central apnea. Reduced ventilatory motor output results in increased upper airway (UA) resistance in susceptible subjects while central apnea is associated with UA narrowing. However, the effect of suppressed neuromuscular activity on UA caliber during sleep has not been studied. Our objective was to determine the effect of reduced ventilatory motor output on pharyngeal cross-sectional area and compliance using fiberoptic naso-pharyngoscopy.
Methods: We studied 6 subjects; 2 normal subjects, 2 snorers and 2 obstructive sleep apnea patients (AHI>30 events/hr). The retropalatal airway was visualized using a fiberoptic scope. The airflow (V) was measured using a pneumotachometer and the pharyngeal pressure (Pph) was measured using a pressure catheter positioned at the palatal rim. During NREM sleep we induced central apnea upon termination of 3 minutes of nasal mechanical ventilation (MV). Central apnea confirmed the inhibition of ventilatory motor output. We measured upper airway compliance (CUA) and cross sectional area at the beginning of inspiration (CSAI) on breaths 1-3 of MV (active breaths) and the last three breaths before the central apnea (passive breaths). CUA defined as the slope of the regression line of CSA v. Pph for each breath analyzed.
Results: CUA of the passive breaths increased significantly compared to the active breaths (4.9 ±4 v. 2.4 ± 2.3 mm2/cmH2O, respectively, $p < 0.05$). CSAI did not change significantly between passive and active breaths (73.9 ±46.8 v. 61.4 ±25 mm2, respectively, p = ns).
Conclusion: Suppression of upper airway neuromuscular activity is associated with increased pharyngeal compliance but no change is found in retro-palatal caliber. Upper airway non-neuromuscular properties may be an important determinant of pharyngeal compliance during NREM sleep.
Support (optional): NHLBI and Veterans Affairs

0091

SLEEP ARCHITECTURE DURING PH ESOPHAGEAL MONITORING IN ADULTS WITH AND WITHOUT SUBJECTIVE SLEEP COMPLAINTS

Robert J,[1] Goodrich S,[1] Fernstrom P,[2] Hasselgren G,[2] Orr W[3]
(1) Lynn Health Science Institute, Oklahoma City, OK, USA, (2) AstraZeneca, Molndal, Sweden, (3) Oklahoma City, OK, USA

Introduction: The aim of the study was to examine sleep architecture in adults who reported sleep disturbances compared to controls. Two groups of healthy adults participated in the study, (1) adults with subjective sleep complaints and (2) adults without subjective sleep complaints served as the control group.
Methods: 52 individuals with self-reported sleep disturbance and 36 controls without symptoms of sleep disorders or heartburn were studied for two nights via polysomnographic evaluations that included distal esophageal pH recordings. Subjects kept a sleep log for two weeks and the sleep disturbance group had to have at least 6 nights of reported unrefreshed sleep to qualify, while the control group had to have at least 10 nights of satisfactory sleep. Two polysomnographic recordings were separated by at least two weeks for each participant.
Results: For both groups there was a significant ($p<.05$) improvement in several sleep measures the second night of sleep, compared to the first night. Adults took a significantly ($p<.05$) longer time to fall asleep, spent more time awake ($p<.05$), and had reduced sleep efficiency ($p<.05$) on the first night compared to the second night. There were no significant group by night interactions. The disturbed sleep group had significantly less ($p<.05$) slow-wave sleep and slept significantly ($p<.05$) less compared to controls on both nights.
Conclusion: (1) Even with nasal intubation there is a significant first night effect in patients with and without sleep disturbances. (2) In studies requiring nasal intubation an adaptation night is highly recommended and effective in allowing more normal sleep on subsequent nights.
Support (optional): This study was supported by a grant from AstraZeneca.

0092

CIRCADIAN VERSUS SLEEP INFLUENCES ON CARDIOVASCULAR ACTIVITY

Trinder J,[1] Kleiman J,[2] Nicholas C,[2] Carrington M,[2] Allen N,[2] Murray G[3]
(1) University of Melbourne, Parkville, Victoria, Australia, (2) University of Melbourne, Victoria, Australia, (3) Swinburne University of Technology, Victoria, Australia

Introduction: In humans, Heart Rate (HR) and Blood Pressure (BP) show a 24 hour variation with higher activity during daytime wakefulness. Constant routine studies have indicated that the diurnal variation in HR, but not BP, is strongly influenced by the circadian

system. We report the effects of the circadian system on HR and BP using a forced desynchrony protocol.
Methods: Fifteen young healthy subjects (8F, 7M) were administered a 28 hr, forced desynchrony protocol for 8, 24 hr days. Subjects were confined to the laboratory for the duration of the study, performed only sedentary activities, were kept blind to time cues, illumination was kept below 20 lux, and temperature maintained at 22-24oC. Rectal temperature was measured to identify circadian rhythmicity. At 2 hourly intervals during wakefulness 30 minute recordings of a range of physiological variables were collected while subjects lay supine on a bed. The ECG and portapres continuous BP recordings were analysed over the last 5 minutes of each 30 minutes. The 24 hour (circadian) oscillation, synchronised to the body temperature minimum, was tested for significance and compared to the 19 hours of continuous wakefulness.
Results: HR and systolic and diastolic BP all showed significant 24 hour variations (F values all p<.05 or less) with the amplitudes of the oscillations being 5 bpm and 9 and 5 mmHg respectively. Peak levels occurred between 180o and 240o from the circadian minimum. Continuous wakefulness also significantly affected HR and Diastolic BP (F values all p<.05 or less). Peak values occurred immediately after awakening and reached the minimum values towards the end of wakefulness. Systolic BP was not significantly affected by continuous wakefulness (p>.05).
Conclusion: BP revealed a circadian oscillation under forced desynchrony conditions, perhaps reflecting the greater sensitivity of this method to circadian influence.
Support (optional): Australian Research Council. Grant # DP0343619

0093

SLEEP-RELATED CLUSTERED VENTRICULAR ARRHYTHMIA IN THE SLEEP HEART HEALTH STUDY

Chang J, Mietus J, Goldberger A, Thomas R
Beth Israel Deaconess Medical Center, Boston, MA, USA

Introduction: Sleep has the potential to both suppress and trigger cardiac tachyarrhythmias. The former effect is typical of slow wave sleep, while both REM sleep and sleep apnea can trigger ventricular and supraventricular tachyarrhythmias such as atrial fibrillation.
Methods: The raw polysomnographic data from the Sleep Heart Health Study were analyzed. The ECG signal was extracted and whole night RR intervals plotted. Each plot was visually scanned, and 32 studies were selected where the RR intervals showed clusters of marked abrupt acceleration and deceleration. Review of the raw data showed that these were clusters of ventricular ectopic beats, occurring nearly continuously throughout the night.
Results: The clusters included ventricular bigeminy and trigeminy. As the recordings were restricted to the sleep period, the occurrence during daytime wake is not known. However, sleep seemed to amplify the abnormality. The clusters were not stage specific (REM vs. non-REM sleep), not always triggered by sleep apnea, and not related to oxygen desaturation. The timing of the clusters varied from every 60-120 seconds to as long as every 4-5 minutes. The onset of a cluster seemed to be associated with respiratory recovery/arousal when triggered by sleep apnea, but most respiratory events did not trigger arrhythmia. The repetitions of clusters seemed to be a multiple of the respiratory cycle (from four to six times) length. A detailed epoch by epoch analysis of these selected studies has been initiated and will be presented. Correlates of arrhythmia and stable or unstable sleep state using cyclic alternating pattern will be assessed.
Conclusion: Sleep-related tachyarrhythmias have complex relationships to sleep state, sleep stage, and sleep-disordered breathing. Low frequency oscillations of autonomic drive may be coupled to various components of the sleep system at cortical and subcortical levels, and modulate the propensity to tachyarrhythmias during sleep.
Support (optional): National Institutes of Health

0094

SLEEP-WAKE REGULATION IN A GENETIC MODEL OF OBESITY AND DIABETES

Laposky A, Bradley M, Williams D, Bass J, Turek F
Northwestern University, Evanston, IL, USA

Introduction: The physiological and molecular mechanisms that link sleep and metabolism are still largely unknown, and few animal models have been developed to understand this relationship. Leptin, a neuropeptide produced in adipose tissue, is a key hormone in long-term regulation of body weight and appetite. The *db/db* mouse, which harbors a mutation in the gene (db) encoding the leptin receptor, represents a model of leptin resistance accompanied by obesity and diabetes. In this study, we characterized the sleep-wake phenotype in *db/db* mice.
Methods: At 12 weeks of age, male wt (N=6) and *db/db* (N=6) mice were implanted with EEG/EMG electrodes for sleep-wake recordings. Four weeks after surgery, sleep was recorded for a 48-hour baseline period under entrained 12:12 L:D conditions with free access to food and water. Mice were then sleep deprived for 6-hours (beginning of light phase) followed by a 24-hr recovery opportunity. The data below represent genotype differences (independent-sample t-tests) for the baseline condition.
Results: When averaged over the two 24-hr recording periods, *db/db* mice exhibited a significant increase in NREM sleep time (+76 minutes) compared to wt mice (wt, 611±13 vs. *db/db*, 687±29 minutes, p<.05). This was due to an increase in the number of NREM bouts (wt, 220±13 vs. *db/db*, 275±11, p<.01) with no genotype difference in average NREM bout duration (p=.16). In contrast, REM sleep time tended to be reduced in *db/db* mice (wt, 67±4 vs. *db/db*, 52±5, p=.08). Sleep fragmentation, as measured by brief arousals from sleep (wt, 129±7 vs. *db/db*, 163±12, p<.05) and sleep-wake stage shifts (wt, 513±32 vs. *db/db*, 643±30, p<.01) were significantly increased in *db/db* mice. No genotype differences were detected in absolute EEG delta (0.5-4Hz), theta (6-10 Hz) or sigma (11-15 Hz) power.
Conclusion: These data indicate that *db/db* mice have alterations in both sleep amount and sleep consolidation and indicate that leptin may represent an important mechanistic link between sleep regulation and energy metabolism.

0095

SLEEP RESPONSE TO CHRONIC PARTIAL SLEEP RESTRICTION IN OLD RATS

Kim Y, Laposky A, Bergmann B, Turek F
Northwestern University, Evanston, IL, USA

Introduction: In this study, we examined the compensatory sleep response in old rats during and after 5 days of chronic partial sleep restriction.
Methods: Old (20 months) male F344 rats (N=7) underwent 16-h of sleep deprivation (SD) and 8-h of sleep restriction (SR) per day for 5 days, followed by 3 days of sleep recovery (R). Sleep deprivation involved a slowly rotating wheel with sleep being restricted to the first 8-h of the 12-h light phase.
Results: Following the first 16-h block of sleep deprivation, rats showed a homeostatic response during the 8-h recovery opportunity, including increased NREM sleep time (p<.05) and NREM EEG delta (0.5-4.0Hz) power (+16%, p<.05) compared to corresponding baseline levels.

Interestingly, rats failed to exhibit a positive rebound in NREM sleep time and in NREM delta power after 1-2 days of sleep restriction, despite accumulating a sleep debt across days. By the end of 5 days of sleep restriction, rats had lost 25.1 hours of sleep and regained only 0.5 hours relative to their baseline sleep amount. Because rats slept about 6-h of the 8-h daily sleep opportunities, they failed to utilize a large amount of time that was available to them to sleep. In combination, the lack of a positive rebound in NREM delta power and in NREM sleep time indicate that during a period of repeated sleep restriction, a fundamental change occurs in the homeostatic response to sleep loss. Even during a full 3-day sleep recovery opportunity, rats failed to obtain any net gain in sleep time over baseline levels and exhibited an overall negative rebound (i.e. below baseline levels) in NREM delta power.
Conclusion: Following 1 day of 16-h of sleep deprivation, rats achieved the expected positive rebound to acute sleep loss. Surprisingly, this homeostatic response was not maintained across sleep restriction days, indicating a change in the sleep compensatory response to repeated sleep restriction.
Support (optional): This research was supported by NIH (AG-18200 and AG-11412) and in part by the Educational Grant (05-014R) from Takeda Pharmaceuticals North America.

0096

CHARACTERIZATION OF SLEEP IN ZEBRAFISH AND FRAGMENTED SLEEP IN HYPOCRETIN (OREXIN) RECEPTOR MUTANTS

Yokogawa T,[1] Marin W,[2] Faraco J,[2] Pezeron G,[3] Appelbaum L,[1] Rosa F,[3] Mourrain P,[1] Mignot E[1]
(1) Stanford University, Palo Alto, CA, USA, (2) Stanford University, CA, USA, (3) INSERM, France

Introduction: The study of sleep in organisms amenable to molecular studies may shed light on sleep-regulatory molecules or neuronal networks. A sleep-like state has been demonstrated in flies, where identification of mutants is ongoing. Zebrafish is another powerful genetic model that shares similar central nervous system organization with mammals. We, and others, have shown that monoaminergic, hypocretinergic and cholinergic cell groups, principal actors of sleep regulation in mammals, are largely conserved, as are responses to various hypnotics. A sleep-like state has been characterized in zebrafish larvae, but these pioneering studies did not distinguish immobility with or without changes in arousal threshold, and have not studied sleep architecture.
Methods: Fish sleep/wake behavior was studied using videorecording, tracking of trajectories and measurements of activity. Gene expression patterns were determined by whole mount in situ hybridization in 2 day-old embryos.
Results: We first demonstrated the existence of sleep in adult zebrafish, characterized by brief and reversible periods of immobility, increased arousal threshold and place preference. Rest deprivation using gentle electrical stimulation was followed by a rebound, indicating homeostatic regulation. We also identified the sole hypocretin receptor in zebrafish. Fish containing a null mutation in this receptor have short and fragmented sleep in the dark, but not feeding abnormalities. Unlike mammals, this receptor does not co-localize with known major wake-promoting monoaminergic cell groups. Rather, it co-localizes with GABAergic, alpha-2A positive cells in the anterior hypothalamic area and cholinergic cells of the hindbrain.
Conclusion: This is the first sleep mutant ever studied in fish. As in other species, hypocretin mutants have disrupted sleep/wake. Unlike mammals, however, mutant fish do not display sudden episodes of paralysis and fragmented wake but disrupted sleep. Studies in zebrafish, a poikilotherm vertebrate, may help decipher not only the functions of sleep but how sleep regulatory network organization has evolved.
Support (optional): Funding (optional): Funded by HHMI, NIH-23724. PM is a visiting scholar from INSERM, France.

0097

CHANGES IN BODY TEMPERATURE AND LOCOMOTOR ACTIVITY RESPONSES TO INFLUENZA VIRUS INFECTION IN MICE DEFICIENT IN THE DSRNA-BINDING TOLL-LIKE RECEPTOR 3

Paul M,[1] Majde J,[1] Krueger J[2]
(1) Washington State University, Pullman, WA, USA, (2) Pullman, WA, USA

Introduction: Influenza infections in normal mice cause severe hypothermia and immobility and excess non-REM sleep. These symptoms are known to be mediated, in part, by cytokines, but the viral elements that induce these cytokines have not been defined. One possible inducer is double-stranded RNA (dsRNA) made during viral replication. To test the role of dsRNA in influenza symptoms we infected mice deficient in the Toll-like receptor 3 (TLR3 KOs) that binds dsRNA, or their controls.
Methods: Methods: All studies were performed at 29°C. Mature TLR3 KO male mice and their controls were implanted IP with Minimitters to continuously record body temperature (BT) and locomotor activity (LA) without disturbing the animals. After recovery from surgery, mice were monitored for 5 d for background values and then infected intranasally with a sub-lethal dose of X31 human influenza virus at light onset. Symptoms were then monitored for 14 d post infection (PI).
Results: Results: Hypothermia was first apparent at 72 h PI in the TLR3 KO strain and 12 h later in the control strian. In the control mice BT continued to fall (nadir 33.4°C) over the next10 d. Normal diurnal fluctuations from d4-d10 were essentially absent, but began to resume on d11. In KO mice, BT fell below control levels on d3 and remained at the same level (mean 35°C) through d9 with diurnal variations similar to baseline. LA was similarly diminished in the two strains until d3-d6, when the controls started to resume normal LA while TLR3 KOs remained quiescent.
Conclusion: Mice deficient in the dsRNA-binding TLR3 demonstrated less severe hypothermia but more immobility following influenza virus challenge. BT diurnal rhythms were better maintained in KO mice, but not LA rhythms. These results suggest that BT and LA are primarily controlled by different mediators, and that BT mediators responsible for hypothermia are diminished but LA mediators are increased when mice cannot respond to dsRNA.
Support (optional): NIH Grant HD36520

0098

HYPOCRETIN/OREXIN OVEREXPRESSION INDUCES AN INSOMNIA-LIKE PHENOTYPE IN ZEBRAFISH

Prober D, Rihel J, Onah A, Sung R, Schier A
Harvard University, Cambridge, MA, USA

Introduction: Zebrafish are an excellent system for studying the neuronal and genetic control of behavior. Zebrafish larvae display complex behaviors and are optically transparent, allowing the visualization of neuronal circuits in living animals. The ability to rapidly raise large numbers of fish allows for large-scale genetic and pharmacologic screens to uncover novel regulators of developmental and behavioral processes. Thus, zebrafish combine the genetic amenability of invertebrates with behavioral complexity and brain

structures similar to mammals. To determine the utility of zebrafish to study the neurobiology and genetics of sleep, we analyzed Hypocretin neuron development and function in zebrafish larvae.
Methods: We generated transgenic fish in which the Hypocretin promoter regulates expression of green fluorescent protein (GFP) and transgenic fish in which a heat shock promoter regulates Hypocretin expression. Hypocretin overexpression was induced by a 1 hour heat shock at 37°C. To assay sleep-like behavior, individual larvae were placed in each well of a 96-well plate, and the locomotor activity of each larva was recorded for several days using a videotracking system. Arousal thresholds were measured in response to a sudden darkness stimulus.
Results: Our Hypocretin-GFP transgenic fish revealed that the zebrafish larval Hypocretin system is similar to, but simpler than, that of mammals. We found that zebrafish larvae initiate robust circadian rhythms of locomotor activity on the fifth day of development, and that as little as 1 minute of inactivity is associated with increased arousal thresholds. Hypocretin overexpression promoted and consolidated active states, impaired the initiation and maintenance of sleep-like states at night, and decreased arousal thresholds, thus inducing the hallmark phenotypes of insomnia.
Conclusion: Our zebrafish model of Hypocretin overexpression indicates that the ancestral function of Hypocretin is to promote locomotion and inhibit rest and will facilitate the discovery of neural circuits, genes and drugs that regulate Hypocretin function and sleep.

0099

SPECTRAL CHARACTERISTICS SURROUNDING THE SPONTANEOUS K-COMPLEX IN GOOD SLEEPERS

Forget D,[1] Morin C,[2] Bastien C[2]
(1) Laval University, Quebec, Canada, (2) Laval University, Ste-Foy, Quebec, Canada

Introduction: The spontaneous k-complex (KC) is a hallmark of sleep and is visually identifiable in stage 2 sleep. Although traditionally perceived as an arousal response, recent studies rather tend to support a "sleep-protective" role of the KC. The objective of the present study is to investigate the role of the KC in good sleepers by examining and comparing the spectral features of EEG segments prior to and following their presence.
Methods: Ten adults (mean age = 43.4 years; range = 25 to 55 years) without insomnia complaints underwent four consecutive nights of PSG recording. The present data are based on the third recording night. KCs were scored during continuous (> 5 minutes) early stage 2 sleep (2E) and late stage 2 sleep (2L) using R&K criteria. Relative spectral power (delta [1-4 Hz], theta [4-8 Hz], alpha [8-12 Hz], sigma [12-14 Hz], beta [14-35 Hz], gamma [35-60 Hz] and omega [60-125 Hz]) was calculated for each 1 second EEG segments prior to (PRE) and following (POST) all identified KCs.
Results: A total of 1300 KCs were scored and analyzed. Average KC density was 1.00 KC/minute. Repeated measure ANOVAs showed significant changes in relative EEG power from PRE to POST: relative delta power increased (d = 1.72), whereas relative power for theta, alpha, sigma and beta bands decreased following KCs (d = -1.17; range = -0.59 [alpha] to -1.40 [theta]). No differences were found between 2E and 2L.
Conclusion: An increase in relative delta power combined with a decrease in relative power of theta to beta bands suggests that EEG activity is lower following KC than at baseline level prior to KC. Thus, KC could be involved in the lowering of EEG activity, therefore temporarily deepening the sleep state in good sleepers. Changes in EEG relative power surrounding KC were constant throughout the whole night for stage 2 sleep. These results support the "sleep-protective" role hypothesis for the KC.
Support (optional): Research supported by the Canadian Institutes of Health Research (# 49500) to C. H. Bastien.

0100

SLEEP IS INCREASED BY THE DEVELOPMENT OF OBESITY AND REDUCED BY WEIGHT LOSS IN MICE

Guan Z, Fang J, Vgontzas A, Bixler E
Pennsylvania State University, Hershey, PA, USA

Introduction: Obesity is associated with excessive daytime sleepiness (EDS) in humans. Sleep is also increased in diet-induced obesity (DIO) or ob/ob mice. However, it is unclear whether sleep alterations in obesity can be reversed by weight loss. In the current study, we tested this possibility in DIO mice.
Methods: Adult male C57BL/6 mice (n=11, 6 months old) implanted with EEG and EMG electrodes were housed individually on a 12:12h light-dark cycle. A 24-h baseline sleep was recorded after 2 weeks of recovery from surgery and 4 days of adaptation to the recording system. After the baseline recording, 6 mice were fed with high-fat food for 6 weeks to induce obesity and with regular lab chow again for additional 4 weeks to induce weight loss. Control mice (n=5) were fed with regular lab chow during the same period. Sleep was recorded at the ends of 6, 8 and 10 weeks again. Sleep was manually scored in 10-sec segments. Two-way repeated ANOVA was used to compare the differences among different feeding periods.
Results: The development of obesity and weight loss significantly altered non-rapid eye movement sleep [$F(3,15)=8.822$, $p<0.001$]: being higher at 6 weeks compared to the baseline ($p<0.001$), 8 weeks ($p<0.02$) and 10 weeks ($p<0.001$) due to increased sleep during the dark period. Rapid eye movement sleep displayed a similar pattern [$F(3,15)=14.342$, $p<0.001$], higher at 6 weeks compared to the baseline ($p<0.004$), 8 weeks ($p<0.02$) and 10 weeks ($p<0.002$). Sleep at 8 and 10 weeks was not significantly different from the baseline levels. The sleep patterns were not significantly altered in the control mice during the same period.
Conclusion: Our data indicate that the development of obesity and weight loss can induce reversible sleep alterations. Such reversible alterations suggest that the obesity does not cause permanent damage to the sleep regulatory systems.

0101

SHORT PERIOD TACHYPNEA DURING REM SLEEP IN HUMANS AND MICE.

Sato S, Kanbayashi T, Kondo H, Matubuchi N, Shimizu T
Akita university, Akita, Japan

Introduction: Minute ventilation in REM sleep is known to fluctuate as increased, decreased, or unchanged (Krieger J. 1994), and other study reported that there was only a slight increase (9.4%) in respiratory rate (RR) during REM, which was calculated breath-by-breath analysis (Aserinsky E. 1965). An animal study also showed only 11% increase in RR during REM (Friedman *et al.* 2004). However, in the present study, we found that a mouse and a human often exhibits tachypnea during REM, which surprisingly have never been reported hitherto.
Methods: Eleven healthy volunteers and four freely moving mice underwent measurement of RR during sleep by polysonmnography with thermistor airflow sensors and respiratory belt sensors for one night and a non-invasive piezoelectric transducer sensor device (Sato *et al.* 2006; PCT/JP2005/016520) with monitoring by an infrared camera for 3

hours, respectively. All data were stored in a computer and instantaneous RR was calculated from breathing interval detected by peak-detection algorithm of an analysis software.
Results: Instantaneous RRs in the volunteers showed increases by up to 70 breaths/min (2.0-4.6 times the RR in deep sleep) during REM. Similar increase in RR by up to 14 breaths/sec (3.0-5.8 times) was detected in all four mice tested, especially after atonia and shortly before awakening. Tachypnea in the volunteers (>30 breaths/min) and the mice (>10 breaths/sec) continued for 1-21 breaths and 0.4±0.1 sec, respectively. The incidence of tachypnea in each REM event varied by individual differences (14%-100%) and it was 0% in stages 3 and 4.
Conclusion: Although the period is very short, tachypnea over three times the RR in deep sleep suddenly appears during REM sleep both in humans and mice. Further studies are needed to clarify the mechanism of the respiratory control in REM sleep, during which autonomic storm may appears.

0102

SLEEP AND BREATHING DURING A TREK FROM 1400-5000 METRES

Johnson P,[1] Edwards N,[1] Burgess K,[2] Sullivan C[1]
(1) University of Sydney, Sydney, New South Wales, Australia, (2) Manly Hospital, Manly, New South Wales, Australia

Introduction: Sleep in new arrivals to high altitude is characterised by poor subjective sleep quality, frequent awakenings and periodic breathing. The major underlying physiological change is hypobaric-induced hypoxia. Reported changes in sleep architecture include increased Stage 1 non rapid eye movement sleep and decreased slow wave sleep. This research aimed to systematically study changes in sleep architecture associated with incremental changes in altitude, and identify associations with periodic breathing and arterial oxyhemoglobin saturation.
Methods: We studied twenty sea level-dwelling volunteers at sea level and five altitudes from 1400m to 5000m during treks in the Nepal Himalaya. Morning arterial blood gases and overnight portable polysomnography were performed at sea level and the five altitudes; sleep stages were examined for duration and percentage of total sleep.
Results: For the group as a whole, total sleep time (TST) and sleep stage distribution did not change significantly until the highest altitude. While in a majority of the subjects (n = 14 – Non-affected group) sleep architecture did not change markedly even at the highest altitude (5000 m), a sub-group of six subjects (Affected) had a considerable reduction in TST at this altitude. The reduction in TST was reflected in reductions in both NREM sleep (76 ± 24 minutes in affected subjects compared to 295 ± 71 minutes in non-affected subjects, $p<0.001$) and REM sleep (4.8 ± 4.9 minutes in affected subjects compared with 85 ± 26 minutes in the unaffected subject group, $p < 0.001$). There were no differences in sleeping arterial oxyhemoglobin saturation, morning blood gas values, periodic breathing, age or sex between the two groups.
Conclusion: This finding indicates that high altitude has an affect on sleep in some subjects at a threshold altitude; this may be due to a direct effect of cerebral hypoxemia on sleep centres in the brain in susceptible individuals.

0103

CHANGES IN HEART RATE VARIABILITY IN SPONTANEOUSLY HYPERTENSIVE RAT FOLLOWING ACUTE SLEEP DEPRIVATION

Ward C, Hayward L
University of Florida, Gainesville, FL, USA

Introduction: Increasing numbers of adults in the United States have hypertension. Additionally, many adults do not get enough sleep due to sleep disorders or voluntary sleep restriction / deprivation. The ramifications of sleep loss in people with high blood pressure are not well understood. In the present study, the effects of sleep deprivation on autonomic balance in spontaneously hypertensive rats (SHR) are investigated.
Methods: Male SHR (6 and 9 weeks old) and Wistar-Kyoto rats (WKY) (8 weeks old) were implanted with EEG, nuchal EMG, ECG, and diaphragm electrodes using standard procedures. Cardiovascular activity was recorded in each animal under control conditions and immediately following 3 hrs of gentle handling sleep deprivation. Following recovery from sleep deprivation, rats were briefly anesthetized and implanted with an arterial catheter for measurement of arterial pressure (AP) following recovery from anesthesia.
Results: The resting AP of the older SHRs (146 mmHg) was considerably higher than both the younger SHR and the WKYs (134 and 117 mmHg, respectively). Frequency domain analysis of R-R intervals (RR) was conducted to determine the high-frequency power (HF), low-frequency power (LF), and LF-to-HF ratio (LF/HF) of heart rate variability (HRV). During non-REM sleep following recovery from sleep deprivation, only WKY and 6 week SHR showed increased LF and LF/HF over baseline recordings.
Conclusion: Increased sympathetic activity was noted following sleep deprivation in both young SHRs that has not fully developed hypertension, and their genetic controls, the WKY. Older SHRs, with hypertension failed to show a change in sympathovagal balance after sleep deprivation. The results of this experiment suggest that the presence of hypertension may limit the ability of the autonomic nervous system to effectively respond to stresses such as acute sleep deprivation.

0104

OLD RATS AND DOGS: MODELING AGE-RELATED CHANGES IN HUMAN SLEEP AND WAKE

Stevens J, Garson S, Renger J, Tannenbaum P
Merck Research Laboratories, West Point, PA, USA

Introduction: Aged humans sleep more during the day and have increased awakenings during sleep, correlating with disruptions in sleep architecture. Rodent models of aging show similar changes in sleep. We evaluated the dog to develop a convergent model to study sleep changes that parallels human aging. The present cross-sectional study examined sleep parameters in adult and aged laboratory rats and dogs as a model for human sleep.
Methods: Sleep data were collected via radio-telemetry implants (Data Sciences International) in male rats (adult = 4-6mo; aged >20mo; n=8 each) and male beagle dogs (adult = 6-8yrs, n=4; aged > 12yrs, n=3) across 3-7 continuous days from individually housed animals in home cages on 12:12 light:dark schedules. Wake and sleep stages were quantified with Somnologica (Medcare) species-specific automated software modules evaluating ECoG, EMG, EOG (dog-only) and activity data. “Active-phase” is defined as the 12-hour circadian period of lights-out for rats and lights-on for dogs; “inactive-phase” is the opposing 12-hour period dominated by sleep.
Results: Aged laboratory animals spent significantly less time in Active

Wake (AW) during the active-phase than younger adult animals: aged rats spent 48.4+0.3min less time in AW and aged dogs spent 119.6+5.9min less time in AW. During the 12-hr inactive-phase, aged rats spent 32.6+0.2 additional minutes awake and aged dogs spent 49.4+1.2 additional minutes awake compared to adult counterparts. Aged rats also had significantly less REM sleep (adult=147.3+0.1; aged=124.4+0.1), whereas aged dog cumulative REM duration did not differ from adults. Unlike adult dogs and rats, aged dogs showed no REM increase across the inactive-period.
Conclusion: Rats and dogs show predictable age-related differences in wake and sleep that parallel humans. Converging sleep data from aged rats and dogs can provide a robust model of sleep architecture associated with human aging.
Support (optional): This work was supported by Merck & Co., Inc.

0105

ACUTE EFFECTS OF DIFFERENT TYPES OF PHYSICAL EXERCISE ON SLEEP PATTERN

Rossi M,[1] Tufik S,[2] Ferreira S,[2] Koyama R,[2] Lucchesi L,[2] Bailoni-Neto A,[2] Cavagnolli D,[2] Faria A,[2] De Mello M[2]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, SP

Introduction: In the last years, various studies have been carried with the intention of verify the effects of physical exercise on sleep. However, the majority of these studies utilize only the aerobic exercise as protocol. The aim this study was to verify the influence of diferent types of exercise on sleep pattern of sedentary volunteers and with good sleep quality.
Methods: A total of 102 volunteers (40 male and 62 females, mean age 28.5 ± 7 years, sedentary and with good sleep quality) participated in the study. The protocol consisted of polysomnographic records (PSG) performed in the following night after 3 types of moderate exercise: resistance (50% of the one-repetition maximum (1-RM), 29 males and 41 females), aerobic (treadmill, 30min at 60% of VO2peak, 6 males and 13 females) or anaerobic (bike, 10 repetitions of 35s at 140% of the maximal workload reached, 5 males and 8 females). A comparison between basal PSG and exercise day PSG were realized using t-test and Wilcoxon test ($p<0.05$).
Results: Despite several studies with acute exercise show significant alteration in some sleep parameters, especially slow wave sleep (SWS) and REM sleep, we did not found significant differences in the sleep parameters (sleep onset latency, REM latency, total sleep time, sleep efficiency stage 1, stage 2, SWS, REM sleep, and wakefulness after sleep onset) after performed 3 types of exercise.
Conclusion: Our results showed that one session of exercise with moderate intensity did not interfere on sleep pattern of the sedentary volunteers with good sleep quality.
Support (optional): AFIP, FAPESP/CEPID (98/14303-3), CEPE/UNIFESP, CNPq

0106

PREDATION RISK REDUCES REM SLEEP IN WILD-CAUGHT NORWAY RATS (RATTUS NORVEGICUS)

Lima S, Lesku J, Borders R, Amlaner C
Indiana State University, Terre Haute, IN, USA

Introduction: Sleep is a prominent and widespread behavior that remains virtually unstudied from an ecological perspective. Our research on wild animals is based on (i) the fact that sleeping is dangerous, and (ii) the idea that certain ways of sleeping are safer than others. Adaptive behavioral responses to predation risk in sleeping animals should be manifest in changes in basic sleep architecture. The continuum of sleep states (e.g., from shallow to deep sleep) represents a gradient of anti-predator vigilance that allows sleep to be adjusted to the prevailing risk of predation and current sleep debt such that fitness is maximized. Based upon prior work, our general expectations are that an increase in perceived risk will lead to a decrease in both the percentage of (sleep) time spent in REM sleep and the depth of SWS. We examined these expectations in wild-caught Norway rats (Rattus norvegicus) from a predator-rich farm environment.
Methods: The two basic elements of rat sleep architecture are slow wave sleep (SWS) and rapid-eye-movement sleep (REMS). EEG electrodes were implanted into 10 rats according to standard IACUC approved procedures. Rats were housed individually and provided food and water ad lib in large stainless steel cages and are maintained on a 12:12 LD photoperiod. Sleep was recorded via a tether-commutator connected to a Grass GAMMA recording system. Recordings included two 24 hr habituation days followed by a 24 hr baseline control day, a 24 hr "predator" treatment day, and an additional 24 hr post-treatment control day. The threatening stimulus during the predator treatment was the presence of an experimenter´s gloved hand in the rat´s cage for 2 minutes at 05:50 (lights off - scotophase), just prior to the main sleep period (lights on - photophase) at 06:00.
Results: Wild rats slept primarily during the photophase (SWS-6.18hr, REMS-1.68hr, TST-7.58 hr) and were active during the scotophase. For the first 4 hrs of the photophase, control group SWS was 2.06+/-0.01hr while SWS following treatment by a simulated predator decreased to 1.02+/-0.02hr. REMS was also greatly reduced from 0.56+/-0.00hr to 0.10+/-0.01hr following simulated predator treatment. The percentage of REMS was reduced proportionately from 22% to 7% after treatment. There was no REMS rebound (18%) during the first 4-hr period of post-treatment sleep. Power analysis also suggested that the depth of SWS was substantially diminished by the appearance of the simulated predator.
Conclusion: We predicted that sleep architecture would be affected by the risk of predation. Both SWS and REMS were reduced in the wild rat immediately following a simulated threat. We suggest that REM sleep and potentially the deeper stages of SWS are dangerous sleep states from an anti-predator point-of-view. We believe that much insight into the nature of sleep remains to be gained from reinvigorating an ecological perspective on the study of sleep.
Support (optional): This project was supported by the NSF and ISU Dept of Ecology and Organismal Biology.

0107

CORTICAL ACTIVATION CAN BE VISUALIZED DURING SLEEP USING SIMULTANEOUS EEG-FMRI

Hutchison K,[1] Butterworth E,[2] Morgan V,[1] Greenberg D,[2] Howard P,[2] Gore J[2]
(1) Vanderbilt University, Nashville, TN, USA, (2) Vanderbilt University, TN, USA

Introduction: We used simultaneous EEG-fMRI to study the brain during sleep, taking advantage of the combination of the high spatial resolution of fMRI with temporally correlated EEG sleep characteristics. Specifically, we identified BOLD activation during alpha production, K-complexes, and NREM Stages 1 and 2 sleep.
Methods: We obtained EEG data, high-resolution MR images, and fMRI data from six healthy subjects, of whom four were able to sleep during the fMRI scan. EEG data were obtained using MRI compatible equipment (Compumedics Neuroscan, El Paso, TX) and fMRI data with a 3.0 T scanner (Philips Medical Systems, Cleveland, OH). EEG sleep characteristics were visually identified by a sleep specialist. fMRI signal

artifacts were removed from the EEG using an intrinsic subtraction algorithm; ballistocardiogram artifacts were reduced using a PCA-based spatial filtering routine. fMRI data was processed using Brain Voyager and AFNI software. The contrasts investigated were: 1) periods of alpha production vs. no alpha (during open/closed eyes); 2) presence vs. absence of K-complexes during NREM sleep; and 3) periods of wake vs. NREM sleep.
Results: The alpha contrasts showed negative BOLD signal changes in the occipital region. Robust K-complexes were present in all 4 subjects who slept. These corresponded to increases in BOLD signal in the right thalamus, right cerebellum and left inferior temporal lobe ($p < .00001$). The awake vs. sleep contrast showed the greatest BOLD signal increase in the anterior cingulate region with scattered signal decreases throughout the brain ($p < 0.0001$).
Conclusion: We identified sleep characteristics using simultaneous EEG-fMRI, and confirmed the expected behavior of alpha production. Additionally, hemodynamic changes were noted during K-complexes and NREM sleep in this pilot study. Future studies using this combination of modalities will assist in localizing the origin of sleep characterisics in healthy controls and patients with sleep disorders.
Support (optional): RO1 EB 000461 Integrated Functional Imaging of the Human Brain

0108

HORMONE REPLACEMENT RESTORES SEX DIFFERENCES IN THE SLEEP-WAKE ARCHITECTURE OF MICE

Paul K,[1] Losee-Olsen S,[2] Turek F[2]
(1) Morehouse School of Medicine, Atlanta, GA, USA, (2) Northwestern University, Evanston, IL, USA

Introduction: Several disorders of the sleep-wake cycle exhibit sex differences in prevalence and virulence that may result from the interaction of sex with sleep-wake architecture and sleep homeostasis. Previous studies have demonstrated that gonadectomy eliminates the majority of sex differences in sleep-wake architecture. The goal of the current study is to determine whether androgen and/or estrogen influences sleep-wake architecture in mice.
Methods: Gonadectomized male and female C57BL/6J mice (3-4 months of age) implanted with EEG/EMG recording electrodes and maintained in 14:10 LD were subsequently implanted with continuous-release pellets containing either testosterone (males) or 17beta-estradiol (females). Controls of each sex were implanted with placebo pellets. Following 24 hrs of baseline recording, mice were sleep deprived (first 6 hrs of the light phase) and given an 8-hr recovery opportunity during the remainder of the light phase.
Results: During 24 hrs. of baseline recording, androgen-treated males exhibited reductions ($p < .05$) in wake amount (-51 min.) and concomitant increases in both NREM (+39 min; $p<.05$) and REM (+13 min; $p>.05$) sleep amounts that were predominant during the dark phase compared to placebo control animals. Estrogen-treated females, conversely, exhibited increases ($p<.05$) in wake amount (+53 min) and decreases in both NREM (-31 min; $p<.05$.) and REM (-21 min; $p<.05$) sleep amounts compared to placebo control animals. The effect in females was also predominant during the dark phase. During recovery from sleep deprivation, hormone-treated males and females exhibited similar levels of NREM sleep amount.
Conclusion: Androgen replacement in males and estrogen replacement in females restored the sex differences in baseline sleep-wake amount that were previously eliminated by gonadectomy, but did not have substantial effects on recovery sleep amount in response to acute sleep deprivation.
Support (optional): This research was supported by NIH awards #R01-AG-18200 and T32 NS044851 and a fellowship from the UNCF/Merck Science Initiative.

0109

SEASONAL CHANGES IN EEG VERIFIED SLEEP IN THE WHITE CROWNED SPARROW (Z. LEUCOPHRYS GAMBELII)

Newman S,[1] Hannan C,[2] Paletz E,[1] Johnson S,[2] Benca R[1]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) University of Wisconsin-Madison, WI, USA

Introduction: We have previously reported that in a constant photoperiod, migratory sparrows significantly reduce their sleep time while in a migratory state. In the present study, we compared sleep patterns across seasons during a photoperiod that tracked the natural photoperiod of wild sparrows.
Methods: Migratory sparrows (Z. l. gambelii) were collected from Northern California and brought to Wisconsin. They were housed one per cage and resided in the laboratory under a titrating light-dark cycle that simulated their natural photoperiods, ranging from 9.5:14.5 to 22.5:1.5 (light:dark). They were implanted with EEG recording electrodes and maintained in individual cages. Light schedules were changed on a weekly basis to mimic their natural habitat. At least 4 birds were recorded (EEG and video) in each season (winter, spring, summer). Data were analyzed for the longest (summer) and shortest (winter) photoperiods, as well as during the spring migratory season. Sleep was scored in 4 s epochs for an entire 24 h period for each bird.
Results: Sleep amounts were greatest during winter (about 50% of total time), whereas as in spring migration and during summer, sleep time fell to between 25-30% of total time. The comparison between winter and summer sleep could largely be attributed to changes in day length, since the percentage of time spent asleep in the dark or the light did not differ between these seasons. In contrast, during the spring migratory season, the percentage of time spent awake in the dark increased dramatically, while there was little change in time awake during the daytime.
Conclusion: Both photoperiod and migratory state influence sleep patterns in migratory sparrows. Furthermore, sparrows show up to at least a two-fold change in sleep duration across a typical year.
Support (optional): This work was supported by NIH.

0110

FOLLICLE STIMULATING HORMONE AND SLEEP CONTINUITY IN HEALTHY WOMEN AND MEN

Tompkins L, Tucker A, Belenky G, Van Dongen H
Washington State University, Spokane, WA, USA

Introduction: Human sleep physiology displays trait individual variability. In a repeated sleep deprivation paradigm, trait individual differences in PSG sleep parameters were reported to cluster in three dimensions, which were interpreted as reflecting the duration, intensity and discontinuity of sleep. Since sleep physiology and endocrine activity affect each other bidirectionally, we examined whether endocrine profiles predicted any of the three sleep trait dimensions. Here we focus on the relationship between sleep traits and follicle stimulating hormone (FSH).
Methods: Twenty-one healthy volunteers (ages 22–40y; 11 pre-menopausal women, 10 men) spent eleven consecutive days in a sleep laboratory. They each experienced eight nights of nocturnal PSG (12 h TIB, 22:00–10:00) interspersed with three 36h periods of total sleep deprivation (they were awake during nights 3, 6 and 9). PSG sleep parameters and EEG delta power were linearly combined to yield overall scores for the three sleep trait dimensions: sleep duration, intensity and discontinuity. Prior to the study during medical screening,

FSH levels were measured in all subjects. The relationship of pre-study FSH to sleep trait dimensions across the eight PSG recordings was analyzed using mixed-effects analysis of covariance, subject to Bonferroni correction for multiple comparisons.
Results: FSH was positively related to sleep discontinuity ($F[1,106]=6.41$, $P=0.013$). This finding persisted after gender was added as a covariate ($F[1,106]=6.46$, $P=0.013$), indicating that the relationship existed independently of gender ($F[1,106]=0.32$, $P=0.57$). FSH was not significantly related to sleep duration and sleep intensity.
Conclusion: In young adult and early middle-aged women and men, higher pre-study levels of FSH predicted greater sleep discontinuity (more sleep stage transitions, movement time, and stage 1 sleep). This result is similar to reported observations in post-menopausal, depressed women. The present study extends the finding to non-depressed pre-menopausal women and men.
Support (optional): NIH grants HL70154 and RR00040; congressionally directed funding W81XWH-01-0099.

0111

SLOW WAVE ACTIVITY IN THE FIRST NREM EPISODE IS A TRAIT MARKER IN ADDITION TO A STATE MARKER

Bender A,[1] Tucker A,[1] Knittle K,[2] Belenky G,[1] Dinges D,[3] Van Dongen H[1]
(1) Washington State University, Spokane, WA, USA, (2) Aspen Sleep Centers, Spokane Valley, WA, USA, (3) University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: It is well established that slow wave activity (SWA) in the NREM sleep EEG is a marker of sleep homeostasis. Recent studies have shown that SWA also varies systematically among individuals regardless of sleep homeostatic state. Thus, SWA is both a state marker and a trait marker. These two properties were compared in the present study.
Methods: 21 healthy volunteers (age 28.5±5.5; 11 females) spent eleven consecutive days in a sleep laboratory. They underwent three 36h sleep deprivation periods, each preceded by baseline sleep (12h TIB) and followed by recovery sleep (12h TIB). All sleep periods were recorded polysomnographically and scored visually. SWA (average spectral power in the 0.75–4.5Hz frequency band per 30s epoch of NREM sleep) was determined for the first NREM episode of each night, for four EEG derivations (Fz, C3, C4, Oz referenced against A1/A2). The SWA data were subjected to mixed-effects ANOVA with prior sleep deprivation as main effect.
Results: For every EEG derivation, there was a significant increase of SWA in the first NREM episode of recovery sleep compared to baseline sleep ($F[1,56]>33.1$, $P<0.001$). In addition, there was significant between-subjects variability ($Z>2.7$, $P<0.004$). For the Fz derivation, the standard deviation for systematic individual differences across all six nights was 21.7% greater than the average difference in SWA between baseline and recovery sleep. Similar results were found for the other derivations.
Conclusion: For SWA in the first NREM episode, the magnitude of systematic individual variability (trait estimate) was greater than the magnitude of the effect of prior sleep deprivation (state estimate). This finding indicates that SWA is predominantly a trait marker in addition to being a robust state marker. Whether the trait and state aspects of SWA can both be understood in terms of sleep homeostatic mechanisms remains to be determined.
Support (optional): NIH grants HL70154 and RR00040 and AFOSR DURIP grant FA9550-06-1-0281.

0112

WORK SCHEDULES IMPACT SLEEP SCHEDULES IN FORAGING HONEY BEES

Klein B,[1] Seeley T[2]
(1) The University of Texas at Austin, Austin, TX, USA, (2) Cornell University, Ithaca, NY, USA

Introduction: Shift-work tests humans´ capacity to be flexible when scheduling both work and sleep. Honey bees (Apis mellifera) shift their foraging schedules depending on resource availability and are known to exhibit sleep behavior (Kaiser 1988). We hypothesized that bee sleep schedules may depend on timing of resource availability.
Methods: We transplanted two colonies on two separate dates in observation hives to a biological station devoid of native colonies and with limited natural food resources. We trained individually marked bees to forage for two days at a sugar solution feeder in the morning (6:45-9 AM) and examined behaviors suggestive of sleep (relative immobility, including states of immobility of the antennae) across a 24h period. We then shifted the bees' foraging period for two days to the late afternoon (4-7 PM) and reexamined sleep signs exhibited by the same bees across a second 24h period.
Foraging attempts were measured by numbers of bees that attempted to exit the hive (in trial 1).
Results: Although the numbers of observations of sleep signs exhibited by foragers did not differ between morning and afternoon treatments in either colony ($P= .83$ & $.60$, matched-pairs analysis), the timing of sleep differed within bees.
No sleep was observed during periods of resource availability, but bees did sleep at other times of the day (and night, as expected).
Also, more bees attempted to forage by 9am when trained in the morning than in the afternoon (25 versus 15).
Conclusion: Shifting temporal availability of food resources shifted the sleep schedules of foraging honey bees, suggesting that plasticity in timing of foraging is matched by plasticity in timing of sleep. A correlation between resource availability and sleeping schedules demonstrates, for the first time, temporal plasticity of sleep under ecologically relevant conditions in an insect.
Support (optional): Kaiser, W. 1988. Busy bees need rest, too: Behavioural and electromyographical sleep signs in honeybees. J. Comp. Physiol.A. 163:565-584.

0113

THE EFFECT OF GABAPENTIN ON SUBJECTIVE SLEEP QUALITY AND DAYTIME FUNCTION IN AN ALCOHOL-DEPENDENT SAMPLE ATTEMPTING ABSTINENCE: A DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

Shadan F,[1] Quello S,[2] Light J,[3] Reiter J,[2] Mason B[3]
(1) Scripps Research Institute and Scripps Clinic Sleep Center, La Jolla, CA, USA, (2) Scripps Research Institute, La Jolla, CA, USA, (3) Scripps Research Institute, CA, USA

Introduction: Sleep disturbance is a significant component the syndrome of protracted abstinence and a common precipitant of relapse in individuals with alcohol dependence. Development of safe and effective medications is necessary to improve the quality of sleep in this population. The current double-blind, placebo-controlled study investigates whether gabapentin improves subjective sleep in alcohol-dependent individuals attempting abstinence over a 12 week period. We hypothesized that subjective sleep quality would be improved by gabapentin, as measured by individual components of the Pittsburg Sleep Quality Index.
Methods: Participants (n=73) were randomized to gabapentin (900mg, 1800mg) versus placebo. The Pittsburg Sleep Quality Index was administered at baseline and weekly thereafter.
Results: Dose-dependent improvements in subjective sleep disturbance and daytime function were observed. Additionally, subjective sleep duration was reduced by 900 mg of gabapentin ($P<0.05$), presumably attributable to improved sleep consolidation and characteristics. This response was greater in the younger age group and may represent a biological distinction from the older alcohol-dependent group. No serious side effects were noted.
Conclusion: Our finding that gabapentin improves several components of the Pittsburg Sleep Quality Index, including daytime functioning, warrants further evaluation of gabapentin as a potential sleep medication in alcohol-dependent individuals.
Support (optional): NIAAA

0114

SELECTIVE BLOCKADE OF 5-HT7 RECEPTORS ENHANCES REM SLEEP SUPPRESSION, 5-HT TRANSMISSION AND ANTIDEPRESSANT-LIKE BEHAVIOR INDUCED BY CITALOPRAM IN RODENTS

Dugovic C,[1] Shelton J,[2] Kelly L,[2] Aluisio L,[2] Lovenberg T,[2] Atack J,[2] Bonaventure P[2]
(1) Johnson & Johnson PRD LLC, San Diego, CA, USA, (2) CA, USA

Introduction: Evidence has accumulated supporting a role for 5-HT7 in circadian rhythmicity, sleep and mood disorders presumably as a consequence of the modulation of 5-HT mediated neuronal activity. We hypothesized that a selective 5-HT7 antagonist (SB-269970) should increase activity of 5-HT neurons and potentiate the effects of the selective serotonin reuptake inhibitor (SSRI) citalopram.
Methods: Sleep EEG: Pharmacological treatments were performed in rats implanted with chronic EEG/EMG electrodes for standard sleep monitoring.
Microdialysis: In freely moving rats, 5-HT, DA and NE levels from the frontal cortex were measured using HPLC-ECD.
Tail Suspension Test (TST): Mice were suspended face down from a force transducer for six minutes. Time spent struggling versus time spent immobile was determined for the last four minutes of the test.
Results: Administration of citalopram (3 mg/kg), or SB-269970 (10 mg/kg) either alone or in combination did not influence the NREM sleep latency or NREM sleep duration. Citalopram treatment induced a significant increase in REM sleep latency whereas SB-269970 had no effect. The combination of citalopram with SB-269970 significantly delayed the REM sleep latency (+65 minutes) as compared to citalopram alone. In addition, the treatment with SB-269970 potentiated the decrease in REM sleep duration induced by citalopram. Interestingly, SB-269970 prevented the citalopram-induced sleep fragmentation, as evidenced by a significant decrease in the number of micro-arousals. In microdialysis studies, citalopram (3mg/kg) alone increased the extracellular concentration of 5-HT, and this effect was significantly enhanced by SB-269970 at a dose that had no effect by itself. In the TST, the decrease in immobility time induced by citalopram (3 mg/kg) was significantly enhanced by co-administration of SB-269970 (10 mg/kg).
Conclusion: These EEG, neurochemical and behavioral data indicate that selective blockade of 5-HT7 receptor may enhance the antidepressant efficacy of SSRIs. In addition, this combination may provide a novel therapy to alleviate sleep disturbances that are common in individuals with depression.

0115

EFFECTS OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS ON SLEEP IN OLDER, COMMUNITY DWELLING MEN

Diem S,[1] Blackwell T,[2] Ancoli-Israel S,[3] Stone K,[4] Redline S,[5] Ensrud K[1]
(1) University of Minnesota, Minneapolis, MN, USA, (2) California Pacific Medical Center (CPMC), CA, USA, (3) University of California, San Diego, San Diego, CA, USA, (4) California Pacific Medical Center (CPMC), San Francisco, CA, USA, (5) Case Western Reserve University, Cleveland, OH, USA

Introduction: Use of SSRIs has been associated with negative effects on sleep; however, investigations were conducted primarily in younger adult patients. We tested the hypothesis that SSRI use among community dwelling older men is associated with an increased likelihood of sleep disturbances.
Methods: 2922 men (mean age 76.4 years) in the Mr OS Sleep Study, a prospective cohort study of older men, were evaluated. Medication use was verified by inspection of medication containers and SSRIs were classified using a computerized medication dictionary. Objective measures of sleep were recorded with wrist actigraphy. Men were categorized as SSRI users (N=109) or non-users (N=2813). Depressive symptoms were identified using a cutoff score of >= 6 on the Geriatric Depression Scale (GDS); 174 subjects with GDS >= 6 were excluded from the analysis.
Results: Controlling for age and clinic location, SSRI use was associated with a higher likelihood of prolonged sleep latency (time to fall asleep of >= 1 hour: OR 2.4, 95% CI 1.4, 4.15; p=.001), poor sleep efficiency (percentage of time in bed asleep <70%: OR 1.9, 95% CI 1.16, 3.00; p=.01), and frequency awakenings (>8 wake episodes of > x minutes: OR 1.78, 95% CI 1.16, 2.74; p=.01). In multivariable models controlling for age, clinic, race, GDS score, Goldberg Anxiety Scale score, # of co-morbidities, health status, IADL impairments, physical activity, physical functioning, caffeine intake, and benzodiazepine use, SSRI use remained associated with a higher likelihood of prolonged sleep latency (OR 1.96, 95% CI 1.10, 3.50; p=.02), but associations with reduced sleep efficiency (OR 1.42, 95% CI .86, 2.35; p=.17) and frequent long awakenings (OR 1.45, 95% CI .92, 2.28; p=.11) were attenuated with reduced statistical significance.
Conclusion: SSRI use was independently associated with a higher likelihood of prolonged sleep latency in older men, independent of depressive symptoms.
Support (optional): The National Heart, Lung, and Blood Institute

(NHLBI) provides funding for the MrOS Sleep ancillary study "Outcomes of Sleep Disorders in Older Men" under the following grant numbers: R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, R01 HL070837, R01 HL070838, and R01 HL070839.

0116

SAFETY AND TOLERABILITY IN EARLY PHASE I STUDIES OF NG2-73, A NOVEL GABA(A) SLEEP AGENT

Sprenger K, Aneiro L
Neurogen Corporation, Branford, CT, USA

Introduction: NG2-73 is a GABA(A) receptor partial agonist which is alpha-3 subunit preferring. In vivo animal experiments suggest that NG2-73 will be a potent sedative hypnotic and may have an improved side effect profile compared to zolpidem with respect to ethanol interaction and learning and memory at equipotent hypnotic doses.
Methods: The first in human studies included a single ascending dose (SAD) and a 5 day multiple dose (MAD) study in healthy subjects. The SAD study started at 0.1mg NG2-73 and was to ascend to 100mg NG2-73 as a powder in a bottle formulation. The MAD study was designed to test 5 day, once daily administration of 5, 10 and 20mg tablets of NG2-73.
Results: In the SAD study 48 subjects were enrolled (38 males and 10 females); all 48 subjects completed the study. Doses administered ranged from 0.1 to 60mg. The maximum tolerated dose was 60mg, defined by the depth of sedation. The Tmax ranged from 0.33 to 3 h and the T1/2 was 1.1 to 1.4 h for all dosage groups. NG2-73 exhibited linear increases in Cmax and AUC(0-inf) with increasing doses. In the MAD study 32 (20 male and 12 female) subjects were enrolled. Repeated daily dosing of NG2-73 did not result in accumulation and NG2-73 exhibited linear pharmacokinetics. The ability of NG2-73 to produce drowsiness and sleepiness was confirmed by the sedation assessment scores on the Stanford Sleepiness Scale and Visual Analog Scale in the MAD study. In both studies the safety and tolerability of the compound were confirmed by the absence of serious adverse events, clinically significant laboratory findings, oxygen saturation level alterations, and ECG abnormalities.
Conclusion: NG2-73 is a novel sedative hypnotic which exhibits linear pharmacokinetics and is well tolerated up to 60mg, which is estimated to be 10- to 20-fold the therapeutic dose.
Support (optional): Neurogen Corp.

0117

ALCOHOL INTAKE AFFECTS THE CARDIAC AUTONOMIC NERVOUS SYSTEM DURING SLEEP IN THE DOSAGE DEPENDENCY.

Sagawa Y,[1] Kondo H,[2] Matsubuchi N,[2] Takemura T,[1] Kanayama H,[2] Kaneko Y,[2] Kanbayashi T,[2] Hishikawa Y,[2] Shimizu T[2]
(1) Akita University, Akita, Japan, (2) Akita University, Akita, Japan

Introduction: This study was performed to clarify the acute effect of alcohol on the relationship of sleep and heart rate variability during sleep.
Methods: Ten healthy male university students were enrolled in the study. Alcoholic beverage was given to each subject in a dosage of 0 (control),0.5 (low dose : LD) and 1 (high dose : HD) g/kg of ethanol (converted to pure ethanol). Alcohol drinking experiment was performed at an interval of 3 weeks. On the experiment day, Holter ECG was applied at 12:00 and the subject was instructed to drink alcoholic beverage in the dosages as described above from 100 min before going to bed, and PSG was performed for 8 hours. Power spectral analysis of heart rate variability (HRV) was performed by maximum entropy method (using MemCalc/Chiram® , Suwa Trust, Tokyo), and the ultra low frequency (ULF: =< 0.0003Hz), the very low frequency (VLF: 0.0003 - 0.004Hz), the low frequency (LF: 0.04 - 0.15Hz) , high-frequency (HF: 0.15 - 0.4Hz) components power and LF to HF ratio(LF/HF) were calculated.
Results: In the first half of the sleep, the number of awakening and REM sleep showed significant decrease in HD compared with control. It was found that the power spectral density of HRV in each frequency range decreased linearly with the increase of alcohol drinking quantity. The powers of TF, VLF, LF and HF showed significant decrease in HD compared with control. In the latter half of the sleep, sleep efficiency decreased and the value of LF/HF increased in HD compared with control.
Conclusion: The result of this study suggested that acute alcohol intake dissociated cardiac autonomic nervous system from sleep and inhibited the cardiac autonomic nervous system in the dosage dependency in the first half of the sleeping time.

0118

PHARMACOKINETIC-PHARMACODYNAMIC EFFECTS OF NG2-73, A NOVEL GABA(A) AGONIST, AND ZOLPIDEM

Greenblatt D,[1] Harmatz J,[1] Zammit G,[2] Accomando W,[3] Sprenger K,[4] Aneiro L[4]
(1) Tufts University, Boston, MA, USA, (2) Clinilabs, Inc., New York, NY, USA, (3) Accomando Consulting Enterprises, Mystic, CT, USA, (4) Neurogen Corporation, Branford, CT, USA

Introduction: NG2-73 is a GABA(A) receptor partial agonist which has preference for the alpha-3 subunit. In vivo animal experiments suggest that NG2-73 will have an improved side effect profile compared to zolpidem based on ethanol interaction and on assessments of learning and memory at equipotent hypnotic doses. The objectives of this study were to evaluate the relationship of dose, plasma concentration, and time to the pharmacokinetics (PK) and pharmacodynamics (PD) of NG2-73 at doses of 1, 3, 5, and 10 mg and zolpidem 10 mg versus placebo in healthy subjects.
Methods: This was a single-center, randomized, double-blind, placebo-controlled, 6-way crossover study of single oral doses of NG2-73 administered to 19 volunteers. Safety and tolerability were assessed, and kinetic-dynamic relationships were determined using plasma concentrations and multiple measures of PD including a visual analog scale of sedation (VAS), posturography, digit symbol substitution test (DSST), EEG beta frequency band (EBFB), and psychomotor vigilance testing (PVT).
Results: In the primary analysis, NG2-73 had a statistically significant effect on sedation compared with placebo, as measured by the Observer and the Subject VAS and there was a dose-response relationship. Similar effects were seen with the EBFB, DSST, PVT and posturography. Zolpidem 10 mg had effects that appeared similar to a dose between 3 mg and 5 mg of NG2-73. The duration of action of NG2-73 in the VAS ranged from approximately 1.5 hours for the 1mg dose to approximately 6 hours with the 10mg dose. Zolpidem had a duration of action of approximately 6 hours. NG2-73 was well tolerated with no serious adverse events or withdrawals due to adverse events.
Conclusion: NG2-73 is a novel, potent, well tolerated, effective sedative hypnotic, with dose-dependent sedation lasting between 1.5 and 6 hours. There was consistency of effect across all PD measures.
Support (optional): Neurogen Corp.

0119

EFFECTS OF ESZOPICLONE ON SLEEP AND WAKING STATES IN THE GUINEA PIG

Xi M,[1] Ramos O,[1] Chase M[2]
(1) WebSciences International, Los Angeles, CA, USA, (2) University of California, Los Angeles, Los Angeles, CA, USA

Introduction: The present report is the first in a series of experiments dealing with the effects of eszopiclone (a hypnotic that binds to sites on the $GABA_A$ receptor complex) on sleep and waking states as well as EEG activity in guinea pigs. To the best of our knowledge, there are no reports describing the effects of eszopiclone on sleep and waking states in the mature guinea pig, which is a unique animal insofar as it can be employed to carry out complementary research involving chronic and acute in vivo as well as in vitro studies.
Methods: Adult guinea pigs were implanted with electrodes to monitor sleep and waking states. Eszopiclone was administrated intraperitoneally at doses of 1 and 3 mg/kg (0.5 ml); vehicle (50 mM acetate buffer, 0.5 ml) was injected as a control. The behavioral states of wakefulness, quiet sleep and active sleep were examined and a frequency analysis of the EEG was performed for each state.
Results: Compared to control injections, the administration of eszopiclone (1 and 3 mg/kg) resulted in a significant increase in quiet sleep of 64.7% and 100.3%, and a decrease in wakefulness of 26.7% and 43.0%, respectively, during the initial two hours of recording. In addition, both doses of eszopiclone significantly reduced the latency to quiet sleep and increased EEG power in the 0.5-4.0 Hz (delta) band during this state. There were no significant changes in either the time spent in active sleep or EEG power during this state or EEG power during wakefulness following the injection of eszopiclone at either dose.
Conclusion: The present results demonstrate that eszopiclone has a pharmacological profile in the chronic guinea pig that is principally characterized by a rapid onset of action, an increase in quiet sleep and an increase in EEG delta power during this state.
Support (optional): This work was supported by Sepracor Inc.

0120

THE EFFECTS OF SLEEP DEPRIVATION AND STIMULANTS ON RISKY BEHAVIOR

Killgore W,[1] Richards J,[2] Balkin T,[1] Grugle N,[3] Killgore D[3]
(1) Walter Reed Army Institute of Research, Silver Spring, MD, USA, (2) Walter Reed Army Insitute of Research, Silver Spring, MD, USA, (3) Walter Reed Army Institute of Research, MD, USA

Introduction: Sleep deprivation reduces metabolic activity within the prefrontal cortex, the brain region most involved in planning and control of voluntary behavior. Although anecdotal evidence suggests that sleep deprivation may increase risk taking propensity, there is presently a dearth of information regarding the relationship between sleep loss and behavioral indices of risk-taking. Therefore, we examined risky behavior on the Balloon Analog Risk Test (BART) while participants were sleep deprived, again after stimulant administration, and following a period of recovery sleep.
Methods: Fifty-four (29 men) healthy individuals were deprived of sleep for 61 hours, followed by 12 hours time in bed for recovery sleep. Following 44 hours awake, volunteers received a double-blind oral dose of caffeine 600 mg, modafinil 400 mg, dextroamphetamine 20 mg, or placebo. BART was administered once a day. Risk/benefit was quantified by taking the ratio of the percent of popped balloons (i.e., "risk") to the percent of total possible winnings actually cashed in (i.e., "benefit").
Results: Mixed model ANOVA yielded a significant main effect of test session ($p<.001$), indicating a general reduction in risk behavior following 24 and 47 hours of sleep deprivation, which returned to baseline following recovery sleep. However, none of the stimulant medication were any different from placebo in their effects on the risk/benefit ratio from the BART.
Conclusion: Contrary to expectations, though similar to recently reported data for self-reported risk-taking propensity, sleep deprivation was associated with a lowered risk to benefit ratio on a behavioral task, which returned to baseline following recovery sleep. Furthermore, caffeine, modafinil, and dextroamphetamine were ineffective at changing the risk-benefit behavior, although a full night of recovery sleep returned such behavior to baseline levels. While recent evidence suggests that sleep loss impairs decision-making and inhibitory capacity, it appears to reduce the likelihood of engaging in blatantly higher risk behavior.

0121

DOUBLE-BLIND, PLACEBO (PLO)-CONTROLLED, POLYSOMNOGRAPHIC RANDOMIZED CLINICAL TRIAL (RCT) OF VALERIAN (VAL) FOR SLEEP IN PARKINSON´S DISEASE (PD)

Bliwise D,[1] Saunders D,[1] Wood-Siverio C,[1] Greer S,[1] Pour Ansari F,[1] Rye D,[2] Hitchcock S,[1] Decker M[2]
(1) Emory University School of Medicine, Atlanta, GA, USA, (2) Emory University, Atlanta, GA, USA

Introduction: VAL is an herbal for which mixed evidence suggests hypnotic efficacy. We undertook a RCT in a patient population (PD) with characteristically disturbed sleep.
Methods: 68 PD pts with moderate levels of disability took part. Mean (SD) daily dosages of levo-dopa and dopamine agonists (pergolide equivalents) were 293.3 (380.2) and 1.88 (1.64) mg, respectively. PD meds (type, dosage, and timing) were unchanged throughout the study. This was a 31-night, 3-phase protocol with 1-week of Baseline Sleep Logs at home (Phase I), followed by randomization (Phase II), comprised of 3 consecutive PSG nts (1 adaptation, 2 single-blind placebo run-in), followed by 14 nts of pill (PLO vs 600 mg VAL [LichtwerPharma, Berlin]) ending with 2 PSG nts (5 PSG nts total). In-home 7-day Open Label (Phase III) followed. Baseline was X of 2nd and 3rd nts; follow-up was X of nts 16 and 17. Data were scored/analyzed blindly with the code held by the School of Public Health. Randomization with replacement resulted in equal numbers in PLO and VAL. Repeated measures ANOVA used Intent-to-Treat principles (LOCF) for 3 pts who did not complete (1 drop out, 1 PD dose medication change; 1 death [PLO]). Significance level was set at .05. VAL was confirmed for label claim, contaminants and purity via HPLC/mass spectroscopy by independent testing lab (ConsumerLab.com) twice: before the trial initiated and after the last subject was run (to check product degradation).
Results: Integrity of product was maintained throughout the 4 years from procurement until last subject completed. VAL was not associated with significant improvement on any PSG measure (all Group x Time interactions, NS). Rates of side effects (frequency, intensity, number) showed no significant difference between PLO and VAL.
Conclusion: VAL was not effective as a hypnotic in patients with this neurodegenerative disease.
Support (optional): AT-00611

0122

COMPARISON OF THE EFFECTS OF ESZOPICLONE AND ZOLPIDEM ON SLEEP AND WAKING STATES IN THE GUINEA PIG

Xi M,[1] Ramos O,[1] Chase M[2]
(1) WebSciences International, Los Angeles, CA, USA, (2) University of California, Los Angeles, Los Angeles, CA, USA

Introduction: The present experiments were designed to compare the effects of eszopiclone and zolpidem on the states of sleep and wakefulness in the chronic guinea pig.
Methods: Adult guinea pigs were implanted with electrodes to record sleep and waking states and to perform a frequency analysis of the EEG. Eszopiclone (1 and 3 mg/kg) and zolpidem (1, 3 and 10 mg/kg) were administered intraperitoneally. Vehicle (50 mM acetate buffer, 0.5 ml) was injected as a control.
Results: The administration of eszopiclone resulted in a significant, dose-dependent increase in quiet sleep at doses of 1 and 3 mg/kg during the initial two hours of recording. However, zolpidem significantly increased quiet sleep only at doses of 3 and 10 mg/kg. Eszopiclone (1 and 3 mg/kg) resulted in a decrease in the mean latency to quiet sleep that was significantly shorter than zolpidem (3 and 10 mg/kg). There was a significant increase in EEG power in the 0.5-4.0 Hz (delta) band during quiet sleep following the administration of eszopiclone (1 and 3 mg/kg). In contrast, there were no significant changes in EEG power during quiet sleep following zolpidem administration (1, 3 and10 mg/kg). The only change in EEG power in the 0.5-4.0 Hz (delta) band during wakefulness, which consisted of a significant decrease, occurred following the administration of 10 mg/kg of zolpidem. At all doses, both eszopiclone and zolpidem increased the latency to active sleep, but did not significantly alter EEG power during this state.
Conclusion: There are significant differences in the effects of eszopiclone and zolpidem on sleep and waking states in the guinea pig which principally involve quiet sleep and EEG parameters during this state. These differences likely reflect the fact that eszopiclone and zolpidem bind to different subunits of the $GABA_A$ receptor complex.
Support (optional): This work was supported by Sepracor Inc.

0123

CX717 DURING SIMULATED NIGHT SHIFT WORK. I. PERFORMANCE AND ALERTNESS

Wesensten N, Reichardt R, Balkin T
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: To establish potential utility of CX717 as a treatment for shift work sleep disorder (SWSD), we evaluated CX717 under experimental conditions simulating SWSD (i.e., nighttime work followed by inadequate daytime sleep). The primary question addressed was: Does CX717 improve performance and alertness across 4 consecutive nights of shift work? Also addressed were questions regarding CX717 effects on daytime sleep duration and architecture (Reichardt *et al.*, companion abstract).
Methods: In this randomized, double-blind, placebo-controlled, parallel groups design, volunteers underwent 4 consecutive nights of simulated shift work from 2300 to 0700 during which performance and alertness were measured periodically. The night shift was followed by polysomnographically monitored daytime sleep from 0800 to 1200. At approximately 2145 hours each night (just prior to the start of each simulated night shift), volunteers ingested a single oral dose of CX717 200 mg, CX717 400 mg, CX717 1000 mg, or placebo (n = 12 per drug dosage; total study N = 48). Tests included psychomotor vigilance, sleep latency, subjective alertness, mood, symptom checklist, vital signs, and tasks of executive function.
Results: Psychomotor vigilance, sleep latency, subjective alertness, and mood declined across the simulated night shift ($p < .05$). CX717 failed to reverse these effects at any dosage ($p > .05$). Few drug side effects were noted and none were serious or unexpected. Vital signs were unaffected.
Conclusion: CX717 did not reverse the performance-impairing effects of sleep loss and circadian rhythms during simulated night shift work and thus is not a viable alternative to currently available compounds such as caffeine (non-prescription) or modafinil (prescription only). Prior positive results in humans suggesting CX717 efficacy during total sleep loss at dosages similar to those used in the present study may be partly attributable to the statistical phenomenon known as `regression to the mean.´
Support (optional): This study was funded by the United States Army Medical Research and Materiel Command. CX717 and placebo were supplied by Cortex Pharmaceuticals, Irvine, CA.

0124

THE EFFECTS OF SLEEP DEPRIVATION AND STIMULANTS ON SELF-REPORTED SENSATION SEEKING PROPENSITY

Killgore W,[1] Lipizzi E,[2] Balkin T,[1] Grugle N,[2] Killgore D[2]
(1) Walter Reed Army Institute of Research, Silver Spring, MD, USA, (2) Walter Reed Army Institute of Research, MD, USA

Introduction: We recently reported that sleep deprivation produced declines in self-reported and behavioral risk-taking. A related but not identical construct is known as "Sensation Seeking" and is often correlated with preferences for high stimulation and potentially dangerous behavior. Because sleep deprivation reduces activity within brain regions involved in judgment and decision-making, it is possible that sleep loss may affect the willingness to engage in highly stimulating activities. Therefore, we examined self-reported sensation seeking on the Brief Sensation Seeking Scale (BSSS) during sleep deprivation and following administration of stimulant medication.
Methods: Fifty-four (29 men) healthy participants remained awake for 61 hours. At 44 hours awake, a double-blind oral dose of caffeine 600 mg, modafinil 400 mg, dextroamphetamine 20 mg, or placebo was administered. Participants completed the BSSS at rested baseline, following 23 hours awake, again after stimulant administration (46.5 hrs), and after 12 hours of recovery sleep. Data were converted to a percent of baseline for each participant and analyzed using a mixed model ANOVA.
Results: There was a main effect of test session ($p<.001$), indicating a general reduction in self-reported Sensation Seeking following 24 and 47 hours of sleep deprivation, which returned to baseline following recovery sleep. Moreover, there was a significant interaction between session and drug group ($p=.025$). Post-hoc comparisons revealed that following 46.5 hours awake, the dextroamphetamine group scored significantly higher on Sensation Seeking than the placebo group ($p=.03$).
Conclusion: Consistent with our previous findings for self-reported risk propensity, scores on Sensation Seeking were significantly reduced by sleep deprivation and were only significantly reversed to near baseline levels by dextroamphetamine. Together with our behavioral findings, these data suggest that errors in judgment that result from sleep deprivation may occur primarily from inattention and reduced vigilance, rather than from increased willingness to engage in risky or highly stimulating behavior.

0125

THE EFFECTS OF ACUTE CAFFEINE WITHDRAWAL ON SHORT CATEGORY TEST PERFORMANCE IN SLEEP DEPRIVED INDIVIDUALS

Killgore D,[1] Kahn-Greene E,[2] Kamimori G,[1] Killgore W[1]
(1) Walter Reed Army Institute of Research, Silver Spring, MD, USA, (2) MD, USA

Introduction: Caffeine is a popular stimulant that is often used to counter the effects of sleep loss and fatigue. Withdrawal from caffeine may produce mild declines in simple cognitive capacities such as attention and concentration, but it is unclear whether more complex cognitive functions, such as abstract reasoning or concept formation, may be similarly affected. Therefore, to assess the effect of acute caffeine withdrawal on executive functioning, we administered the Short Category Test (SCT), a measure of abstract reasoning and concept formation, to participants undergoing acute caffeine withdrawal after two nights of sleep deprivation.
Methods: 26 young healthy volunteers (21 males) were deprived of sleep for a total of 77 hours. Each night from 0100 to 0700, participants received repeated doses of caffeine (200 mg) or placebo in double blind administration (800 mg total each night). After the second night of sleep deprivation and overnight administration of either caffeine or placebo, participants completed the SCT (i.e., 56 hours of total sleep deprivation; 9 hours after the last caffeine/placebo administration).
Results: After covariation for education and reading level, the analyses revealed that the caffeine group performed significantly worse (i.e., made more errors) on the SCT than the placebo group ($p<.05$). When SCT were compared to published normative data, neither the caffeine group (M = 33.25 errors, SD = 11.64) nor the placebo group (M = 26.37 errors, SD = 5.56) differed significantly from the published mean score of the normative sample (i.e., mean normative Category Test errors = 29.3; (Heaton *et al.*, 1986). Thus, performance of both groups remained within normal limits, despite sleep deprivation and caffeine withdrawal.
Conclusion: These findings suggest that caffeine withdrawal during prolonged sleep deprivation has a negative effect on abstract reasoning and concept formation, though not of sufficient magnitude to produce clinically significant decrements in performance.

0126

THE EFFECTS OF MODAFINIL, DEXTROAMPHETAMINE, AND CAFFEINE ON VERBAL AND NONVERBAL FLUENCY IN SLEEP DEPRIVED INDIVIDUALS

Rupp T, Killgore D, Balkin T, Grugle N, Killgore W
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: Sleep deprivation impairs simple vigilance, but its effects on higher-order complex cognition are less consistent. Stimulants are generally effective at reversing deficits on simple vigilance tasks, but their effects on complex cognition are not well understood. Because higher-order cognition is mediated by the prefrontal cortex, a region that is particularly affected by sleep loss, stimulants that specifically target systems in this region may be most effective at reversing the effects of sleep loss on executive functions. We compared three stimulant medications for their effect on two complex fluency tasks, the Controlled Oral Word Association Test, which correlates with left prefrontal dysfunction, and the Ruff Figural Fluency Task, which correlates with right prefrontal dysfunction.
Methods: Fifty-four healthy volunteers (29 males) were deprived of sleep for 61 hours. Participants received a single dose of either modafinil 400 mg, dextroamphetamine 20 mg, caffeine 600 mg, or placebo following 44 hours awake, and completed the COWA and RFFT after 48.7 hours of wakefulness, and again following a 12 hour period of recovery sleep. Total completed items and the number of perseverations were examined.
Results: After statistically controlling for education level and performance IQ, figural fluency performance differed significantly among drug groups ($p=.046$), with the dextroamphetamine group significantly outperforming the placebo group ($p=.03$). Drug groups did not differ in the number of RFFT perseverative errors. COWA total words and perseverations did not differ among drug groups. Following recovery sleep, groups were no longer significantly different for any measures on the RFFT or COWA.
Conclusion: Dextroamphetamine was superior to placebo at improving nonverbal figural fluency during sleep deprivation, without leading to a significant increase in perseverative responses. In contrast, none of the stimulants improved verbal fluency. Findings suggest that dextroamphetamine may be more effective at improving right than left prefrontal executive functions during sleep loss.

0127

GABOXADOL IMPROVES SLEEP ARCHITECTURE IN YOUNG AND AGED RHESUS MONKEYS

Doran S,[1] Fox S,[1] Garson S,[2] Devilbiss D,[3] Motzel S,[4] Johnson C,[4] Renger J[2]
(1) Merck & Co. Inc., West Point, PA, USA, (2) Merck Research Laboratories, West Point, PA, USA, (3) Merck & Co. Inc., PA, USA, (4) Merck & Co., Inc, PA, USA

Introduction: Gaboxadol (GBX) has previously been shown to dose-dependently increase slow wave sleep (SWS) without changing rapid eye movement (REM) sleep or total sleep amount in rats, young adults, and elderly adults. Rhesus monkeys are the optimal animal model for human sleep and cognition as they are diurnal, produce abundant SWS in the hours just after sleep onset, abundant REM sleep late in the sleep period, and show age -related changes in cognitive performance.
Methods: Adult (7 +/- 1.7 years old) male and aged (20 +/- 4.2 years old) female rhesus sleep patterns were assessed across 7 contiguous days dosing with 15mg/kg or 5 mg/kg oral doses (respectively) given 1 hour prior to lights out. EEG/EOG/EMG data were collected telemetrically 22 hours per day and sleep/wake states quantified automatically (Somnologica V3.2.1 Medcare) in 30 minute bins. Next day cognitive assessment was achieved using the 5-choice serial reaction time task (5CSRT) with a touch-screen system (CANTAB, Lafayette Instruments) for the aged animals.
Results: Gaboxadol 5mpk in elderly and 15 mpk in young rhesus monkeys each produced significant increases in SWS without changing REM or total sleep time. 15mpk GBX produced robust SWS increases beginning 2 hours after dosing and lasting for the next 5 hours. 5mpk GBX in aged animals produced a comparatively smaller SWS increase but with a similar duration of action. Spectral analysis revealed differences consistent with SWS effects. No significant changes in next day 5CSRT reaction time or percent correct performance were detected.
Conclusion: Gaboxadol produces an increase in rhesus SWS qualitatively similar to reported GBX effects on rat and human sleep. During peak plasma concentrations GBX-induced SWS expression in rhesus produce increased SWS entries and a small reduction of REM entries – a pattern that mimics post sleep-deprivation patterns.
Support (optional): This project was supported by Merck & Co., Inc.

0128

CX717 DURING SIMULATED NIGHT SHIFT WORK. II. DAYTIME SLEEP

Reichardt R, Wesensten N, Balkin T
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: To establish potential utility of CX717 as a treatment for shift work sleep disorder (SWSD), we evaluated CX717 under experimental conditions simulating SWSD (i.e., nighttime work followed by inadequate daytime sleep). In this abstract, we addressed whether CX717 affects daytime sleep duration and architecture. Performance and alertness are addressed in a companion abstract (Wesensten *et al.*, this issue).
Methods: In this randomized, double-blind, placebo-controlled, parallel groups design, volunteers underwent 4 consecutive nights of simulated shift work from 2300 to 0700 during which performance and alertness were measured periodically. The night shift was followed by polysomnographically monitored daytime sleep from 0800 to 1200. At approximately 2145 hours each night (just prior to the start of each simulated night shift), volunteers ingested a single oral dose of CX717 200 mg, CX717 400 mg, CX717 1000 mg, or placebo (n = 12 per drug dosage; total study N = 48). Sleep was scored offline in 30-sec epochs for stages W, 1, 2, SWS (stages 3 and 4 combined) and REM.
Results: Compared to placebo, CX717 1000 mg significantly reduced time in SWS across all 4 daytime sleep periods, increased latency to stage 2 for daytime sleep period 2, and increased minutes of wake time after sleep onset for daytime sleep periods 2 and 4 ($p < .05$). No other effects were significant.
Conclusion: CX717 exerted minimal effects on daytime sleep (0800-1200 hours) following simulated night shift work, and only at the highest dose administered. Although lack of effects on daytime sleep is a desirable characteristic, CX717 did not reverse the performance-impairing effects of sleep loss and circadian rhythms during simulated night shift work (Wesensten *et al.*, this issue). Thus, CX717 is not a viable alternative to currently available compounds such as caffeine (non-prescription) or modafinil (prescription only) for treating SWSD.
Support (optional): This study was funded by the United States Army Medical Research and Materiel Command. CX717 and placebo were supplied by Cortex Pharmaceuticals, Irvine, CA.

0129

CAFFEINE, DEXTROAMPHETAMINE, AND MODAFINIL IMPROVE PVT PERFORMANCE AFTER SLEEP DEPRIVATION AND RECOVERY SLEEP

Rupp T, Grugle N, Krugler A, Balkin T, Killgore W
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: In a previous study, caffeine, modafinil, and dextroamphetamine showed comparable efficacy in reversing performance deterioration following 64 hours of sleep deprivation without affecting recovery sleep. This study assessed the effects of stimulants on psychomotor vigilance performance and sleep quality after less severe sleep deprivation (44 hrs.).
Methods: Fifty-three healthy adults ages18-36; (29 men, 24 women) were given double-blind doses of caffeine (600 mg, n = 12), modafinil (400 mg, n = 11), dextroamphetamine (20 mg, n = 16), or placebo (n = 14) after 44 hours awake. Recovery sleep (12 hrs.) occurred 15 hours post-drug administration. Psychomotor Vigilance Tests (PVT) were administered every two hours (30 tests total) during sleep deprivation with 4 tests post-recovery. Mean reaction time (RT), speed (1/RT*1000), and minor (>.5 sec) and major (3 sec) lapses were collected.
Results: Repeated measures ANOVA showed performance deterioration as a result of sleep loss pre-drug administration. Post-drug administration, all stimulants improved RT and reduced major lapses relative to placebo ($p´s < .01$), while modafinil and dextroamphetamine improved speed versus placebo ($p < .01$). Post-recovery performance generally returned to baseline levels except RT was slower with placebo versus all experimental groups ($p = .02$) and minor lapses were greater with modafinil ($p = .02$) compared to other groups. Relative to caffeine, dextroamphetamine was associated with less total recovery sleep time ($p = .02$). The dextroamphetamine group showed shorter latency to REM sleep than placebo and modafinil ($p´s < .05$).
Conclusion: Dextroamphetamine and modafinil most effectively restored PVT speed after 44 hours awake; all drugs were otherwise equally effective in restoring PVT performance and generally did not have deleterious effects on post-recovery performance; indeed, RT post-recovery was slowest in the placebo group. These findings are generally consistent with drug effects after 66 hours awake; however, effects of dextroamphetamine on recovery sleep warrant further investigation.

0130

GABOXADOL AND INDIPLON SLEEP EFFECTS IN THE AGED RAT ECOG MODEL

Garson S,[1] Doran S,[2] Fox S,[2] Motzel S,[3] Johnson C,[3] Renger J,[1] Ken K[4]
(1) Merck & Co., Inc, West Point, PA, USA, (2) Merck & Co. Inc., West Point, PA, USA, (3) Merck & Co., Inc, PA, USA, (4) PA, USA

Introduction: Aging disrupts sleep architecture by decreasing delta and REM sleep, increasing the number and duration of awakenings during sleep, and decreasing low frequency spectral power of the ECoG.
Methods: Sleep was examined in aged rats comparing the selective extrasynaptic $GABA_A$ agonist (SEGA) gaboxadol (IP; 5 & 10mg/kg) and the non-benzodiazepine $GABA_A$ modulator indiplon (IP, 0.5 & 3mg/kg) against vehicle dosed 1 hr prior to lights on in 1-week cross-over studies (N=8, >20 months). ECoG, EMG and locomotor activity were collected via radio-telemetry, implanted in individually housed animals recorded in home cages. Wake and sleep stage durations were quantified in 30 min bins across 16hrs using Somnologica's automated sleep analysis software to classify 10 second epochs into 1 of 4 arousal states.
Results: Active wake was reduced for 0.5hr with 10mg/kg gaboxadol and for 1hr with 3mg/kg indiplon. Both significantly increased delta sleep for 2hrs following lights on. Gaboxadol increased cumulative low frequency (0.5 – 4Hz) ECoG spectral power faster and for a longer duration than vehicle for 12hrs whereas indiplon increased faster than vehicle for 4hrs after lights on then decreased faster than vehicle. 12 hrs after dosing with indiplon cumulative low frequency spectral power was lower than vehicle.
Conclusion: In summary, indiplon and gaboxadol both increased delta sleep amounts in aged rats but only gaboxadol increased delta activity throughout the night. We hypothesize that the differences in the effects on sleep architecture are due to the unique subset of $GABA_A$ receptors that are selectively activated by gaboxadol (extrasynaptic 4 3, ; Storustuvo and Ebert, 2006). The unique effect of gaboxadol on delta activity reported here may represent a novel mechanism for the restoration of slow wave activity in the aged human.
Support (optional): This work was supported by Merck & Co., Inc

0131

THE EFFECTS OF CAFFEINE, DEXTROAMPHETAMINE, AND MODAFINIL ON EXECUTIVE FUNCTIONING FOLLOWING 45 HOURS OF SLEEP DEPRIVATION

Newman R, Smith K, Balkin T, Grugle N, Killgore W
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: Sleep loss consistently impairs cognitive performance on tasks of attention and vigilance, but findings are less compelling for tasks of executive functioning that involve complex concept formation, mental control, and set-shifting. We recently reported that immediate spatial working memory and short-term planning abilities during sleep deprivation were significantly enhanced by modafinil 400mg and, to a lesser extent, by dextroamphetamine 20mg, but not caffeine 600mg. Here, during 45 hours of sleep deprivation, we examined the effects of these same stimulants on the Wisconsin Card Sorting Test (WCST), a test of concept formation and mental flexibility.
Methods: Fifty-four healthy volunteers (29 males) were deprived of sleep for 61 hours. At 44 hours awake, participants received a double-blind administration of one of the study medications or placebo. One hour later, participants completed the computerized 64-item WCST. Drug groups were compared using one-way ANOVAs, controlling for education, performance IQ, and study week. The following standardized T-scores were compared: Total Errors, Perseverative Responses, Perseverative Errors, Nonpereverative Errors, Conceptual Level Responses, Categories Completed, Trials to Complete First Category, Failure to Maintain Set, and Learning to Learn.
Results: Scores for all groups were well within normal limits relative to the normative sample for all WCST variables. When drug groups were compared, a significant main effect was found only for Perseverative Responses (p=.030) and Perseverative Errors (p=.029), and a non-significant trend for Conceptual Level Responses (p=.062). Post-hoc analyses revealed that the modafinil group significantly outperformed all other groups on Perseverative Responses and outperformed placebo and caffeine for Perseverative Errors.
Conclusion: Findings suggest that sleep loss did not significantly impair executive functioning on this task. However, relative to caffeine, dextroamphetamine, or placebo, modafinil was associated with significantly less perseveration on ineffective strategies. These data suggest a potential advantage of modafinil for tasks requiring concept formation and mental flexibility.

0132

RAMELTEON DIFFERENTIALLY REGULATES THE SENSITIVITY OF HMT1 AND HMT2 MELATONIN RECEPTORS EXPRESSED IN MAMMALIAN CELLS

Tiano J, Markowska M, Lambert A, Dubocovich M
Northwestern University, Chicago, IL, USA

Introduction: Melatonin regulates physiological functions through activation of G protein-coupled MT_1 and MT_2 receptors. These receptors are differentially desensitized and internalized by melatonin. Here we have assessed the efficacy of ramelteon to regulate hMT_1 and hMT_2 melatonin receptor sensitivity in heterologous mammalian cells.
Methods: CHO cells stably expressing hMT_1 or hMT_2 melatonin receptors were serum starved and pretreated with ramelteon. Specific 2-[^{125}I]-iodomelatonin binding or agonist stimulation of ^{35}SGTP-γ-S binding was determined in washed membranes.
Results: Pretreatment of CHO-hMT_1 cells with ramelteon (0.03, 0.3, 3, 30, 100 nM) did not affect specific 2-[^{125}I]-iodomelatonin binding. However, this pretreatment (0.03, 0.3, 3, 30 nM) induced a robust concentration-dependent decrease in specific 2-[^{125}I]-iodomelatonin binding to hMT_2 receptors (40±0.03; 5±2; 2.2±0.9; 0.7±0.4% of vehicle control, respectively, n=4; $p < 0.0001$; one way ANOVA). Ramelteon at 30nM did not inhibit 2-[^{125}I]-iodomelatonin binding to hMT_1 receptors after 1, 2, 4, or 8h pretreatment. Furthermore, 8h pretreatment did not affect binding to hMT_1 receptors after 8 or 16h withdrawal. By contrast, the inhibition of binding induced by pretreatment of CHO-hMT_2 cells with 0.3 or 30 nM ramelteon recovered to only 53±1.3% (n=4, $p < 0.0001$) and 16±6.5% (n=4) of vehicle control, respectively, after 4-20h withdrawal.

Ramelteon (0.1 nM-1 μM) stimulated ^{35}S-GTPγS binding to both MT_1 and MT_2 melatonin receptors in a concentration-dependent manner. Ramelteon pretreatment (30 nM and 0.3 nM) significantly decreased the efficacy of this ligand to stimulate ^{35}S-GTPγS binding to hMT_1 and hMT_2 receptors, respectively.
Conclusion: Ramelteon pretreatment differentially decreased 2-[^{125}I]-iodomelatonin binding to and affects the recovery from withdrawal of hMT_2 but not to hMT_1 receptors. However, under the current experimental conditions (eg., cell background, pretreatment length) ramelteon decreased ^{35}S-GTPγS binding possibly by uncoupling the receptors from their cognate G protein. The regulation of signal transduction events following exposure of hMT_1 and hMT_2 receptors to clinically relevant concentrations of ramelteon will be discussed.
Support (optional): Supported by Takeda Investigator-Sponsored Research Grant 06-016R.

0133

REM VERSUS NREM RAT SLEEP EFFECTS ACROSS ANTIDEPRESSANT CLASSES.

Garson S,[1] Doran S,[2] Fox S,[1] Motzel S,[3] Johnson C,[3] Koblan K,[3] Renger J[4]
(1) Merck Research Laboratories, West Point, PA, USA, (2) Merck & Co. Inc., West Point, PA, USA, (3) Merck & Co., Inc, PA, USA, (4) Merck & Co., Inc, West Point, PA, USA

Introduction: Important connections exist between sleep and depression, including early onset REM sleep, insomnia and hypersomnia. Sleep varies across different types of depression and no single antidepressant class relieves all types of depression. This work demonstrates that five mechanistically different antidepressants suppress REM sleep to various degrees; however active wake, light NREM sleep and delta sleep effects differed between mechanistic classes.
Methods: Paroxetine (5mg/kg), bupropion (30mg/kg), buspirone; (3mg/kg), trazodone (10mg/kg) and amitriptyline (10mg/kg) were examined in male rats (4-6month; n=8) against vehicle in five 1-week cross-over studies dosed PO with compound 1 hour prior to lights on (12:12 L:D cycle). ECoG, EMG and locomotor activity data was collected via radio-telemetry implanted in individually housed animals and recorded in their home cages. Wake and sleep stage durations were quantified in 30 min bins across 16hrs using Somnologica automated sleep analysis software to classify 10 second epochs into 1 of 4 arousal states.
Results: All antidepressants suppressed early REM sleep (paroxetine, 5.5 hrs; amitriptyline, 3.5 hrs; bupropion, 3.5 hrs; trazodone, 2.5 hrs; and buspirone, 1.5 hrs). REM sleep increased in the second half of the night only with trazodone and amitriptyline. Light NREM sleep duration increased with paroxetine and bupropion. However, paroxetine, trazodone, and amitriptyline increased delta sleep at the beginning of the light phase.
Conclusion: With an understanding of antidepressant related sleep effects it is therefore possible that sleep could be used as a pseudo-diagnostic measure to identify depression-related sleep problems linked

to the subjective complaints of depression. In addition, because antidepressants usually take weeks to demonstrate subjective efficacy the opportunity to use sleep as a rapid measure of efficacy of the antidepressant activity on the depressed patient´s sleep, there is a more rapid readout of the efficacy of the compound to treat the disrupted sleep component of the depressed state.
Support (optional): This work was supported by Merck & Co., Inc

0134

USE OF SLEEP AIDS AMONG ADULTS WITH HIV INFECTION

Nelson K, Gay C, Coggins T, Kelly R, Bruce S, Lee K
University of California, San Francisco, San Francisco, CA, USA

Introduction: Sleep disturbance is common among adults with HIV, but few studies have evaluated the effectiveness of sleep aids in this population. This study compares adults with HIV using sleep aids to those not using sleep aids on measures of sleep and fatigue.
Methods: Wrist actigraphy was used to estimate total sleep time (TST), wake after sleep onset (WASO), sleep onset latency (SOL), and number of wakes over 72 hours. The Pittsburgh Sleep Quality Index and the General Sleep Disturbance Scale were used as subjective measures of sleep disturbance, and the Fatigue Severity Scale was used to measure fatigue.
Results: Among 196 HIV-infected adults (122 men, 62 women, 12 transgender), 28% reported using a sleep aid, the most common being Trazodone, Ambien, and Seroquel. Sleep aid use was unrelated to gender, age, and CD4 count. Those using sleep aids reported more sleep disturbance and more fatigue than those not using sleep aids. Among the 168 subjects with actigraphy, the groups did not differ in TST (mean 6.2±1.7 hrs) or WASO (mean 21.4%±15.6), although those using sleep aids had shorter SOL and fewer awakenings. In both groups, approximately 46% slept <6 hrs/night and 57% had WASO>15%.
Conclusion: Regardless of sleep aid use, sleep disturbance was common in this sample. Those using sleep aids reported more sleep disturbance and had shorter SOL and fewer awakenings, but their TST and WASO were similar to those not using sleep aids. However, this was not a clinical trial, and it is unclear whether the sleep aids improved sleep in individual patients. Future research should evaluate the effectiveness of sleep aids for adults with HIV. Lifestyle issues likely influence sleep, and therefore behavioral interventions should also be considered. Given the number of medications prescribed to this population, clinicians need to monitor sleep aid efficacy.
Support (optional): NIH Grant #R01 MH074358, KA Lee, P.I.

0135

EFFECTS OF THE GABA-A AGONIST, ESZOPICLONE, ON SLEEP, BODY TEMPERATURE AND PATTERNS OF C-FOS EXPRESSION IN RATS

Kumar S,[1] Alam M,[2] Bashir T,[2] McGinty D,[3] Szymusiak R[4]
(1) Department of Medicine, UCLA, North Hills, CA, USA, (2) Department of Psychology, UCLA, North Hills, CA, USA, (3) Department of Psychology, UCLA, Sepulveda, CA, USA, (4) Departments of Medicine and Neurobiology, UCLA, North Hills, CA, USA

Introduction: GABAergic neurons in the preoptic area function to promote sleep via inhibition of arousal systems, including histamine (HIS) and orexin (ORX) neurons in the posterior and lateral hypothalamus (PLH). Potential mechanisms of action of sleep-promoting GABA agonists include inhibition of PLH neurons. We examined the effects of systemic administration of the GABA-A receptor agonist, eszopiclone (ESZ), on sleep-wake measures, body temperature (Tb) and c-Fos protein immunoreactivity in the PLH.
Methods: Adult rats were surgically prepared for recordings of cortical EEG, EMG and core Tb. Following recovery and adaptation, groups of 6 rats each were given one of 2 doses of ESZ (3 or 10 mg/kg, n=6, IP) or vehicle (VEH). Injections were made 1 hour following lights-off. Animals were left undisturbed for 2 hours, then anesthetized with pentobarbital, followed by thoracotomy and cardiac perfusion. Brain sections were processed for visualization of c-Fos protein, adenosine deaminase (ADA) and ORX.
Results: ESZ at 10 mg/kg induced significant increases in total sleep time (TST) over the 2 hours period, compared to VEH (46.8±2.3% vs 24.5±3.6%; independent t-test, $p < 0.01$). EEG delta power in nonREM sleep, expressed as % of waking values, was also elevated in the 10 mg/kg group (411±40% vs 281±43%; $P < 0.05$). Tb was significantly reduced following 10 mg/kg ESZ (37.2±0.2° vs 37.9±0.2°C, $p<0.05$). TST following 3 mg/kg ESZ was elevated only during the first 30 min following injection compared to VEH (38.7±2.3% vs 19.8±4.1%); 2 hours values between the two conditions were not different. Preliminary analysis of cell counts indicates that the number of ADA/Fos+ neurons was similar in ESZ and VEH rats, but the number of ORX/Fos-IR neurons was reduced in ESZ rats (19.5±4.3 vs. 38.1±4.0).
Conclusion: Systemic administration of 10 mg/kg eszopiclone promotes sleep and EEG delta power, reduces Tb and suppresses activity in ORX neurons.
Support (optional): Sepracor Inc.

0136

SLEEP AND ALCOHOL DURING FORCED DESYNCHRONY IN YOUNG ADULT HUMANS

Van Reen E,[1] McInrue E,[2] Arantes H,[3] Ronda J,[4] Acebo C,[5] Carskadon M[6]
(1) Brown University, Providence, RI, USA, (2) E.P. Bradley Sleep and Chronobiology Laboratory, Providence, RI, USA, (3) E.P. Bradley Sleep and Chronobiology Laboratory, RI, USA, (4) Brigham and Women's Hospital, MA, USA, (5) Brown University, RI, USA, (6) Brown Medical School, Department of Psychiatry and Human Behavior; E.P. Bradley Sleep and Chronobiology Research Lab, Providence, RI, USA

Introduction: To explore time of day effects of alcohol on sleep, we examined sleep following alcohol administered at two times of day and three intervals from bedtime during a 20-hr forced desynchrony (FD).
Methods: Participants.
Healthy adults (21-25 yrs) were dosed at two clock times: 1000 (MornGroup, n=6, 1 female) or 2200 (EveGroup, n=7, 2 females).

Procedures.
Participants slept 2300 to 0800 at home before the in-lab FD study (adaptation, FD 1-12 nights). Double blind placebo and alcohol (vodka tonic targeting .05g% concentration) beverages were administered during FD; thus, MornGroup and EveGroup drinking occurred 11hrs (TP11), 7hrs (TP7), and 3hrs (TP3) before bedtime. Sleep stage scoring used standard criteria.
Results: Breath Alcohol Concentration (BrAC) confirmed targeted maximal levels. At bedtime, BrAC was 0 with alcohol given at TP7 and TP11; however, with TP3 dosing, mean bedtime BrAC was .019g% for MornGroup and .014g% for EveGroup. Sleep of MornGroup was unaffected with alcohol given at TP7; with alcohol at TP11, only stage 3 minutes showed statistically significant differences (alcohol mean = 22; placebo mean = 25). At TP3 for MornGroup, stage 1 minutes (alcohol = 29, placebo = 20) and number of awakenings (alcohol = 16, placebo = 5) were greater with alcohol. By contrast, no sleep effects occurred in EveGroup with TP3 and TP7 alcohol dosing; however, alcohol at TP11,

was associated with higher sleep efficiency (alcohol = 81%, placebo = 72%), greater minutes total sleep time (alcohol = 325, placebo = 288), and decreased minutes wake (alcohol = 73, placebo = 110).
Conclusion: These data indicate that direct and residual effects of alcohol on sleep architecture differ as a function of time of day and timing relative to bedtime. Additional analyses will include groups given alcohol at other times and will also examine circadian phase and spectral components of sleep EEG.
Support (optional): AA13252 (to MAC)

0137

THE EFFECTS OF DIETHYL-LACTAM ON RODENT SLEEP OVER A 48-HOUR PERIOD

Dodson E,[1] Morrissey M,[2] Anch M[3]
(1) Saint Louis University, St. Louis, MO, USA, (2) Children's Hospital, Saint Louis, MO, USA, (3) Saint Louis University, MO, USA

Introduction: An investigational anticonvulsant, diethyl-lactam (3,3-diethyl-2-pyrrolidone), has been shown to modulate GABA-A receptors. Other well-studied compounds that bind with GABA-A receptors are barbiturates and benzodiazepines, which have soporific properties. Initial results showed that 200mg/kg increased total sleep (TST), specifically High Voltage (HS), while 300mg/kg suppressed Paradoxical sleep (PS) in rats.
Methods: Eighteen male Sprague-Dawley rats weighing approximately 450 grams received either a 200mg/kg or 300mg/kg dose of diethyl-lactam dissolved in saline or a vehicle injection of saline. Each animal served as its own control. Sleep was recorded and analyzed for the 48 hours immediately following drug and 24 hours following saline administration.
Results: Three separate repeated measures ANOVA were conducted for total sleep, total HS and total PS on the 24-hour control and drug as well as the second 24-hour period (called 48-hour condition) after drug administration. A significant main effect for condition showed rats slept less in the 48-hour condition compared to the control and drug conditions ($p=.001$). A significant interaction followed up by post hoc analyses found that rats with the 200mg/kg dose were significantly different in each condition with less sleep in the 48-hour compared to the control which was less than the drug condition ($p<.05$). Significant main effects for Total HS also found less HS in the 48-hour condition compared to the control, which was less than the drug condition ($p<.05$). A significant interaction and post hoc found that the 200mg/kg dose had more HS scored in the drug compared to both the control and 48-hour conditions ($p<.05$). A significant interaction for total PS and post hoc analyses found that more PS was scored during the drug than the 48-hour condition for the 200mg/kg dose ($p<.05$).
Conclusion: It appears that diethyl-lactam is no longer affecting sleep during the 48-hour condition (hours 25-48 post injection).

0138

COMPARING NREM EEG SPECTRAL POWER ALTERATIONS OF TIAGABINE VERSUS SLEEP RESTRICTION

Hall J,[1] Schweitzer P,[2] Walsh J[1]
(1) Sleep Medicine and Research Center, St. John's Mercy Medical Center/St. Luke's Hospital; Saint Louis University, Chesterfield, MO, USA, (2) Sleep Medicine and Research Center, St. John's Mercy Medical Center/St. Luke's Hospital, Chesterfield, MO, USA

Introduction: Tiagabine, a GABA reuptake-inhibitor, increases SWS and spectral EEG power in delta and theta ranges. We compared the spectral profile produced by tiagabine with that associated with sleep restriction.
Methods: Power density was calculated for stages 2, 3, and 4 during a baseline night and either a night with 8mg tiagabine (T8; 7m, 7f; Age=27.57±8.81) or the fourth night of sleep restriction (SR; 5 hours in bed; 6m, 7f; Age=25.92±5.85). Paired t-tests were conducted to compare absolute power between nights for each group, and independent t-tests were used to compare relative (to baseline) power between groups. One-sample t-tests were then used to determine which frequency bands demonstrated the greatest percent-increase for each group.
Results: Absolute power within the delta (0.75-4.75Hz) and theta (4.75-8Hz) frequency ranges was significantly greater than baseline for both T8 and SR ($p<0.05$ for all). Analyses of individual 1Hz bands showed that relative power was significantly greater for T8 compared to SR, at all bands ≤ 10Hz ($p<0.05$ for all). Examination of relative spectral power profiles for frequencies ≤ 12Hz revealed that the largest percent-increases for T8 occurred in the 2 and 7Hz bands (104.3% and 117.3%, respectively), each significantly greater than the mean percent-increase (63.3%; $p<0.05$ for both). For SR, percent-increases in the 1, 2, 3, and 4Hz bands (29.1%, 42.3%, 40.1%, and 30.2%, respectively) were the largest, significantly greater than the mean percent-increase (19.2%; $p<0.05$ for all).
Conclusion: Although both T8 and SR increased absolute power in the delta and theta bands, relative power analyses using 1Hz bands revealed different patterns of increase, with peaks in delta and theta for T8 but only in delta for SR. This may represent different neural processes of the drug versus sleep loss, or it could indicate that the magnitude of the two manipulations is not comparable.
Support (optional): Cephalon, Inc.

0139

A CROSS-SECTIONAL STUDY OF THE PREVALENCE OF CARDIOVASCULAR/METABOLIC RISK AND SLEEP/FATIGUE RELATED IMPAIRMENT IN THE CALGARY POLICE SERVICE (CPS) DISTRICT SERGEANTS AND DUTY INSPECTORS

Samuels C,[1] Brasher P,[2] Dirks-Farley S,[2] Seib M,[2] Joyce S,[3] Smith R[3]
(1) Centre For Sleep and Human Performance and University of Calgary, Faculty Medicine, Calgary, Alberta, Canada, (2) Centre For Sleep and Human Performance, Alberta, Canada, (3) Calgary Police Service, Alberta, Canada

Introduction: Law enforcement agencies are concerned that the impact of shift work on cognitive/mood impairment, and cardiovascular/metabolic disease will effect officer health and the ability of agencies to recruit and retain officers. This CPS research initative is designed to determine the prevalence of this health risk and fatigue related impairment, and evaluate the feasibility of a practical, valid, and reliable method of screening.
Methods: Thirty (30/36, 83% eligible), senior officers (29 male), mean age 44.6 years, completed: Pittsburgh Sleep Quality Index (PSQI) (day sleep/nightshift and night sleep/dayshift), Profile Of Mood States (POMS), SF-36 (v2), Framingham Risk Score, Adjusted Neck Circumference, and Metabolic Syndrome X score. Blood pressure, height, weight, neck circumference, waist circumference, fasting lipid screen and serum glucose were collected for each officer (lipids/glucose missing data: 2/30). Testing required one hour at a cost of $35.98 CND/officer.
Results: Global PSQI score (day sleep/night shift): mean 6.23(SD 3.0, range 0-11), (night sleep/day shift): mean 7.10(SD 3.46, range 2-19). POMS total mood disturbance mean t-score =49.47. SF-36 (v2) physical and mental component mean summary scores 52.54 and 51.94, respectively. Ninety-three percent (28/30) officers meet BMI criteria for overweight or obesity. Sixty percent (18/30) officers have a moderate to high risk Adjusted Neck Circumference. Twenty-nine percent (8/28) officers meet the criteria for metabolic syndrome. Twenty-five percent (7/28) officers have a greater than 20% 10-year risk of coronary heart disease.
Conclusion: In a group of senior officers, doing shift work, poor sleep quality is prevalent (PSQI>5). Robust measures of mood and quality of life are within normal limits. The health risks of obesity, metabolic syndrome, coronary heart disease and obstructive sleep apnea are prevalent. The feasibility and effectiveness of this screening process appears to be worth pursuing on a larger scale to assist the CPS with risk reduction and health management strategies.
Support (optional): The City of Calgary, Calgary Police Service
The Centre For Sleep and Human Performance

0140

MEASUREMENT OF HPER2 EXPRESSION IN HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS THROUGHOUT AN UNINTERRUPTED 72-HOUR PERIOD.

James F,[1] Boivin D,[2] Charbonneau S,[3] BéLanger V,[3] Cermakian N[3]
(1) Center for the Study and Treatment of Circadian Rhythms, Douglas Hospital Research Centre, Verdun, Quebec, Canada, (2) Center for Study and Treatment of Circadian Rhythms, Douglas Hospital Research Centre, Verdun, Quebec, Canada, (3) Laboratory of Molecular Chronobiology, Douglas Hospital Research Centre, Verdun, Quebec, Canada

Introduction: The rhythmic variation in levels of clock gene mRNA suggests the presence of functional circadian oscillators in peripheral blood mononuclear cells (PBMCs). We used an uninterrupted 72-hour sampling period to compare the expression of peripheral circadian oscillators in PBMCs in the presence of a habitual sleep/wake cycle (LD) and under constant routine (CR) conditions.
Methods: Six healthy men (n=4) and women (n=2, follicular phase) aged 18-30 years (mean age ± SEM: 23.7 ± 1.6 years) maintained a regular 8-hour sleep episode for two weeks prior to the study. Repeated whole blood samples were drawn from an indwelling catheter during a 72-hour period including 40 hours of LD where subjects were exposed to 144 ± 28 lux of full-spectrum light during daytime wake periods and slept in darkness, and a 32-hour CR of sustained wakefulness and limited activity under dim light. Real-time PCR was used to assess *HPER2* expression in PBMCs isolated from whole blood samples every ~120 minutes. Plasma melatonin sampled every ~60 minutes was used as a marker of the central circadian pacemaker.
Results: Dual-harmonic regression analyses revealed that four subjects displayed a statistically significant expression of *HPER2* under LD conditions and mean peak expression occurred (±SEM) 1.9 ±1.7 hours before awakening. During the CR, all participants demonstrated a significant amplitude of expression with peak expression occurring 0.1 ±1.4 hours after the time of habitual awakening. The temporal relationship between peripheral clock gene expression and the midpoint of peak melatonin was comparable under LD and CR conditions (p=0.7).
Conclusion: These results demonstrate that the pattern of clock gene expression in PBMCs can be evaluated over extended periods, and maintains a stable relationship with the melatonin rhythm under different behavioral conditions. Despite controlled investigative conditions, the phase of clock gene expression in PBMCs remains more variable than markers of central circadian pacemaker.
Support (optional): *Fonds de Recherche en Santé du Québec,* Canadian Institutes of Health Research.

0141

EXPONENTIAL DECAY OF SLOW-WAVE ACTIVITY DURING A RECOVERY NIGHT FOLLOWING SLEEP FRAGMENTATION IN CHRONOTYPES

Mongrain V, Dumont M
Universite de Montreal, Montreal, Quebec, Canada

Introduction: We recently reported, using an exponential decay modeling of slow-wave activity (SWA) during a baseline night, that a higher initial level and a steeper decay rate of SWA were associated with an earlier sleep schedule in a subgroup of chronotypes with intermediate circadian phase position. Here, we verify if these differences persist during a recovery night following an increase in sleep pressure.
Methods: Twelve morning types and 12 evening types were selected with the Horne & Östberg questionnaire. Participants were classified according to their circadian phase (salivary Dim Light Melatonin Onset; DLMO): 6 morning and 6 evening types with intermediate phases, and 6 morning and 6 evening types with early or late phases. Five consecutive polysomnography nights were recorded according to each subject's preferred sleep schedule: a baseline night, two nights of sleep fragmentation (5 minutes of forced wakefulness every half-hour), and a recovery night. SWA (1-5 Hz) was computed by spectral analysis on NREM sleep EEG recorded in the Fz derivation. An exponential decay function was then applied to recovery night relative SWA data averaged per sleep cycle.
Results: In subjects with intermediate circadian phases, the initial level of sleep pressure in recovery was higher in morning than in evening types and was correlated with earlier wake time, shorter sleep duration,

and a shorter interval between DLMO and waketime ($p<0.05$). However, the decay rate was similar between chronotypes and was not associated with sleep schedule parameters. No difference appeared between chronotypes with extreme phases and no significant correlation was found between individual estimates of SWA decay and sleep schedule.
Conclusion: These results support the assumption that in some individuals, differences in homeostatic regulation are at the origin of morningness-eveningness preference and are directly related to the resulting differences in the phase angle between circadian phase and sleep schedule.
Support (optional): Canadian Institutes of Health Research

0142

PSYCHO-BEHAVIORAL PREDICTORS OF CHRONIC JET-LAG IN LONG-HAUL AIR CREW

Ruscitto C, Ellis J
University of Surrey, Guildford, England, United Kingdom

Introduction: Although long-haul air crew report significant chronic jet-lag, a discordance between their levels of objective and subjective jet-lag exists. The extent to which psychological and behavioral variables mediate this discordance is of importance in the diagnosis and treatment of circadian rhythm disorders. Additionally, a major confounding factor is the self-selected nature of this type of sample by which predispositional factors may influence occupational choice. The aim of the present study was to examine the role of psychological and behavioral factors in reports and experienced jet lag.
Methods: In a prospective design, ten long-haul air crew completed measures of well-being, sleep (actigraphy and diary), coping, chronotype, and perceptions of jet lag, before, during and after a long-haul flight. Additionally, melatonin was assayed over the course of the study. A comparison group, matched for age, gender, and length of working week, were used to compare predispositional factors.
Results: Although there was a discrepancy between objective and subjective jet-lag, most psychological characteristics failed to mediate the relationship. However, a relationship between coping style and perceptions of jet-lag was observed as was increased fatigue related to decreased well-being ($r = -0.68$, $p<0.05$) and extent of time change to sleep-onset latency ($r = -0.86$, $p<0.05$). There were no differences between groups on well-being ($t(18) = 0.78$, n.s.), chronotype ($t(18) = 0.43$, n.s.) or coping style. However, differences between the groups were observed on sleep-onset latency ($U = 8.5$, $Z = 3.36$, $p<0.005$) on `nights off´ from work.
Conclusion: The findings demonstrate that whereas predispositional and psychological factors are not involved in choosing a career as long-haul air crew, they are related to the experience of jet-lag. The results are discussed in relation to the psycho-social aspects of frequent long-haul travel and in psychological characteristics in occupational choice amongst air crew.
Support (optional): None

0143

WHY DO SOME PEOPLE SECRETE MORE MELATONIN THAN OTHERS?

Burgess H, Alderson D, Fogg L, Eastman C
Rush University Medical Center, Chicago, IL, USA

Introduction: Melatonin is secreted from the pineal gland at night. Low levels of melatonin are associated with greater risk for cancer and cancer growth. Thus, we looked for factors that influence melatonin levels.
Methods: Melatonin secretion (area under the curve, AUC) was estimated from baseline melatonin profiles derived from saliva samples collected half-hourly for 20 hours in dim light (<10 lux) from 85 males and 86 females. Subjects were young (18-45y) nonsmokers with no medical, psychiatric or sleep disorders, and were medication free (except hormonal birth control, n=15). Prior to saliva collection subjects abstained from alcohol for at least 24 hours, and avoided NSAIDs and were on fixed sleep schedules for at least 3 days.
Results: Peak melatonin levels ranged from 2.4 to 83.6 pg/ml. AUC ranged from 88 to 2126 pg/ml/h. Females tended to secrete more melatonin ($p=0.06$), because hormonal birth control increased melatonin ($p=0.024$). Drinking 10 or more alcoholic drinks per week was associated with secreting less melatonin ($p=0.02$). Full-time workers secreted less melatonin ($p=0.03$) than students, part-time workers and those unemployed. Definite morning types secreted less melatonin than other morningness-eveningness types ($p=0.047$). There was a trend for people who wore eyeglasses and/or contact lenses to secrete more melatonin ($p=0.06$, $p=0.07$) than people without corrective vision. There were no significant associations between melatonin secretion and race, education, Epworth, PSQI, MMPI-2 scores, and the presence of bed partner and/or housemate.
Conclusion: Several factors may influence melatonin levels. Potential mechanisms include that full-time workers and definite morning types may receive light that suppresses their melatonin, and that this photoperiodic history is reflected in their subsequent dim light melatonin profiles. UV filters in corrective vision may reduce exposure to short wavelength light which can suppress melatonin. The causes of the large variation in melatonin levels remain unknown and are probably genetic.
Support (optional): RO1 NR007677, RO1 OH003954, RO1 NS35695, RO1 NS23421

0144

SCHEDULED BRIGHT LIGHT AND DARKNESS TO ACHIEVE A COMPROMISE PHASE POSITION FOR PERMANENT NIGHT SHIFT WORK

Smith M, Eastman C
Rush University Medical Center, Chicago, IL, USA

Introduction: This is the second in a series of studies designed to achieve and maintain a compromise phase position for permanent night shiftwork, in which the sleepiest time of the circadian cycle is delayed out of the night work period and into the first half of daytime sleep, improving night shift alertness and subsequent daytime sleep, but not precluding late nighttime sleep on days off.
Methods: All subjects underwent 3 consecutive night shifts (23:00-7:00) followed by two days off.An experimental group (n=9) received five 15-minute light pulses (~3,200 lux, ~1,100 μW) beginning at 23:45, interspersed by 45 minutes of room light. They wore sunglasses (~15% transmission) when outside. Sleep in darkened bedrooms was from 8:30-15:30 after the first two night shifts, 8:30-13:30 after the third night shift, and 3:00-12:00 on days off. Subjects went outside for ≥15 minutes after awakening to receive a "light brake" to keep them from delaying past the compromise phase position, a delay of ~6 h.A control group (n=12) remained in room light during night shifts, wore sunglasses (~37% transmission), and had unrestricted sleep and outside light exposure.The dim light melatonin profile was collected before and after night shifts and days off to measure the phase shift.
Results: Phase delays of the melatonin onset for the experimental group were larger than for the control group (4.2 ± 0.8 vs 0.9 ± 1.2 h, $p < .001$).
Conclusion: Our previous study showed a delay of ~3 h after two night shifts with bright light. This study found a similar delay of ~4 h after

three night shifts and two days off. While the compromise position has not yet been reached, a relatively delayed circadian phase was maintained after two days off. More night shifts will be required to achieve the compromise phase position.
Support (optional): R01 OH003954 to C.I.E.

0145

ENTRAINMENT OF HPER2 EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR CELLS FOLLOWING SIMULATED NIGHT SHIFT WORK.

James F,[1] Cermakian N,[2] Boivin D[1]
(1) Center for the Study and Treatment of Circadian Rhythms, Douglas Hospital Research Centre, Verdun, Quebec, Canada, (2) Laboratory of Molecular Chronobiology, Douglas Hospital Research Centre, Verdun, Quebec, Canada

Introduction: Judicious light and darkness exposure throughout the day can promote the appropriate alignment of the endogenous hormonal rhythms to night shift work. However, the synchronization of human peripheral circadian oscillators to shifted sleep-wake schedules is currently unknown. We evaluated *HPER2* expression in peripheral blood mononuclear cells (PBMCs) with respect to the simultaneous resetting of the plasma cortisol rhythm throughout simulated night shift work.
Methods: Five healthy candidates (4 male, 1 female in follicular phase) aged (mean ± SD) 24.9 ± 4.8 years maintained stable sleep and meal schedules before the study start. Upon admission to the laboratory, sleep/wake schedules were delayed by 10 hours to simulate nighttime "work". The light intervention included exposure to full-spectrum white light of (mean ± SEM) 6,036 ± 326 lux during 8-hour night shifts and dim light exposure after each night shift with the use of sunglasses (5% visual light transmission). *HPER2* expression in PBMCs and plasma cortisol concentration were estimated from 24-hour blood sampling periods performed before and after nine simulated night shifts. The expression of *HPER2* in isolated PBMCs was determined relative to *HCDK4* via real-time PCR.
Results: Following nine simulated night shifts, the cortisol rhythm was delayed by 10.2 hours and the fitted maximum of cortisol expression occurred (mean ± SEM) 3.5 ± 0.7 hours after awakening. Dual-harmonic regression analyses revealed that all participants demonstrated significant circadian rhythmicity in *HPER2* expression. Peak *HPER2* expression occurred 0.6 ± 0.7 hours after awakening and was in a conventional temporal relationship with the sleep/wake cycle, even though it was shifted.
Conclusion: This is the first demonstration of the entrainment of peripheral circadian oscillators in PBMCs to an atypical sleep-wake schedule. In light of recent evidence implicating peripheral oscillators and tissue function, this line of investigation may have important implications for understanding the medical disorders affecting night shift workers.
Support (optional): *Fonds de Recherche en Santé du Québec,* Canadian Institutes of Health Research.

0146

EXTENDED DURATION WORK SHIFTS AND PREVENTABLE ADVERSE EVENTS: A RISK TO PATIENTS AND PHYSICIANS

Barger L,[1] Ayas N,[2] Cade B,[1] Cronin J,[1] Rosner B,[1] Speizer F,[1] Czeisler C[1]
(1) Brigham and Women's Hospital, Boston, MA, USA, (2) Vancouver General Hospital, Vancouver, British Columbia, Canada

Introduction: We recently reported that interns working extended duration shifts have an increased risk of motor vehicle crashes, needle stick injuries, and medical errors. We assessed the impact of working extended duration shifts on patient safety (preventable adverse events) and the well-being of the interns themselves.
Methods: 2,737 physicians in their first post-graduate year participated in a nationwide web-based survey, completing 17,003 monthly reports. A regression analysis was performed to determine the relationship between the number of extended duration work shifts (>=24 hours), reported medical errors and a self-reported measure of stress. Case crossover within-subject analysis was used to assess the association between the number of extended duration shifts worked per month and the reporting of preventable adverse events. In addition, we compared self reported stress in months with and without reported preventable adverse events.
Results: The reporting of medical errors and the number of extended duration shifts worked in a month were both significant predictors of stress ($p<0.001$). Compared to months in which no extended-duration shifts were worked, interns working five or more extended duration shifts had seven times greater odds (OR=7.0; 95%CI: 4.3-11) of reporting at least one fatigue-related significant medical error that resulted in an adverse patient event and reported 300 percent (OR=4.1; 95%CI: 1.4-12) more fatigue-related preventable adverse events resulting in the death of the patient. Moreover, interns who reported a medical error that resulted in an adverse patient outcome were more than 3 times as likely to report high stress (6 or 7; 7-point Likert scale) in that month (OR=3.43, 95%CI: 3.31-3.56).
Conclusion: These results suggest that extended duration shifts negatively impact patient safety and the well-being of medical interns. They have important public policy implications for post-graduate medical education and suggest the need for counseling or other care for interns who make medical errors.
Support (optional): This study was supported by grants from the National Institute for Occupational Safety and Health within the U.S. Centers for Disease Control (R01 OH07567) and by the Agency for Healthcare Research and Quality (RO1 HS12032).

0147

INDIVIDUAL DIFFERENCES IN ALERTNESS AND PERFORMANCE AT NIGHT IN PATIENTS WITH SHIFT-WORK SLEEP DISORDER

Schweitzer P,[1] Czeisler C,[2] Dinges D,[3] Roth T,[4] Walsh J[5]
(1) Sleep Medicine and Research Center, St. John's Mercy Medical Center and St. Luke's Hospital, Chesterfield, MO, USA, (2) Harvard Medical School and Brigham and Women's Hospital, Boston, MA, USA, (3) University of Pennsylvania, Philadelphia, PA, USA, (4) Henry Ford Hospital, Detroit, MI, USA, (5) St. John's Mercy Medical Center and St. Luke´s Hospital; St. Louis Univerisity, Chesterfield, MO, USA

Introduction: Decrements in alertness and performance associated with sleep loss vary considerably among individuals and are reasonably stable within individuals. We examined interindividual variability in sleepiness and performance during the night shift in patients with shift-work sleep disorder (SWSD).
Methods: SWSD patients randomized to 8 weeks of placebo treatment in a study investigating the effectiveness of a drug treatment for SWSD were evaluated. MSLT, Karolinska Sleepiness Scale (KSS; range=0 to 9), and 20-minute Psychomotor Vigilance Tests (PVT) were administered during two laboratory night shifts, one at week 4 and one at week 8. The laboratory night shifts directly followed the last night of each subject´s usual 3- to 5-night work week.
Results: Eighty-three Ss completed both laboratory nights (27 females, 56 males, mean age 39.7, range 20-62). Mean values (and range) for the week-4 and week-8 night shifts were 2.3 (0 – 11.6) and 2.4(0 – 13.2)

minutes for MSLT, 6.6 (3.6 – 9) and 6.7 (3.7 – 9) for KSS ratings, and 23.4 (0.3 – 109.5) and 24.2 (0.3 – 91) for number of PVT lapses. Intraclass correlations between the two nights were .64 for MSLT, .61 for KSS, and .72 for PVT ($p < .001$ for all).
Conclusion: SWSD patients demonstrate significant interindividual variability in alertness and performance during night shift hours, but considerable intraindividual stability across nights. This suggests that just as individuals appear to have a trait response to sleep loss, they appear to have a trait response to night shift work. Additional data in non-SWSD individuals as well as baseline data during non-night-shift hours are needed to better understand the possible trait vulnerability to reduced alertness and performance during night-shift hours.
Support (optional): Cephalon, Inc.

0148

WOMEN WITH A PRIMARY VASOSPASTIC SYNDROME AND SLEEP ONSET INSOMNIA EXHIBIT AN ALTERED PHASE RELATIONSHIP BETWEEN THE CIRCADIAN SYSTEM AND THE SLEEP-WAKE CYCLE

Vollenweider S,[1] Dattler M,[2] Renz C,[2] Selim O,[3] Savaskan E,[2] Wirz-Justice A,[2] Krauchi K[2]
(1) Psychiatric University Clinic Basel, Basel, Switzerland, (2) Psychiatric University Clinics, AE (Europe), Switzerland, (3) University Hospital Basel, AE (Europe), Switzerland

Introduction: Women with a primary vasospastic syndrome (VS), a functional disorder of vascular regulation in otherwise healthy subjects (main symptom: cold hands and feet), often suffer from sleep onset insomnia (SOI). We have previously shown that increased distal vasodilatation before lights off promotes a rapid onset of sleep. As VS are more vasoconstricted in distal skin regions than controls (CON) before their habitual lights off, the SOI could be due to a misalignment between the circadian system and the sleep-wake cycle, i.e. subjects are physiologically not ready for sleep. In a laboratory study we aimed at a chronobiological characterisation of women having both VS and SOI to test this hypothesis.
Methods: 18 healthy women (N=9 VS; 9 CON; luteal phase; similar age: 20-33yr, BMI: 18-24, and habitual bedtimes: 22:00-24:07h) performed a 40-h constant routine protocol (CR, adjusted to habitual bedtime), with a baseline (BL) and a recovery (RE) night before and after. Skin temperatures [ST; 8 probes] and core body temperature (CBT, rectal) were continuously recorded. Half-hourly saliva samples were collected for melatonin assay and subjective sleepiness was assessed on the Karolinska Sleepiness Scale (KSS) and on 100 mm visual analogue scales (VAS). Dim Light Melatonin Onset (DLMO) was defined as the first interpolated point above 3 pg/ml that continued to rise.
Results: In comparison to CON, VS showed before BL, during the CR and before RE a 1h circadian phase delay in DLMO [h after lights on: VS 14.6+/-0.3h; CON 13.5+/-0.2h; $p<0.02$]. Similar phase shifts were observed in CBT, distal ST (hands and feet), KSS and VAS ratings.
Conclusion: Women having both VS and SOI exhibit a changed internal phase angle between endogenous circadian rhythms and their habitual sleep-wake cycle, which could be a cause of SOI.
Support (optional): Research supported by the Swiss National Science Foundation (SNF# 33100a0-102182/1 to K.K.)

0149

CIRCADIAN TIMING, SLEEP QUALITY, AND MORNING VIGILANCE AFTER WEEKEND "CATCH-UP" SLEEP IN TEENS: PRELIMINARY RESULTS

Crowley S,[1] Carskadon M[2]
(1) Brown University, Department of Psychology; E.P. Bradley Hospital Sleep and Chronobiology Research Lab, Providence, RI, USA, (2) Brown Medical School, Department of Psychiatry and Human Behavior; E.P. Bradley Sleep and Chronobiology Research Lab, Providence, RI, USA

Introduction: High school students´ sleep is typically restricted during the school week and is compensated by late and long sleep on weekends. We examined circadian phase, sleep quality, and morning vigilance before and after simulating this weekend sleep pattern.
Methods: To date, four healthy adolescents (15-16 years, 2 males) have kept a fixed sleep/wake schedule (time in bed=7.5 hours) 7 nights before and 4 nights after a weekend. On the intervening weekend, participants retired 1.5 hours later and rose 3 hours later than fixed sleep/wake (time in bed=9.0 hours). We measured evening melatonin from saliva samples collected every 30 minutes for 6 hours before (Friday) and after (Sunday) late weekend sleep. We determined dim light melatonin onset (DLMO) phase using a 4pg/mL threshold and computed phase shifts from Friday to Sunday. Participants rated sleep quality at waking from 1 (very poor) to 5 (very good) and completed a 5-minute PDA-based PVT about 30 minutes after wake. We report descriptive trends for average sleep quality ratings and median reaction time (RT) on Monday and Tuesday before (pre-weekend) and after (post-weekend) late weekend sleep.
Results: Three participants ("shifters") showed a DLMO phase delay shift ≥ 30 minutes (-30, -41, and -85 minutes) across the weekend; one participant ("non-shifter") showed no phase shift (+3.6 minutes). Two shifters reported poorer sleep quality post-weekend (mean=3.5) compared to pre-weekend (mean=4.5); one shifter reported no change. The non-shifter reported slightly better sleep quality post-weekend (mean=3.5) compared to pre-weekend (mean=3.0). One shifter showed slower post-weekend median RT (Monday=355 msec, Tuesday=375 msec) compared to pre-weekend (Monday=275 msec, Tuesday=240 msec); two shifters showed little change. Morning PVT data were unavailable for the non-shifter.
Conclusion: Three of four participants showed phase delay shifts after late weekend sleep. More participants are needed to draw conclusions about associations between weekend phase shifts and weekday behavioral outcomes.
Support (optional): 1 F31 MH078662-01 awarded to S.J. Crowley; Apollo Health, Inc.

0150

AMBULATORY MEASUREMENT OF SKIN TEMPERATURES AND THE SLEEP-WAKE-CYCLE IN WOMEN WITH VASOSPASTIC SYNDROME AND CONTROLS

Gompper B,[1] Vollenweider S,[2] Renz C,[1] Someren E,[3] Wirz-Justice A,[1] OrgüL S,[4] Flammer J,[4] Krauchi K[1]
(1) Psychiatric University Clinics, Basel, AE (Europe), Switzerland, (2) Psychiatric University Clinic Basel, Basel, AE (Europe), Switzerland, (3) Netherlands Institute for Neuroscience and VU Medical Center, Amsterdam, AE (Europe), Netherlands, (4) University Eye Clinic Basel, Basel, AE (Europe), Switzerland

Introduction: The primary vasospastic syndrome is defined as a vascular dysregulation of blood vessels in otherwise healthy subjects (main symptoms: cold hands and feet). It occurs mostly in young

women and is often accompanied by sleep onset insomnia (SOI). In this study, we investigated when vasospasm occurs under normal everyday conditions. In addition we asked whether women having both vasospastic syndrome and SOI (VS) have different internal phase relationships between thermoregulation, sleep midpoint, sleepiness and the light-dark cycle in comparison to controls (CON).
Methods: Study subjects were 20 VS and 21 CON women (Age: 25.4±0.7 s.e.m., BMI:21.0±0.3). Skintemperatures were recorded in a week-long ambulatory protocol using 11 wireless temperature sensors (ibuttons; left and right wrist, ankle, calf, thigh, infraclavicular region, sternum; 2.5-min intervals). Purified data 2hr before and after lights off and lights on, respectively, were analysed, as well as mean 24-hour profiles of raw data (7 days). Subjective items such as sleepiness, sleep times etc. were recorded daily in sleep-activity diaries.
Results: Compared with CON, VS showed increased distal vasoconstriction at midday and in the evening, as indicated by lower distal skin temperatures (DIST, mean of hands and feet), feet-calf and distal-proximal skin temperature gradients ($p<0.05$). VS revealed distal vasoconstriction before lights off, which lasted longer after lights off than in CON. Sleep onset latency was longer in VS vs. CON (29.2±4.3 vs. 7.8±1.1min), but times of lights off and lights on did not differ. Calculated sleep midpoint was later in VS compared to CON (4.68±0.22 vs. 4.00±0.23h), but no differences were found in sleep duration. Subjective ratings of sleepiness (VAS) showed a phase delay in VS vs. CON ($p<0.02$).
Conclusion: Under everyday conditions VS demonstrate a phase delay in DIST, sleep midpoint and sleepiness with respect to the light-dark cycle compared with CON. Therefore, VS exhibit certain aspects of a chronobiological disorder.
Support (optional): Research supported by SNF Grant #3100A0-102182 to K.K. and the Schwickert-Stiftung.

0151

WOMEN WITH VASOPASTIC SYNDROME SHOW A PREDISPOSITION FOR EVENING CHRONOTYPE AND SOCIAL JETLAG

Krauchi K,[1] Gompper B,[1] Vollenweider S,[2] Flammer J,[3] OrgüL S[3]
(1) Psychiatric University Clinics, Basel, AE (Europe), Switzerland, (2) Psychiatric University Clinic Basel, Basel, AE (Europe), Switzerland, (3) University Eye Clinic Basel, Basel, AE (Europe), Switzerland

Introduction: The primary vasospastic syndrome (VS) is a functional disorder of blood flow regulation in otherwise healthy subjects (mostly women; leading symptoms: cold hands and feet). There is evidence from epidemiological, ambulatory and controlled laboratory studies of a close relationship between cold extremities in the evening and difficulties initiating sleep. The aim of the study is to explore whether women with VS exhibit preponderance in a certain chronotype and/or exhibit more or less `social jetlag´ (Wittmann, 2006).
Methods: Hundred forty-five women were recruited from participants of a larger survey in a random population sample of Basel-Stadt (Kräuchi *et al.*, APSS, 2005). Various questionnaires were mailed to the subjects (e.g. Munich Chronotype Questionnaire, MCTQ; thermal discomfort; sleep behaviour, etc). VS and CON were classified from questionnaire-derived scores (feeling of cold hands and feet, and finger color changes).
Results: In comparison to CON (N=84), women with VS (N=63) showed significant higher VS –scores (2.85±0.06 vs. 1.60±0.03units) and increased sleep onset latency (SOL; 23.2±2.3 vs. 14.7±1.6min; all U-tests $p<0.05$). VS compared with CON showed significantly higher MSFsc -values (4.4±0.1 vs. 3.7±0.1) as well as larger differences in sleep timing between free and work days (corrected for sleep onset latency, 1.71±0.15 vs 1.19±0.10h). Additionally, VS were significantly younger (31.4±0.8 vs. 34.7±0.6y), slimmer (BMI: 21.5±0.6 v s. 22.8±0.4) and were more often smoker than controls (35±6 vs. 14±4%).
Conclusion: Women with VS exhibit not only long SOL, but also a significant tendency to late chronotypes and larger `social jetlag´ than CON, indicating some aspects of a chronobiological disorder i.e. different phase of entrainment. It can be hypothesised that distal vasoconstriction lead to a larger internal phase angle between circadian clock and sleep-wake cycle, and hence, to a sleep onset disturbance.
Support (optional): "Research supported by the Schwickert-Stiftung and the SNF Grant #3100A0-102182 to K.K."

0152

INTER-INDIVIDUAL VARIABILITY IN THE PARAMETERS OF A MATHEMATICAL MODEL OF NEUROBEHAVIORAL PERFORMANCE AND ALERTNESS

St. Hilaire M,[1] Klerman E[2]
(1) Brigham and Women's Hospital, Boston, MA, USA, (2) Brigham and Women's Hospital, MA, USA

Introduction: A wide range of inter-individual variability in measures of performance and alertness has been observed under conditions of total sleep deprivation and sleep restriction. Most current mathematical models of circadian rhythms, performance and alertness do not include inter-individual differences. Using the Kronauer-Jewett neurobehavioral performance model (Jewett 1999), we investigated inter-individual differences in parameter values of best-fit models and the relationship of these values to subject characteristics.
Methods: The Kronauer-Jewett model includes circadian, homeostatic and sleep inertia components and predicts neurobehavioral performance on a 0.0 to 1.0 scale. The model parameters were originally based on grouped data. We used a non-linear optimization procedure to fit these parameters to individual serial addition task (ADD) data from 12 subjects during 52h sleep deprivation. Six parameters of the model were fit: uC (upper asymptote of circadian amplitude), A (circadian scaling), Hac (circadian-homeostatic interaction scaling), rHw (rate of homeostatic decline), uH (homeostatic recovery asymptote), and rW (sleep inertia dissipation rate). R^2 was calculated to determine goodness of the model fits to data. Correlations were performed between estimated parameters and subject trait characteristics (age, gender, owl-lark score, habitual bedrest duration (HBD), habitual sleep/wake times).
Results: The individual model fits to the data (average R^2=0.43) were significantly better than the predictions of the model with parameters based on grouped data (average R^2=0.18). Correlation analysis revealed a negative correlation between age and Hac (R^2=-0.87, p=0.003) and age and A (R^2=-0.76, p=0.016). These results both suggest less influence of circadian-homeostatic interactions in older people.
Conclusion: This preliminary analysis will be expanded to include a larger number of subjects, more measures of alertness and performance, and will compare parameter fits with more subject characteristics, including intrinsic period, circadian phase, and baseline performance.
Support (optional): NSBRI HPF00405 and NIH grants P01-AG09975, K02-HD045459 (EBK), and NCRR-GCRC M01 RR02635

0153

LOST IN TIME

SpäTi J,[1] Blatter K,[2] MüNch M,[2] Knoblauch V,[2] Cajochen C[2]
(1) Centre for Chronobiology, Psychiatric University Clinics Basel, Basel, Switzerland, (2) AE (Europe)

Introduction: Knowing of our position in time (i.e., temporal orientation) helps us adequately interact with the environment and may contribute to the daily entrainment of the circadian pacemaker to a near 24 h day. In this study, we investigated subjective clock-time estimates at different circadian phases during prolonged wakefulness in healthy young and older volunteers under constant routine conditions.
Methods: Time-of-day estimates were collected in 16 young (8 m, 8f; 20-31 years) and 16 older (8 m, 8f; 57-74 years) healthy volunteers during 40 h of extended wakefulness under constant routine conditions in an environment devoid of temporal cues. At intervals of approximately 3.75 h subjects were asked to give a verbal estimate on time-of-day.
Results: In general, an overestimation of clock time was found in both age groups, with significantly higher values for the older group (young: 0.4±0.3 h vs. older: 1.5±0.3 h, $p<0.05$). Estimation errors varied in a diurnal fashion in both age groups, the oscillation roughly paralleling the time course of core body temperature. However, a significant interaction between elapsed time awake x age group was found (rANOVA, $p<0.05$). Post-hoc analyses revealed significantly higher magnitudes of estimation errors for the older at 8.6, 12.4, and 16.1 h of elapsed time of wakefulness ($p<0.05$); beyond 16.1 h elapsed time into protocol, the mean estimation error in the young group increased up to the level found in the older subjects group.
Conclusion: Temporal orientation was more impaired in the older than in the young volunteers, particularly from the afternoon till late evening (16:30-24:00h). However, time-of-day estimates in young people seem to be more susceptible to the effects of elevated sleep pressure than in the older.
Support (optional): Research supported by Swiss National Science Foundation Grants START 3100-055385.98 and 3130-054991.98 to CC, the Velux Foundation and by the EU 6th Framework Project EUCLOCK (#018741).

0154

OBJECTIVE MEASUREMENT OF FATIGUE IN HIV USING ACTIGRAPHY

Boero J, Shannon W, McLeland J, Doerr C, Kampelman J, David C, Duntley S
Washington University in St. Louis, Saint Louis, MO, USA

Introduction: Behavioral changes associated with HIV infection include lethargy or fatigue. Fatigue appears early in HIV infection and worsens with disease progression. Sleep dysfunction, in particular insomnia, are associated with CNS infection by HIV years before diagnosis. Fatigue is usually recognized only when impairment becomes severe. The need for an objective and early method for detecting neurologic impairment due to HIV is vital for the proper treatment and management of HIV/AIDS. We propose the use of actigraphy as an objective and early method for detecting neurologic impairment due to HIV.
Methods: Wrist actigraphy data was collected from 20 HIV infected individuals recruited from the CNS HIV Anti-Retroviral Therapy Effects Research (CHARTER) site in St. Louis. Actigraphy was measured on average for 10.8 days recording motion at 1 minute intervals (1,440 minutes per day). Functional Principal Component Analysis (functional PCA) was used to reduce the data complexity while retaining the information content. Principal compoments of the actigraphy data variability were identified and correlated with observed behavioral patterns identified by inspection of actigraphs.
Results: Functional data analysis of actigraphy data identified 4 principal compoments that explain 95.6 % of the variation among the actigraphy (80.7%, 8.2%, 3.9% and 2.8%). The first and largest principal component represents maximal activity during the day, and helps to distinguish patients with overall high average activities from those with overall low average activity levels. In contrast, the second principal component identifies patients with higher than average activity in the evening and night, but are less active during the day, from those who are restful at night but more active in the morning and day. Furthermore, analysis of the third component for the actigraphy data variability showed that this component is associated with rapid acceleration of activity levels. Patients with high third functional component scores have rapid acceleration in activity levels in the morning, below average activity the rest of the afternoon, and average activity at night. Patients with low third functional scores are below average in the morning, and above average in the afternoon. The fourth functional component identified a group of patients with low scores who have a late burst of activity around 1200 minutes (8:00 pm).
Conclusion: Functional data analysis of the principal components associated with wrist actigraphy provides more detail into individual patient activity profiles than simple summary statistics of counts per minute data. Four functional compoments identified changes in rate in activity that correlate with individual patterns of behavior. Using functional data analysis for actigraphy has a potential to objectively measure fatigue in HIV/AIDS and other diseases.
Support (optional): National Institute of Mental Health Grant 22005

0155

DISRUPTION OF THE DIURNAL PATTERN OF SLEEP AND WAKEFULNESS INCREASES OBESITY AND IMPAIRS INSULIN TOLERANCE IN MICE

Veasey S, Pack A, Mackiewicz M
University of Pennsylvania, Philadelphia, PA, USA

Introduction: Chronic sleep debt and the dissociation of timing in sleep and wakefulness from the normal diurnal light/dark cycle (like such experienced by shift workers) has become increasingly common in modern societies. This subset of adults is at increased risk for multiple illnesses. The aim of this study was to establish whether the disruption of the diurnal pattern of sleep and wakefulness in mice affects food intake, body weight and glucose metabolism. We hypothesized that this altered light pattern would disrupt sleep and wakefulness and lead to metabolic syndrome.
Methods: In male C57/B6/J mice (n=10) the cycle of light and dark was disrupted for three months. It consisted of alternating periods of 2 hrs of light and 4 hrs of dark. Controls (n=10) were maintained on 12:12 hrs light/dark. Sleep was estimated non-invasively by monitoring locomotor activity. The intake of regular or high-fat food and weight gain was assessed weekly. Normal and fasting glucose levels and its changes after insulin challenge, as well as body composition (by DEXA) were determined at the end of study.
Results: We have demonstrated that total sleep time, number and duration of sleep bouts did not differ between experimental groups; however, there were significant differences in the temporal distribution of sleep and wakefulness across a day. Disruption of the light-dark cycle lead to: (1) increase in body weight ($p=0.03$); (2) increase in whole body and abdomen fat ($p=0.005$ and $p=0.01$, respectively); (3) higher normal and fasting glucose levels and impaired insulin tolerance ($p=0.01$).

Conclusion: Alteration of the diurnal pattern of sleep and wakefulness leads to symptoms of metabolic syndrome. These changes are likely due to a decrease in metabolic rate. Additional experiments on the energy expenditure, circadian variation in metabolic hormones, and cholesterol/triglyceride are in progress.
Support (optional): NHLBI grant HL60287

0156

CIRCADIAN VERSUS PSYCHOSOCIAL FACTORS IN HABITUAL SLEEP TIMING

Paine S, Gander P
Massey University, Wellington, New Zealand

Introduction: There is significant interest in the genetic mechanisms underlying differences in sleep timing. However, decisions about when to go to bed and when to wake up are also influenced by a myriad of exogenous factors including personal/family commitments and work schedules. This study aimed to examine the relative contribution of the dim light melatonin onset (DLMO) versus psychosocial factors in determining habitual sleep timing.
Methods: Wrist actigraphy and sleep diary data were collected for two weeks from 28 healthy, non-shiftworking adults (19 females, 9 males, mean age 41.1yrs ± 4.7yrs) recruited from a random population sample. Participants slept in their own homes and were were given no instructions regarding sleep, except to sleep at their preferred time on the last night before circadian phase assessment using a modified constant routine protocol (Day 15). Half-hourly saliva samples were collected between 1730 and 1000hrs under dim-light conditions (<20 lux) and analysed by radioimmunoassay. Mixed model ANCOVAs were used to investigate the influences of age (30-39yrs vs. 40-49yrs), circadian phase (DLMO), and week (Sunday-Thursday nights) versus weekend nights (Friday and Saturday nights) on sleep timing. DLMO was defined as the first time that melatonin levels rose to 25% of maximum, followed by a continuous rise in levels.
Results: For sleep start times, significant main effects were found for DLMO ($p=0.0172$) and week versus weekend nights ($p<0.0001$). For sleep end times, significant main effects were found for DLMO ($p=0.0003$), age group ($p=0.0039$) and week versus weekend nights ($p<0.0001$). Later sleep times were associated with later DLMO.
Conclusion: This study suggests that psychosocial factors may have a greater effect on sleep timing in daily life than circadian physiology. While this is perhaps not surprising, it does reaffirm that better understanding of clock gene polymorphisms will not fully explain preferred sleep timing.
Support (optional): Sarah-Jane Paine conducted this research during the tenure of a Mäori Health PhD Scholarship from the Health Research Council of New Zealand (HRC 03/020). Funding for this research was provided by the Lotteries Health Research Committee.

0157

PER3 POLYMORPHISM PREDICTS SUSCEPTIBILITY TO SLEEP DEPRIVATION-INDUCED IMPAIRMENT OF EARLY MORNING EXECUTIVE PERFORMANCE

Groeger J,[1] Lo J,[2] Viola A,[1] Von Schantz M,[1] Archer S,[3] Dijk D[1]
(1) University of Surrey, Guildford, United Kingdom, (2) University of Surrey, United Kingdom, (3) University of Surrey, Guildford, Surrey, United Kingdom

Introduction: Extreme preferences for waking and sleeping times are associated with a length variant polymorphism of the PERIOD3 gene. Following sleep deprivation, morning types report greater sleepiness, but no performance data contrast impairment across genotypes. Among the population at large, sleep deprivation particularly compromises those executive cognitive functions which depend on the dorsolateral prefrontal cortex. Here, we test the hypothesis that, when contrasted with subjects homozygous for the short variant (PER34/4), the waking performance of subjects homozygous for the long variant (PER35/5) shows greater executive function impairment after one night´s total sleep deprivation.
Methods: Fourteen PER34/4 and 10 PER35/5 healthy, young (mean 25.0±1.0 y) volunteers served in a 40-h constant routine, during which they remained awake in a semi-recumbent position in dim light. Blood was drawn hourly to establish individual peak melatonin concentrations. Every 2 hours, volunteers underwent 20 min of cognitive testing. Tests had been practiced during the baseline days, and assessed: Working Memory (Verbal and Spatial N-Back), paced serial addition (PVSAT), un-paced digit-symbol substitution, sustained attention (SART), reaction time, motor sequence learning and control (Pursuit tracking and Serial Reaction).
Results: Performance of both groups was indistinguishable on all tests until later in the biological night. During the period 2 to 4 hours after the melatonin peak, performance of the 2 and 3- back verbal and spatial Working Memory tasks, and Paced Visual Serial Addition deteriorated significantly more in PER35/5 ($p<0.01$ after family-wise correction). These subjects also switched more slowly between the learned sequence and random trials during the Serial Reaction task. Thereafter, PER35/5 performance in these tasks recovered to PER34/4 levels. No reliable differences between the genotypes were observed for any of the non-executive tasks.
Conclusion: Individuals homozygous for the long variant of the PER3 polymorphism, have selectively impaired executive performance in the early morning following sleep deprivation.
Support (optional): Supported by BBSRC BSS/B/08523

0158

ENDOGENOUS CIRCADIAN RHYTHM OF PER3 RNA IN HUMAN LEUCOCYTES: ASSOCIATION WITH SLEEP TIMING, MELATONIN RHYTHM, AND PER3 GENOTYPE

Archer S, Viola A, Von Schantz M, Dijk D
University of Surrey, Guildford, Surrey, United Kingdom

Introduction: PERIOD3> has been implicated in the regulation of human sleepwake timing and diurnal preference. Rhythmic expression of PER3 in leukocytes persists in the absence of masking by the sleep/wake and light/dark cycle. We investigated whether inter-individual variation in PER3 expression timing is associated with sleep/wake timing and melatonin rhythms.
Methods: 24 individuals homozygous for the long ($PER3^{5/5}$) or short variant ($PER3^{4/4}$) of *PER3* participated in a field and laboratory study. After habitual sleep/wake cycle assessment, they underwent a constant routine, during which hourly blood samples for quantifying *PER3* RNA and melatonin were collected. Circadian rhythmicity was assessed by sinusoidal fitting to individual time series (NLIN, SAS).
Results: Habitual sleep timing varied between 22:45 and 04:40 (onset), and 06:00 and 10:40 (offest). The amplitude of the *PER3* RNA rhythm differed significantly from zero in 19/24 subjects (11/14 $PER3^{4/4}$ and 8/10 $PER3^{5/5}$). The timing of the *PER3* RNA rhythm maximum varied from 02:00 to 12:00. The melatonin mid-point varied from 02:32 to 06:59. When the data were split by mean sleep- or melatonin-timing, clear differences in the timing of *PER3* expression emerged, which were confirmed by correlational analyses (timing of RNA and sleep onset, $r = 0.045$, $p < 0.03$; timing of RNA and melatonin onset, $r = 0.45$, $p < 0.05$). By comparison, the correlation between sleep timing and melatonin onset was 0.78 ($p < 0.001$), which is stronger than the

correlation between *PER3* RNA and sleep timing ($p < 0.05$). None of these correlations differed between the two genotypes.
Conclusion: The endogenous circadian rhythm of *PER3* RNA correlates with habitual sleep timing, but this is weaker than the correlation between sleep timing and melatonin.
Support (optional): This work was funded by a grant from the UK Biotechnology & Biological Sciences Research Council (BBS/B/08523)

0159

EFFECT OF AN INTERVENTION ON MELATONIN SECRETION DURING NIGHT SHIFTS IN POLICE OFFICERS

Tremblay G,[1] Boivin D,[1] Bourdhouxe M[2]
(1) McGill University, Montreal, Quebec, Canada, (2) Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST), Montreal, Quebec, Canada

Introduction: In a prior study we looked at the effect of an intervention based on the timing of light/darkness in permanent night shift workers. This study aims at determining the effect of a similar intervention on melatonin secretion in rotating shift workers.
Methods: Eight police officers (4 per group) were studied in the laboratory before and after a series of 7 consecutive night shifts (8-8.5 hours). Saliva melatonin was sampled every 1-2 hours over a 24-hour period. Participants in the "intervention" group exposed themselves to bright light (Litebook 1.2, Litebook Company Ltd.) for the first 6 hours of their shifts. They wore orange-tinted glasses from sunrise until bedtime (Blue-blockers, Telemedoptique Inc.). An 8-hour daytime sleep episode was planned 2 hours after the end of their shift. Participants in the "control" group did not receive any instructions regarding their light exposure and sleep schedule.
Results: One factor ANOVA (factor: group) was used to analyze the percentage of the 24-hour AUC of salivary melatonin that occurred during the work period. This ANOVA revealed a significant difference ($F(1)= 18{,}1851; p=0.0053$), with the "intervention" group having lower values than the "control" group.
Conclusion: Our preliminary results indicate a better circadian adjustment to working nights of participants exposed to our intervention. "Control" participants secreted more melatonin during their work period then participants from the "intervention" group.
Support (optional): This study was supported by the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST). GT is supported by a fellowship from the IRSST. DBB is supported by a career award from the Canadian Institutes of Health Research (CIHR).

0160

CIRCADIAN VARIATION OF CORE AND BRAIN TEMPERATURES IN HUMANS

Boudreau P,[1] Shechter A,[1] Dittmar A,[2] Gehin C,[2] Delhomme G,[2] Nocua R,[2] Dumont G,[3] Boivin D[1]
(1) McGill University, Montreal, Quebec, Canada, (2) National Institute of Applied Science of Lyon, Lyon, France, (3) University of British Columbia, Vancouver, British Columbia, Canada

Introduction: The human circadian phase and amplitude is commonly assessed with the core body temperature cycle in the laboratory. However, in ambulatory conditions, invasive measurements are unsuitable. In this study, we compared the assessment of circadian phase and amplitude drawn from a rectal temperature (CBT) sensor and from a newly designed, non-invasive, cerebral temperature (BT) sensor using an ultra-rapid sleep-wake cycle procedure (URSW).
Methods: Three healthy women (mean age ± SD: 27.0 ± 2.5 years), with regular menstrual cycles were studied individually for 5 days in time isolation for a total of four visits (one subject came twice during each phases of the menstrual cycle). After an 8-hour baseline sleep episode, participants underwent an URSW consisting of 60-min waking episodes in dim light (<10 lux) alternating with 60-min nap episodes in total darkness. Throughout this procedure, participants remained in a semi-recumbent position and BT and CBT were monitored continuously. A dual harmonic regression model was used to assess circadian phase and amplitude of both body temperature series.
Results: The dual harmonic regression revealed a significant variation of CBT and BT (95% CI not including the zero axis). Comparison of circadian phases and amplitudes revealed no significant difference between parameters assessed from the BT and CBT ($p=0.85$ and $p=0.86$, respectively). The mean value of BT across all waking episodes was significantly lower than that of CBT (minus 0.23°C, $p=0.034$), while no significant difference was found for the mean values of CBT and BT during all nap episodes.
Conclusion: This study suggests that BT can be an acceptable alternative to CBT for the assessment of circadian phase and amplitude. While the BT is lower than CBT during waking episodes, it is not the case during napping episodes. This finding suggests a different masking effect of sleep on temperature levels recorded rectally versus by our brain sensor.

0161

THERMOREGULATORY CHANGES ACROSS THE MENSTRUAL CYCLE: IMPLICATIONS FOR SLEEP QUALITY

Shechter A, Boivin D
McGill University, Montreal, Quebec, Canada

Introduction: Variations in body temperature, and in sleep onset, duration and structure, are seen across the menstrual and circadian cycles. Also, it was shown that sleep onset is associated with increased heat loss at the extremities. Our goal was to test the hypothesis that an interaction between menstrual and circadian factors would simultaneously affect body temperature and sleep quality.
Methods: Seven women were studied during the mid-follicular (MF) and mid-luteal (ML)phases of their menstrual cycle. Participants underwent a 72-hour multiple-nap procedure (36 cycles of 60-min wake/60-min nap), designed to assess the circadian variation of sleep propensity. Core-body temperature (CBT; rectal) and distal temperature (DT; hands/feet) were recorded, and a distal-core temperature gradient (TG) was calculated as an index of heat loss. Subjective sleep quality (SSQ; z-transformed) was assessed via numeric rating following each nap.
Results: Dual-harmonic regression revealed a significantly reduced CBT amplitude in ML vs. MF ($p=0.02$). Two-way ANOVA´s revealed significant circadian phase × menstrual phase interactions for CBT, DT and TG ($p<0.01$). A significant main effect of menstrual phase was observed for CBT ($p<0.001$), DT ($p=0.025$) and TG ($p=0.006$). A significant main effect of circadian phase was observed for CBT, DT and TG at both menstrual phases ($p<0.001$). Pearson´s correlations revealed significant negative correlations between CBT & SSQ in both menstrual phases (MF $r=-0.7289$; ML $r=-0.7788$) as well as significant positive correlations between DT & SSQ and TG & SSQ (DT: MF $r=0.7906$; ML $r=0.7493$; TG: MF $r=0.7352$; ML $r=0.7531$).
Conclusion: This study demonstrated that an interaction between menstrual and circadian phases is involved in temperature regulation. It supports an association between heat loss and improved sleep quality. Interestingly, we found elevated CBT and decreased TG (less efficient heat dissipation) in ML compared to MF. This implies that a compromised thermoregulatory system may play a role in producing ML-associated sleep impairments.

0162

PERCEIVED HEALTH AND PSYCHOLOGICAL CONSEQUENCES ASSOCIATED WITH WORK SCHEDULES FOR

Vallieres A,[1] Morin C,[2] Ivers H,[3] Melanie L[1]
(1) Universite Laval, Quebec, Canada, (2) Laval University, Ste-Foy, Quebec, Canada, (3) Laval University, Quebec, Canada

Introduction: The impact of shift work sleep disorder (SWSD) on physical and psychological functioning is poorly documented. Only a few studies demonstrated a high rate of depressive symptoms and low work productivity among night workers suspected of suffering from SWSD. This study aims at assessing the impact of the work schedule on perceived health and psychological variables of night and rotating shift workers.
Methods: The sample consisted of 192 adults (44% of women; age, M = 37.2), 20 permanent night workers, 76 rotating night shift workers, and 96 day workers selected from a larger epidemiological study. Each rotating shift worker and night worker was paired with a day worker based on gender, age, income, and insomnia symptoms. Each group of workers was further classified into a good sleepers or insomnia symptoms groups. Participants completed self-reported questionnaires about sleep variables (e.g., total sleep time), health related variables (e.g., self-perceived health, quality of life measured with the SF-36, medication use), and psychological variables (e.g., anxiety, depression, fatigue).
Results: Results suggested that there were differences mainly on sleep and health related variables for workers without insomnia complaint. Night workers in this subgroup reported a shorter sleep duration ($F(2,185) = 5.72$, $p < .01$) and a lower perceived mental health on the SF-36 ($F(2,185) = 3.48$, $p < .05$) than good sleepers working day or rotating shifts. These differences were no longer present for subgroups of workers with insomnia symptoms. For these workers, permanent night workers used more hypnotics than the other two insomnia symptoms subgroups ($F(2,185) = 2.96$, $p < .05$). Also, workers with insomnia symptoms presented high levels of anxiety, depression, and fatigue regardless of work schedules.
Conclusion: These results suggest that the impact of a work schedule on perceived health and psychological variables appears less significant than has been previously reported. However, it seems that the presence of insomnia symptoms may better explain the impact on perceived health and psychological variables. Further analyses are needed to specify the proportion of perceived health and psychological consequences explained by insomnia symptoms for each group of workers.
Support (optional): Research supported by the Canadian Institutes of Health Research (MT42504).

0163

INFLUENCE OF CIRCADIAN MISALIGNMENT ON THE ADIPOCYTE HORMONE LEPTIN

Nguyen J, Wright K
University of Colorado at Boulder, Boulder, CO, USA

Introduction: Sleep restriction to <4h per night has been reported to reduce circulating leptin levels and increase hunger. Low leptin levels have also been hypothesized to contribute to obesity by increasing food intake. The influence of circadian misalignment, which commonly occurs during shift work, on leptin levels is unknown. Therefore, we tested the hypothesis that circadian misalignment would reduce leptin levels.
Methods: Fourteen healthy participants (12 males, 2 females), aged 31.6±5.9 (mean±SD) with BMI 24.3±2.2 lived in the laboratory for up to two months. After three weeks of a consistent sleep-wake schedule at home, six laboratory baseline days and nights, a 40-h constant routine to estimate circadian melatonin phase, and an 8-h recovery sleep episode, participants were scheduled to a 24.0-h or 24.6-h dim light-dark wakefulness-sleep schedule. Leptin levels were measured in plasma collected hourly at baseline and following ~13 days of the dim light-dark schedule. Sleep was recorded at baseline, and ~3 days before and after leptin assessment. Changes to melatonin phase, leptin levels, and sleep were assessed using repeated measure ANOVA.
Results: The phase angle between the dim light melatonin onset and scheduled sleep was maintained in 7 participants (entrained group); whereas, phase angle was advanced by ~4-h on average in 7 participants (misaligned group)($p<0.05$). Sleep latency, TST, and stage 2 were decreased (~9 min, ~40 min, ~35 min respectively); whereas, WASO increased (~49 min)($p<0.05$) in the misaligned group. The diurnal profile of rising leptin levels during scheduled sleep was not significantly altered by circadian misalignment; however, circadian misalignment significantly reduced leptin levels ($p<0.05$) during scheduled wakefulness.
Conclusion: Circadian misalignment and associated sleep loss—of a degree much less than previously reported—reduces circulating levels of leptin, which may be a factor that increases the risk of obesity in shift workers.
Support (optional): Research Supported by NIH HL-073196, NIH M01-RR00051, and NASA Cooperative Agreement NCC 9-58 with the National Space Biomedical Research Institute.

0164

OBJECTIVE ALERTNESS CORRELATES WITH MOOD CHANGES DURING 44 HOURS OF SLEEP DEPRIVATION

Richards J, Lipizzi E, Balkin T, Grugle N, Killgore W
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: Although sleep deprivation has been found to have a negative effect on subjective mood, the relationship between objective alertness and specific mood dimensions remains poorly characterized. Using the Psychomotor Vigilance Task (PVT) and the Stern Visual Analog Mood Scales (VAMS), we examined the relationship between alertness and eight mood dimensions: Afraid, Angry, Confused, Energetic, Happy, Sad, Tense, and Tired over a period of two nights without sleep.
Methods: Fifty-four volunteers (29 males) were administered the Psychomotor Vigilance Test (PVT) and the Stern Visual Analogue Mood Scales (VAMS) every two hours in order to track their objective alertness and subjective mood ratings during 44 hours of total sleep deprivation. Mean PVT Speed (1/RT*1000) performance was calculated across all subjects for each administration session. Similarly, mean mood ratings were calculated at each session. Pearson correlations between PVT and VAMS were then compared.
Results: Pearson correlations of session means showed a significant negative correlation between PVT speed and mood scales measuring responses to: Afraid (r=-.71), Angry (r=-.76), Confused (r=-.70), Sad (r=-.91), Tense (r=-.87), and Tired (r=-.89). There was a significant positive correlation between PVT speed and ratings on the Energetic (r=.85) and Happy (r=.88) scales (all p´s<.001, and remained significant following Bonferroni correction).
Conclusion: Objective alertness was significantly related to subjective mood on eight dimensions measured by the VAMS. Declines in alertness were highly related to worsening of mood, particularly feelings of sadness and subjective feelings of reduced energy level. Findings

suggest that simple alertness and mood may share a common substrate that is affected by sleep loss. Future research may examine whether these two aspects of functioning account for separate variance in predicting changes in higher order cognitive performance due to sleep loss.

0165

COMORBIDITIES IN DELAYED SLEEP PHASE SYNDROME

Jaksa A, Eisengart J, Kane P, Lu B, Naylor E, Zee P, Reid K
Northwestern University, Chicago, IL, USA

Introduction: Psychiatric comorbidities are common in Delayed Sleep Phase Syndrome (DSPS). Systematic characterization of psychiatric comorbidities in DSPS is limited. The current study examines psychiatric comorbidities and sleep related quality of life in DSPS patients.
Methods: 30 DSPS (mean age 34 ± 11.4, 53.3% female) patients as determined by International Classification of Sleep Disorders Criteria and 12 controls (mean age 34 ± 15.2, 41.7% female) completed the Beck Depression Inventory (BDI), Center for Epidemiologic Studies-Depression Scale (CES-D), and the Functional Outcomes of Sleep Questionnaire (FOSQ). Approximately one month later, patients completed a Structured Clinical Interview for DSM-IV Disorders (SCID). Groups were compared using t-tests.
Results: The SCID indicated that there was a greater number of DSPS patients than controls with a history (22 vs 4) or current (12 vs 3) diagnoses of Axis 1 disorders. Mood, anxiety, and substance abuse disorders were the most common diagnoses in DSPS. Half of the DSPS patients with a current diagnosis had one or more of these disorders. Major Depressive Disorder was present in 33% of the DSPS subjects. DSPS patients scored significantly higher on the: BDI (9.9 vs 3.4) and the CES-D (14.5 vs 5.8) compared to controls (p=0.01). DSPS patients scored significantly lower (p = 0.02) on the FOSQ (94.1) than controls (106.2). The FOSQ was similar between those with and without a current disorder.
Conclusion: This study indicates that mood, anxiety and substance abuse disorders are very common in DSPS patients. It is not clear whether DSPS is a precipitating or perpetuating factor for these psychiatric comorbidities. While sleep related quality of life is reduced in patients with DSPS, this does not seem to be due to psychiatric disorders. These disorders, if left untreated, may pose a challenge for effective treatment of DSPS. A detailed history and interview to determine psychiatric disorders is warranted.
Support (optional): Funding: 1R01 HL069988-01A1

0166

CIRCADIAN PHASE INFLUENCES MOOD AND WELL BEING

Nguyen S,[1] Nguyen J,[1] Hull J,[2] Czeisler C,[2] Wright K[1]
(1) University of Colorado at Boulder, Boulder, CO, USA, (2) Brigham and Women's Hospital / Harvard Medical School, Boston, MA, USA

Introduction: A circadian variation in happiness has been reported in a prior study that used a forced desynchrony protocol to control for the influence of prior wakefulness. We used factor analysis to assess the influence of circadian phase on multiple measures of mood and well-being also using data from a forced-desynchrony protocol. We hypothesized that the factor structure would change across circadian phase and that the number of factors would be largest near the temperature minimum when alertness and performance are at their worst.
Methods: Fifteen healthy subjects (12 men, 3 women), aged 31.9±6.3 years (Mean±SD), were scheduled to a 28-h day forced desynchrony for 12 consecutive days. Body temperature, recorded every minute, was averaged into 1-h bins. Twenty-one mood and well-being measured were assessed using visual analog scales every 2-h during scheduled wakefulness and data were averaged into 60 degree circadian bins. Scales include measures of: tranquil, competent, friendly, sociable, content, stress, sadness, relaxed, physically exhausted, strong, sick, fresh as a daisy, clearheaded, alert, energetic, quickwitted, sharp, attentive, interested, well-coordinated, and motivated. Factor analysis (varimax rotation, normalized) was performed on circadian bins and factors with eigenvalues > 1.0 were included.
Results: Exploratory factor analysis reduced the 21 mood and well-being measures to two or three factors for circadian bins near the temperature minimum, whereas only one factor was observed near the temperature maximum. In addition, measures that loaded on specific factors were inconsistent across circadian phase. Factors loadings shortly after the temperature minimum were representative of mental/physical fatigue, social interest, and psychological stress. Derived factors explained over 85% of the variance in mood and well-being independent of circadian phase.
Conclusion: The emergence of one dimension of mood and well-being near the temperature maximum and of more than one dimension near the temperature minimum demonstrates that factors regulating mood are influenced by circadian phase.
Support (optional): Research Supported in part by NASA Cooperative Agreement NCC 9-58 with the National Space Biomedical Research Institute and by the NIH-HHMI Scholars Program for Diversity in the Biosciences at the University of Colorado.

0167

PERIODIC LEG MOVEMENTS IN BIPOLAR PATIENTS ACROSS VARIOUS CIRCADIAN PHASES

Waddington Lamont E,[1] Lalinec M,[2] Beaulieu S,[2] Boivin D[1]
(1) McGill University, Montreal, Quebec, Canada, (2) McGill University, Quebec, Canada

Introduction: Limb discomfort and periodic leg movements (PLM) tend to increase during the evening and at night in patients with restless leg syndrome (RLS). A negative correlation between PLM and core body temperature (CBT) was observed suggesting a circadian variation of PLM. The aim of the present study was to explore the circadian variation of PLM in bipolar patients.
Methods: Four bipolar patients (3 men, 1 woman; 40-47yrs), stabilized on lithium and/or risperidal, and 3 healthy controls (2 men, 1 woman; aged 20-42yrs) were recruited. Following two 8-hour sleep episodes, participants underwent a 48-hour ultra-rapid sleep-wake cycle procedure (URSW; 60 min wake/60 min nap). CBT was recorded using a rectal sensor. Sleep was polysomnographicaly recorded. PLM were measured using right and left anterior tibialis EMG and quantified during 20-sec epochs scored as sleep (PLMS) or waking (PLMW). PLMS leading to arousals (PLMA) were also quantified. Correlations were calculated between PLM, sleep onset (SO), total sleep time (TST), and CBT. One-factor ANOVA was used to assess the circadian variation of PLM. Results are reported as mean ± SEM.
Results: Baseline sleep recordings revealed PLM is all bipolar patients (index per hour of PLMS: 8.44±3.46; PLMW: 2.56±1.30; PLMA: 0.55±0.75). The average number of PLMW per nap was 10.08±4.12, and PLMS per nap was 4.15±1.19. PLMA were virtually absent. Significant correlations were observed between PLMW (but not PLMS or PLMA), SO ($r= 0.67$, $p<0.01$), and TST($r= -0.72$ $p<0.01$). No significant variation of PLM parameters were observed across the naps, nor were correlations between PLM parameters and CBT.
Conclusion: The present study did not indicate a clear variation of PLM

across circadian phases in bipolar patients. However, the use of medications limits the interpretation of results and PLM in these patients may be quite different from those observed in RLS patients.
Support (optional): Study supported by the Canadian Psychiatric Research Foundation and the Gustav Levinschi Foundation. DBB is supported by CIHR and the FRSQ. EWL is supported by the IRSST.

0168

LESIONING THE SUPRACHIASMATIC NUCLEUS ABOLISHES ULTRADIAN RHYTHMS OF LOCOMOTOR ACTIVITY IN RATS

Shea S,[1] Hu K,[1] Buijs R,[2] Scheer F[1]
(1) Brigham and Women's Hospital, Boston, MA, USA, (2) Netherlands Institute for Brain Research, Netherlands

Introduction: Locomotor activity in rats exhibits a circadian rhythm at ~24h and ultradian rhythms at shorter time scales. Circadian rhythms in activity are generated by the suprachiasmatic nucleus (SCN), but the neural sites responsible for ultradian rhythms are unknown. We tested whether the SCN contributes to the generation of ultradian rhythms in locomotor activity.
Methods: Locomotor activity was recorded in 7 control and 7 SCN-lesioned (SCNx) Wistar rats throughout separate 10-day protocols in light/dark (12-h light, 12-h dark; LD) and constant dark (DD). Locomotion was measured using infrared beam crossings within individual cages. Power spectrum analysis was used to assess rhythmicities in locomotor activity.
Results: Control rats exhibited a significant ~24h complex waveform in activity with 3-4 specific peaks in LD and DD. This waveform resulted in a power spectrum with a sharp peak at 24h and many `apparent´ ultradian rhythms that occurred only at precise harmonic frequencies of 24h (i.e., 24/2=12h, 24/3=8h, 24/4=6h, 24/5=4.8h, 24/6=4h and 24/7=3.4h), with negligible spectral power between these harmonics. All rhythms in the circadian and ultradian ranges were abolished by SCN-lesions in both LD and DD, while mean activity levels did not change.
Conclusion: The SCN is critically involved in regulating locomotor activity not only at a frequency of ~24h but also in the ultradian range (<24h) at precise harmonic frequencies of the underlying circadian rhythm. This suggests that ultradian rhythms in activity may emanate from the SCN itself as it regulates a circadian rhythm in activity with a 24 hour shape that is not purely sinusoidal. An alternative hypothesis is that ultradian rhythms in activity are generated from locations outside the SCN, but the fact that they occur at precise harmonics of the fundamental circadian oscillation suggests that such ultradian rhythms must interact with and be coupled to the SCN pacemaker.
Support (optional): Supported by HL076446, FAJL supported by Pickwick Fellowship

0169

EXERCISE DISTRIBUTED ACROSS DAY AND NIGHT DOES NOT ALTER CIRCADIAN PERIOD IN HUMANS

Cain S, Duffy J, Czeisler C
Brigham and Women's Hospital / Harvard Medical School, Boston, MA, USA

Introduction: In rodents, increased activity due to running wheel access is associated with a change in observed circadian period. In humans, exposure to exercise has failed to demonstrate similar effects on period. Methodological issues with prior studies such as light exposure during exercise, length of study, and method of measuring period confounded prior evaluation of effect of exercise on period in humans.
Methods: In the present experiment, we examine the effect of exercise on period in a 44-day long within-subjects inpatient study. We used a 20-hour forced desynchrony protocol, under dim light conditions in which subjects are exposed to exercise across circadian phases. Intrinsic circadian period was measured using both core body temperature and hourly plasma melatonin samples.
Results: Consistent with previous reports, we find no effect of exercise on endogenous circadian period as measured by either core body temperature or melatonin.
Conclusion: Exercise distributed across the biological day and night does not appear to affect circadian period.
Support (optional): This research was supported by a United States Air Force grant (AFOSR F49620) awarded to CAC, and was conducted in the Brigham and Women´s Hospital General Clinical Research Center supported by RR02635.

0170

THE CIRCADIAN PACEMAKER CONTRIBUTES TO INTRINSIC SCALE-INVARIANT PATTERNS OF CARDIAC DYNAMICS ACROSS A WIDE RANGE OF TIME SCALES – SPANNING MINUTES-24 HOURS

Hu K,[1] Scheer F,[1] Buijs R,[2] Shea S[3]
(1) Brigham and Women's Hospital, Boston, MA, USA, (2) Netherlands Institute for Brain Research, Netherlands, (3) Boston, MA, USA

Introduction: Heartbeat fluctuations in mammals display a robust temporal structure characterized by scale-invariant/fractal patterns over a wide range of time scales from seconds to 4 h. The scale-invariant heartbeat fluctuations in humans persist during varied behaviors and environments but change with autonomic blockade, suggesting the fluctuations are endogenously controlled. Such scale invariant patterns break down in heart disease and are a marker of reduced survival. We recently discovered that scale invariant patterns of activity in rats are influenced by the internal circadian pacemaker (suprachiasmatic nucleus, SCN). Moreover, this influence occurs at a wide range of time scales from minutes to 24 h, rather than solely at a period of ~24 h. Thus, we tested whether scale invariant cardiac dynamics also are influenced by the SCN, and across the same wide range of time scales.
Methods: We analyzed heart rate recordings from 7 control and 7 SCN-lesioned (SCNx) Wistar rats. Each rat was housed individually under 12-h dark:12-h light cycles for 10 days (LD protocol) and under constant darkness for 10 days (DD protocol). Heart rate was collected every four minute across these protocols, and scale-invariant patterns of cardiac dynamics were assessed using detrended fluctuation analysis.
Results: A scale-invariant pattern of heart rate occurred in control rats across a wide range of time scales: from minutes to 24 h. In SCNx rats, the scale-invariant pattern completely broke down at time scales >4 h resulting in heart rate fluctuations resembling white noise without feedback control.
Conclusion: The SCN appears to more complex than a simple 24 h pacemaker as it imparts scale-invariant patterns of activity and cardiac dynamics in rats across a wide range of time scales spanning 4 to 24 h, rather than solely at a period of ~24 h. A different neuro-anatomical source must be responsible for the previously detected scale free behavior from minutes to 4 h.
Support (optional): Supported by HL076409, HL076446, FAJL supported by Pickwick Fellowship

0171

FUNCTIONAL KNOCKOUT OF THE VPAC2 RECEPTOR INCREASES OVERALL SLEEP TIME UNDER ENTRAINED CONDITIONS

Naylor E,[1] Harmar A,[2] Turek F,[3] Zee P[1]
(1) Northwestern University, Chicago, IL, USA, (2) University of Edinburgh, Edinburgh, Scotland, United Kingdom, (3) Northwestern University, Evanston, IL, USA

Introduction: Functional knockout of the Vasoactive Intestinal Peptide (VIP) receptor VPAC2 in mice results in an activity rhythm phenotype characterized by blunted amplitude, reduced activity intensity and little or no rhythmicity during conditions of constant darkness. These alterations have been attributed to changes in the circadian timing mechanism. We tested the hypothesis that mice lacking the VPAC2 receptor will also demonstrate changes in the timing of sleep and sleep architecture.
Methods: Seven adult male C57BL6 mice homozygous for the deletion of the VPAC2 receptor along with six colony-matched, age-matched controls were implanted with electroencephalograph (EEG) recording electrodes. Sleep was recorded under both entrained (12 hours light/ 12 hours dark) and free-running (constant darkness) conditions.
Results: VPAC2 knockout mice demonstrated significantly less wakefulness (Vipr2-/- 812.2 ± 13 min, wt 855 ± 17 min; p=0.03, t-test) under entrained conditions. This decreased wakefulness was almost entirely replaced by increased NREM sleep amounts. Whereas wild-type controls showed much greater circadian variation in sleep times between light and dark, the time asleep and number of sleep bouts in VPAC2 knockout mice was more evenly distributed throughout the day. Compared to wild-types, Vipr2-/- mice showed significantly more NREM sleep during the lights off period (Vipr2-/- 34.8% ± 4.0%, wt 17.8% ± 2.2%; p =0.004) and less NREM sleep (Vipr2-/-41.9% ± 3.0%, wt 53.9% ± 2.2%; p =0.009) during the lights on period. Under constant darkness conditions, VPAC2 knockout mice continued to demonstrate more NREM and REM sleep bouts during the rest phase, however, there was no significant difference in overall sleep time.
Conclusion: VIP and its receptor appear to play an important role in not only the diurnal distribution of the sleep/wake cycle but also in the regulation of the total amount of NREM sleep and wake under entrained conditions.
Support (optional): National Institutes of Health grant #: T32 AG020506-02

0172

CHANGES IN NIGHTTIME ULTRADIAN PARAMETERS OF HEART RATE OVER TIME IN THE ELDERLY

Stein P,[1] Oliveira L,[2] Domitrovich P,[2] Lundequam E,[2] Redline S[3]
(1) Washington University in St. Louis, Saint Louis, MO, USA, (2) Washington University School of Medicine, St. Louis, MO, USA, (3) Case Western Reserve University, OH, USA

Introduction: Heart rate (HR) displays ultradian rhythms which are prominent during the nighttime. These rhythms reflect cardiac autonomic functioning but are not surrogates for sleep stage, at least among the elderly. We have developed parameters to characterize these rhythms. Little is known about changes in nighttime ultradian HR rhythms over time in the elderly.
Methods: N=24 participants (baseline age 70±3 yrs, 7M,17F) with Holter recordings in the Cardiovascular Health Study (CHS yr 2 and CHS yr 7) and polysomnograms (PSGs) in the Sleep Heart Health Study (SHHS1=CHS yr 8, SHHS2=CHS yr 13) were studied. ECGs from all 4 recordings were analyzed using a commercial Holter scanner (MARS 8000, GE Medical systems, Milwaukee, WI). HR was calculated for every 2-min for each recording. Bed and wake times were estimated from HR patterns on the Holter recordings. Ultradian patterns of HR, were quantified beginning 1.5 hours before bed until wake on the Holters and over the duration of recording for the PSGs which tended to start about 1.5 hrs before lights out. Results from each of the 4 recordings were compared by ANOVA with repeated measures with LSD post hoc testing.
Results: Although the number and durations of ultradian HR cycles were not different with increased age, some ultradian measures of HR showed progressive declines between the first and second and second and third recordings. Among them were the maximum cycle amplitude (14.7±4.6, 13.7±3.9, 8.8±4,8 and 11.2±4.5 bpm), mean cycle amplitude (6.7±1.9, 6.1±1.9, 4.6±2.1 and 5.7±2.2 bpm), maximum upward slope (0.64±0.29, 0.52±0.21, 0.46±0.32 and 0.49±0.27 bpm/s) and mean upward slope (0.27±0.8, 0.22±0.8, 0.19±0.09 and 0.21±0.10 bpm/sec) of the HR cycles. There were no significant differences in any ultradian parameter of HR over the 5 years between SHHS1 and SHHS2 for these participants.
Conclusion: Ultradian HR rhythm changes are consistent with diminished cardiac autonomic functioning with aging in these predominantly healthy participants. Changes may level off at more advanced ages. The utility of these novel HRV measures and changes in these measures to identify abnormal cardiac autonomic functioning during sleep will be investigated.

0173

MODAFINIL IMPROVED THE ABILITY TO SUSTAIN ATTENTION AND DECREASED WAKE STATE INSTABILITY IN PATIENTS WITH SHIFT WORK SLEEP DISORDER

Dinges D,[1] Wright K,[2] Walsh J,[3] Czeisler C[4]
(1) University of Pennsylvania School of Medicine, The Division of Sleep and Chronobiology, Philadelphia, PA, USA, (2) University of Colorado at Boulder, Boulder, CO, USA, (3) St. John's/St. Luke´s Hospital, Sleep Medicine and Research Center, Chesterfield, MO, USA, (4) Harvard Medical School, Division of Sleep Medicine, Boston, MA, USA

Introduction: Patients with excessive sleepiness (ES) and shift work sleep disorder (SWSD) have impaired alertness that is associated with an increased risk of accidents. This analysis evaluated the effect of modafinil, a wake-promoting agent, on the ability to sustain attention and decrease wake state instability in patients with ES associated with SWSD.
Methods: Night-shift workers with nighttime ES and daytime insomnia for ≥3 months due to SWSD participated in a double-blind, placebo-controlled study. Patients were randomized to receive modafinil 200 mg (n=89) or placebo (n=104) before each night shift for 3 months. Median reaction time (RT), the ability to sustain attention (number of lapses), optimal response time (10% fastest RT), response time in the lapse domain (10% slowest RT), and wake state instability (mean standard deviation of correct RTs) were assessed via the Psychomotor Vigilance Test. Adverse events were monitored.
Results: Modafinil improved optimal response time, response time in the lapse domain, lapses in attention, and wake state instability versus placebo, although performance worsened for some measures in both groups. The changes from baseline to final visit were significantly better with modafinil versus placebo for 10% fastest RT (–1.9 vs +14.9 msec, *P*<.01), 10% slowest RT (+501.9 vs +1332.4 msec, *P*<.001), mean number of lapses (–3.8 vs +7.2; *P*<.01), and wake state instability (+173.4 vs +441.8 msec; *P*<.05). The change from baseline in median RT (+0.3 vs +60.2 msec) was similar for the modafinil and placebo

groups (P>.05). Patients continued to show evidence of ES during the night shift following administration of modafinil. Commonly reported adverse events in the modafinil and placebo groups were headache (modafinil, 26%; placebo, 19%) and nausea (modafinil, 9%; placebo, 3%).
Conclusion: Modafinil improved the ability to sustain attention, decreased wake state instability, and was well tolerated in patients with ES associated with SWSD.
Support (optional): Cephalon, Inc

0174

CEREBROSPINAL FLUID HISTAMINE LEVELS IN RATS ACROSS 24 HOURS AND AFTER VARIOUS BEHAVIORAL AND PHARMACOLOGICAL MANIPULATIONS

Soya A,[1] Song Y,[1] Kodama T,[2] Honda Y,[2] Fujiki N,[1] Nishino S[3]
(1) Stanford University, Palo Alto, CA, USA, (2) Tokyo Metropolitan Institute for Neuroscience, Fuchu-shi, Japan, (3) Stanford University, Stanford, CA, USA

Introduction: We previously reported that CSF histamine levels are reduced in human narcolepsy and other primary hypersomnia (APSS 2002, 04). Since histamine is one of the wake-promoting amines, reduced histaminergic neurotransmission may be involved in the pathophysiology of these hypersomnias as a result. However, the nature and origin of the CSF histamine (i.e., terminal release or release from neuronal mast cells) and how their levels fluctuate across different times and after various manipulations that alter the vigilance states, are not yet known. We measured CSF histamine levels in rats collected by repeated CSF taps across 24 hours, and after various behavioral and pharmacological manipulations. As reference, CSF hypocretin-1 levels were also measured in the same CSF samples.
Methods: A total of 20 male Sprague-Dawley rats were used, and they were maintained in a 24-hour light–dark cycle (LD 12:12). Four sets of experiments were carried out 1) Diurnal fluctuation: CSF samples were collected at 2-hour intervals over 24 hours. 2) Sleep deprivation: After 6 hours of sleep deprivation, CSF samples were collected at ZT 6. 3) Food deprivation: After 48 hours of food deprivation, CSF samples were collected at ZT 10, 22. 4) Pharmacological manipulations; thioperamide (H3 antagonist) 1.25, 5 mg/kg i.p., amphetamine (5 mg/kg i.p.) and modafinil (200 mg/kg i.p.) were administered at ZT 2, and CSF sample were collected at ZT 4 and 6. CSF histamine levels were measured by HPLC, and hypocretin-1 levels were measured by RIA.
Results: As previously reported, we observed that CSF hypocretin significantly fluctuates across 24 hours (high during dark period and low during light period) and the levels were also increased by sleep deprivation, but not after 48 hours of food deprivation. Amphetamine and modafinil moderately increased CSF hypocretin levels, while thioperamide had no effect on CSF hypocretin levels. In contrast, the high dose of thioperamide significantly increased CSF histamine levels. However, any significant fluctuation in CSF histamine levels across 24 hours or any changes in CSF histamine levels after sleep and food deprivation were not found.
Conclusion: Contrary to hypocrestin-1 levels in the CSF, histamine in the CSF in rats does not fluctuate across 24 hours, either by sleep and food deprivation or amphetamine and modafinil administrations. Since high doses of thioperamide increase neuronal histamine release in the brain, increased CSF histamine levels and changes in the CSF histamine levels may partially reflect the activity of central histamine neurotransmission. However, CSF histamine did not fluctuate physiologically or by the manipulations that alter alertness. Although the functional significance of reduced CSF histamine levels in human cases still needs to be determined, the results of the current study suggests that CSF histamine levels, at least in rats, are not sensitive reflections of central histamine neurotransmission.
Support (optional): This research was supported by NIH grant MH072525.

0175

MORNINGNESS-EVENINGNESS'S RELATIONSHIP TO DEPRESSION IS MEDIATED BY POSITIVE, NOT NEGATIVE, AFFECT

Hasler B,[1] Allen J[2]
(1) University of Arizona, Tucson, AZ, USA, (2) University of Arizona*, Tucson, AZ, USA

Introduction: Research suggests that morningness-eveningness, which is correlated with circadian phase, predicts overall psychological health. Specifically, greater morningness appears to be associated with less psychological distress. A separate literature connects circadian rhythms to the Behavioral Approach System (BAS) and positive affect (PA), but not to the Behavioral Inhibition System (BIS) or negative affect (NA). Integrating this research and theoretical underpinnings, morningness-eveningness should relate to depression severity and also BAS and PA, but not to BIS and NA.
Methods: In the context of a larger study investigating risk for depression, 109 adults (mean age = 21.62 ± 22.05 years, 81 females) completed the Horne-Ostberg Morningness-Eveningness Questionnaire (MEQ), Behavioral Inhibition and Behavioral Approach System Questionnaire (BIS/ BAS), Positive and Negative Affect Schedule (PANAS), and Beck Depression Inventory, 2nd Edition (BDI-II). As predicted, greater morningness (higher MEQ scores) was associated with lower BDI-II scores ($r = -.22$, $p < .05$). To assess potential causal pathways, hierarchical linear regressions were run to assess relative contributions of the MEQ, BAS-Reward Responsivity and Drive (BAS-RR and BAS-D) subscales, and PA in predicting the BDI-II. Indirect (mediation) effects were also assessed.
Results: As predicted, greater morningness (higher MEQ) was significantly associated with greater reward responsivity (higher BAS-RR; $r = .23$, $p < .05$) and higher levels of PA ($r = .22$, $p < .05$), but not with NA nor BIS scores. Indirect effects of morningness-eveningness on depression were found via the BAS-RR (Sobel test statistic = -2.17, $p < .05$) and PA (Sobel test statistic = -2.30, $p < .05$). The reverse pathways were not significant. Follow-up analyses supported that PA took priority over BAS-RR as the intervening variable.
Conclusion: In accordance with previous research, greater morningness was associated with less psychological distress in this sample. Results were consistent with the BAS and PA mediating this association.
Support (optional): This research was supported, in part, by grant R01 MH066902 from the National
Institutes of Health.

0176

PERSONALITY TRAITS AND COMORBIDITY OF CIRCADIAN RHYTHM SLEEP DISORDERS

Hashizume Y
Kurume University School of Medicine, Department of Psychiatry, Kurume, Fukuoka, Japan

Introduction: Changes in Japanese lifestyles by prevailing Internet mobile telephones and 24-hour convenient stores causes shorter sleeping time and longer time awake at midnight and irregular sleep-wake cycles. For this reason, an increasing number of patients with delayed sleep phase disorder and irregular sleep-wake type due to changing lifestyles are being referred to our sleep disorder clinic. In this study, we

examined personality traits and comorbidity of patients admitted to our hospital.
Methods: The subjects consisted of 35 males and 29 females (average age 21.5±9.9 years old) diagnosed with delayed sleep phase disorder or irregular sleep-wake rhythm by the international classification of sleep disorders using actigraphy monitoring or sleep log. Circadian rhythm sleep disorders are relatively complicated with other psychiatric diseases, the percentage of complication of which is 40-60%. Patients are treated by drugs (melatonin, vitamin B12, short acting hypnotics) and blight light therapy which resynchronizes the circadian rhythm in most patients. Some of subjects were admitted to our hospital and some underwent psychological tests (Yatada-Guilford personality inventory, Minnesota multiphasic personality inventory and Rorschch test) .
We measured certain hormones (growth hormone, melatonin, and cortisone) and conducted polysomnography(PSG). PSG was conducted for a few days after the admission day.
Results: The circadian sleep-wake rhythm returned to 24-hour regular sleep-wake schedule. Most of the patients also showed regular hormonal circadian rhythm. The average PSG results were; total sleep time of 528.4±134.4 minutes, sleep efficiency of 84.6±9.3%, sleep latency of 55.0±42.0 minutes, wake after sleep onset of 37.1±42.6minutes, and REM sleep latency of 88.6±48.3 minutes.
Conclusion: Seven out of 11 inpatients were diagnosed with psychiatric disorders. Resynchronized by the regular schedule of hospitalization, the circadian rhythm of most patients returned to a regular 24 sleep-wake cycle.

0177

CIRCADIAN SLEEP PHASE PREFERENCE AND ADJUSTMENT IN COLLEGE STUDENTS

Kim J
Pohang University of Science and Technology, Pohang, Kyungbuk, South Korea

Introduction: The present study evaluates the relationships between Morning/Evening(M/E) types and adjustment (such as sleep patterns, mental/physical health, academic performance) in Korean college students.
Methods: 399 college students in Korea (mean=21.6) completed a survey including morningness/eveningness(M/E) scale(Smith, Reilly and Midkiff, 1989), College Maladjustment(Mt) Scale(Wilderman, 1984), Pittsburg Sleep Quality Index(PSQI), Behavioral Health Questionnaire-20(Kopta and Lowry, 2002), Beck Depression Index, and questions on sleep habits and academic performance (GPA etc).
Results: The M/E scores(mean=30.94, sd=6.52) from 399 students ranged from 14 to 48 (lower scores indicating greater eveningness).

Major findings on the correlation between M/E scores and various adjustment variables are as follows :

1. The greater eveningness, the lower sleep quality on PSQI (p=.001). Among the component scores of the PSQI, the same trend was found on `subjective sleep quality´, `sleep latency,´ and `daytime dysfunction,´ while not on `sleep duration´.
2. The greater eveningness, the more maladjusted on college life on Mt (p=.000). Among the 4 component scores of the Mt, the same trend was shown on `confidence´, `physical/mental health´, `concentration´, while not on `anti-social tendency´.
3. The greater eveningness, the worse mental health on BHQ (p=.000).
4. The greater eveningness, the lower the GPA (p=.02). Further analyses shows that the difference comes mostly from the difference between the M/E scores of 22 and below (mean bedtime: 02:17am; mean wake-up time: 09:11am) and the M/E scores of 23 and above.

Conclusion: The present study shows that the greater eveningness, the more maladjusted in college life, in terms of global mental health, sleep quality, and academic performance. It seems important to give relevant information and a helpful guidance on good sleep habits to students from the beginning of college life.

0178

DESYNCHRONY BETWEEN SLEEP-WAKE CYCLE AND CIRCADIAN CYCLE LEADS TO SUPPRESSED PLASMA LEPTIN; POTENTIAL RELEVANCE FOR SHIFT WORKERS

Scheer F,[1] Hilton M,[1] Benjamin T,[1] Barb D,[2] Evoniuk H,[1] Mantzoros C,[3] Shea S[1]
(1) Medical Chronobiology Program, Division of Sleep Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA, (2) Endocrinology Diabetes and Metabolism, Beth Israel Deaconess Medical Center and Joslin Diabetes Center, Harvard Medical School, Harvard School of Public Health, Diana Barb, MA, USA, (3) Endocrinology Diabetes and Metabolism, Beth Israel Deaconess Medical Center and Joslin Diabetes Center, Harvard Medical School, Harvard School of Public Health, Boston, MA, USA

Introduction: Decreased circulating leptin signals negative energy balance, producing increased appetite and decreased energy expenditure. Shift work—characterized by sleeping out of synchrony with the endogenous circadian cycle—is associated with an increased risk for obesity. We wondered whether shift work causes changes in leptin that might predispose to obesity. Thus, we determined the effects upon plasma leptin, insulin, glucose, and cortisol of: (1) the sleep-wake cycle (independent from circadian effects); (2) the circadian cycle (independent from sleep/wake effects), and (3) the combined circadian and sleep/wake effects caused by sleeping out of synchrony.
Methods: 10 adults (5 female) underwent a 10 day 'forced desynchrony' protocol in dim light, wherein subjects slept at all phases of the circadian cycle—achieved by scheduling a recurring 28-hour `day´. On each 28-hour day subjects ate three standardized meals and a snack. Plasma leptin, insulin, glucose, and cortisol were measured hourly. Core body temperature was used to assess circadian phase.
Results: Independent from circadian phase, leptin increased throughout wakefulness and decreased during sleep, likely attributable to the eating/fasting cycle (ANOVA; P=0.0001). These sleep-wake cycle effects interacted with the circadian phase (P<0.0001), such that leptin levels were ~15% lower throughout the entire sleep/wake cycle when subjects slept during the biological day (12 hours out of synchrony) compared to sleeping during the biological night. This reduced leptin was not caused by decreased glucose, insulin or cortisol. Indeed, glucose actually increased by ~5% when subjects slept during the biological day (P=0.001).
Conclusion: Leptin is reduced across the entire sleep/wake cycle when subjects sleep ~12 hours out of phase from their habitual sleep time. These data suggest that shift work would reduce leptin, which could provoke increased appetite and decreased energy expenditure, and provide a possible physiological explanation for the reported risk of obesity in shift workers.
Support (optional): NIH RO1 HL064815; K24 HL076446 in support of SAS; Pickwick Fellowship in support of FAJLS; NCRR GCRC M01 RR02635

0179

HOMEOSTATIC AND CIRCADIAN RESPONSES TO 6-H SLEEP DEPRIVATION OF OCTODON DEGUS

Perryman J, Lee T, Opp M
University of Michigan, Ann Arbor, MI, USA

Introduction: Octodon degus are long-lived, diurnal rodents that display more consolidated sleep (longer sleep bouts) during the night versus the day, and have crepuscular bouts of activity around the light/dark transitions. The aim of the present study was to systematically determine in a laboratory setting homeostatic and circadian components of sleep-wake behavior of this diurnal species.
Methods: Our pilot study used four male degus. Animals were individually housed on a 12:12 Light/Dark cycle, without running wheels, at 18°C. Degus were surgically implanted with EEG electrodes and thermistors to record brain temperature. Infrared devices were used to detect activity in the cage, and infrared LEDs provided illumination. After recovery and 1 week of habituation, baseline recordings were made for 24 h. Animals were subsequently sleep-deprived by gentle handling for 6 h in the middle of the light phase (ZT3-ZT10) and dark phase (ZT15-ZT21). Following deprivation, animals were allowed 48 hours uninterrupted recovery sleep. Sleep-wake behavior was determined by visual scoring of records with a 12 s resolution.
Results: Following light phase sleep deprivation, animals displayed longer NREMS bouts during the first recovery hour (10.2±2.2min vs. 5.7±2.8min). After dark phase deprivation, NREMS bout length increased for 2-h following the protocol (8.8±1.9 min vs. 4.0±0.7min). Increased sleep consolidation did not persist more than two hours post deprivation. Significant changes in NREMS total amount and REMS total amount were not observed. Animals across conditions maintain their crepuscular activity bouts.
Conclusion: Degus display a circadian response to sleep deprivation. Our data suggest sleep deprivation during the dark "rest" phase consolidates NREMS more than during the light "active" phase. Degus model human circadian rhythms, pubertal development, and reproduction. Our new data suggest this species may be suitable as a model of human sleep because of the diurnal nature of responses to sleep deprivation.

0180

EFFECTS OF NOCTURNALLY-ADMINISTERED GREEN LIGHT ON LUTEINIZING HORMONE AND FOLLICLE-STIMULATING HORMONE IN YOUNG MEN

Grandner M,[1] Kripke D,[2] Elliott J,[2] Cole R[3]
(1) San Diego, CA, USA, (2) University of California, San Diego, La Jolla, CA, USA, (3) Alliant Health Systems, CA, USA

Introduction: Previous research found that bright light administered during early morning awakenings stimulated luteinizing hormone (LH). Light presented in the last two hours of sleep might stimulate a particularly sensitive time interval, and green light might be more effective than white light in photic, non-visual effects. No previous light mask studies have investigated LH and follicle-stimulating hormone (FSH).
Methods: Participants were 30 young adult males with minimal-mild depression. A light mask device was worn at night. Green masks had bright 10,000 lux green LEDs centered at 500nm wavelength. Placebo masks produced approximately 0.5 lux red light. Participants wore the masks for 11 nights. Each mask produced light for the 2.5 hours prior to the participant´s usual wake time. Participants were instructed to collect urine for 24-hours at the beginning and end of the study. Urinary LH and FSH were measured using double antibody immunoassay (EIA) kits. Twenty-one samples met reliability criteria and were included in analysis (green=11,red=10).
Results: Both groups demonstrated a decrease in LH following light treatment. The decrease in the green group (-1.5mIU/hr) was smaller than the red group (-6.01mIU/hr); however, a MANCOVA, with mean, mesor and acrophase as dependent variables, group as independent variable and time (baseline versus end of study) as covariate was not significant (T-squared= 0.128,F(3,37)=1.578,p=0.211). Preliminary FSH data suggested a stronger relationship than LH (mean green change=+0.17mIU/hr,SD=.89, red=-0.81mIU/hr,SD=1.45), with mean excretion difference significant between groups (1-tailed t(19)=2.89,p=0.035). Observed power was low, suggesting that there may not have been sufficient power to detect more difference between groups.
Conclusion: The results of the present study may be helpful in further understanding effects of nocturnal light on LH and FSH. Although differences were nonsignificant for LH and small for FSH secretion in this sample, the trends suggest that larger studies might be useful.
Support (optional): MH68545

0181

NEGATIVE SLEEP AND HEALTH OUTCOMES IN NIGHT SHIFT POLYSOMNOGRAPHIC TECHNICIANS

Powell E,[1] Barber L[2]
(1) Clayton Sleep Institute, St. Louis, MO, USA, (2) Saint Louis University, St. Louis, MO, USA

Introduction: It has been well documented that shift work is associated with decreased performance, impaired alertness, increased incidence of accidents, and disrupted sleep. Negative health outcomes, such as affective disorders, cardiovascular disease, and gastrointestinal disease have also been associated with performing shift work. Primary focus in studying shift work in healthcare workers has centered on residents or nursing staff. However, little research is available looking at the impact of shift work in polysomnographic technicians.
Methods: A total of 21 polysomnographic technicians working at various sleep labs in a Midwestern metropolitan region, who have worked at least six months during the night shift, completed a modified version of the Standard Shiftwork Index. This questionnaire assesses various modalities affected by shift work such as circadian rhythms, health, work satisfaction, and coping ability. The Pittsburgh Sleep Quality Index was integrated to assess sleep quality before, during, and after shift work each week.
Results: Using a model assessing job context factors, work/shift perceptions, and personality variables, significant correlations were found between poor cardiovascular health and shift incongruity (prefer days) ($r = .40$, $p < 0.05$), duration of performing shift work ($r = .41$, $p<0.05$), and work related performance ($r = .54$, $p<0.01$). In addition, those who reported increased fatigue leaned towards introversion ($r = .62$, $p<0.01$) and circadian rigidity ($r = .53$, $p<0.01$), and also reported poorer sleep quality before and during their shifts for the week. Path analyses regression indicated that a disengagement coping strategy in relation to perceived work performance may mediate the effect of shift incongruity and introversion on cardiovascular health, fatigue, and poorer sleep quality.
Conclusion: The data suggest polysomnographic technicians performing night shift work who have personal or circadian preference for a dayshift tend to have poorer coping strategies leading to decreased work performance, poorer sleep habits, and increased incidence of poor health outcomes.

0182

ARE THE CIRCADIAN RHYTHMS OF BLIND ADULT MALES LESS SENSITIVE TO SOCIAL CUES THAN FEMALES?

Lewy A,[1] Yuhas K,[2] Emens J,[1] Woods K,[3] Arntz D,[3] Songer J,[2] Johnson K,[1] Rough J,[3] Brick C,[3] Bussell C[3]
(1) Oregon Health & Science University, Portland, OR, USA, (2) Oregon Health & Science University, OR, USA, (3) OR, USA

Introduction: Since 1983, it has been known that totally blind people have different types of melatonin circadian rhythms. Because of preliminary data that we recently reported in pre- and post-pubertal blind children, we undertook a gender-specific analysis of our adult population, using more stringent definitions of circadian status (free-running vs. entrained). We also assessed range of oscillation in the free-running subjects, all of whom show relative coordination to unknown weak zeitgebers (as reported by us in 2005).
Methods: The retrospective analysis included 46 healthy subjects (25 males) with no ability to detect light. Plasma or saliva melatonin onsets (MOs) for each subject were determined using a 2/0.7 pg/ml (plasma/saliva, respectively) or a 10/3 pg/ml threshold. Average circadian period (tau), as well as two-point taus for each pair of consecutive MOs, were calculated using fitted slopes. Subjects were classified either as free-running (tau < 23.95 or ≥ 24.05 h for > 50% of a beat cycle) or entrained (≥ 6 MOs with 23.95 ≤ tau < 24.05 h and the 95% confidence interval overlapping 24.00 h). Relative coordination could be assessed in 19 (12 males) of the free-running subjects; range of oscillation was calculated as the difference between a subject's longest and shortest two-point taus.
Results: 75% of females and 100% of males studied to date were free-running. This sex difference was statistically significant ($p < 0.05$, Fisher´s exact test). A two-tailed t-test ($p < 0.05$) indicated that the range of oscillation was significantly greater in females [0.50 ± 0.22 h (S.D.)] than in males (0.33 ± 0.13 h).
Conclusion: Particularly if the weak zeitgebers are shown to be consistent in strength, phase and period, it appears that adult males may be less sensitive to them than adult females. These findings are consistent with those reported by Theresa Lee and co-workers: in the diurnal rodent Octodon degus, males are less sensitive to social cues than females.
Support (optional): This work was supported by Public Health Service Grants R01 HD42125, R01 AG21826, and R01 MH56874 (to A.J.L.) and 5 M01 RR000334 (to the GCRC of OHSU). A.J.L. was supported by the NARSAD 2000 Distinguished Investigator Award.

0183

DLMO/MID-SLEEP INTERVAL OF SIX HOURS PHASE TYPES SAD PATIENTS AND PARABOLICALLY CORRELATES WITH SYMPTOM SEVERITY

Lewy A,[1] Woods K,[2] Kinzie J,[2] Emens J,[1] Songer J,[3] Yuhas K[2]
(1) Oregon Health & Science University, Portland, OR, USA, (2) OR, USA, (3) Oregon Health & Science University, OR, USA

Introduction: Seasonal affective disorder (SAD, or winter depression) may be the first psychiatric disorder in which symptom severity correlates with a physiological marker before and after treatment in the same patients. In our SAD study published in 2006, we administered melatonin in the morning (to cause phase delays) and in the afternoon/evening (to cause phase advances). At the end of this report, we suggested that extant data sets could be re-analyzed to confirm the same three hypotheses: that 2/3rds of SAD patients are phase delayed and 1/3rd are phase advanced, in whom a parabolic (rather than a linear) curve most significantly fits base SIGH-SAD depression score data plotted against the phase angle difference (PAD) between the 10 pg/ml plasma dim light melatonin onset (DLMO) and mid-sleep, and that these data have a parabolic minimum 6 h (the "sweet spot" for the DLMO).
Methods: We applied these hypotheses to the baseline data from a study of 49 SAD subjects published in 1998. Subjects were asked to sleep between 10 p.m. and 6 a.m. for one baseline week, at the end of which a SIGH-SAD and a DLMO were obtained. Based on their baseline PAD, patients were categorized as advanced (PAD > 6 h) or delayed (PAD ≤ 6 h).
Results: Hypothesis 1 was confirmed: 2/3rds (32) of the 49 patients were delayed and 1/3rd (17) were advanced. Hypothesis 2 was confirmed: the parabolic curve, but not the linear fit, was significant (parabolic: $R2 = 0.218$, $p = 0.006$; linear: $R2 = 0.072$, $p = 0.07$). Hypothesis 3 was confirmed: parabolic minimum = 5.73 h.
Conclusion: Re-analysis of an independent data set confirmed our three a priori hypotheses. Unlike our more recent study in which the placebo effects were minimal, we could only use the baseline (pre-treatment) data of our earlier study because of the interference of the large placebo response associated with bright light. Other research groups are encouraged to re-analyze their baseline data to provide additional tests of these three inter-related circadian hypotheses for SAD.
Support (optional): This work was supported by Public Health Service Grants R01 MH55703, R01 MH56874, R01 AG21826, and R01 HD42125 (to A.J.L.) and 5 M01 RR000334 (to the GCRC of OHSU). A.J.L. was supported by the NARSAD 2000 Distinguished Investigator Award.

0184

WOMEN HAVE A LONGER PHASE ANGLE OF ENTRAINMENT THAN MEN

Emens J, Lewy A, Yuhas K
Oregon Health & Science University, Portland, OR, USA

Introduction: The maintenance of consolidated periods of sleep and wakefulness is dependent upon the proper alignment of the endogenous circadian pacemaker to the external 24-hour day. The alignment of circadian phase to the external light/dark cycle and the habitual sleep/wake schedule is the phase angle of entrainment (ψ). It has been shown that ψ correlates with intrinsic circadian period: longer ψ correlates with shorter periods. Furthermore, in 2006 we reported that depression ratings in winter depression (seasonal affective disorder, SAD) correlate with ψ. Here we show that among sighted, healthy people selected for morning or evening preference ψ is longer in women compared to men.
Methods: Subjects (36 F, 17 M) were healthy adults who participated in a study of diurnal preference. They were morning or evening types, measured by the Horne-Ostberg Morningness & Eveningness Questionnaire. Subjects maintained a written sleep diary and a constant sleep schedule of their choosing for one week before admitting to Oregon Health & Science University for circadian phase assessment. Plasma samples were collected every 15 minutes for 8 h. Melatonin concentrations were measured by radioimmunoassay (American Laboratory Products, Windham, NH), and the dim light melatonin onset (DLMO) was assessed using a 2 pg/ml threshold. Subjects´ bedtimes and wake times over 7 days were used to calculate a mean mid-sleep. Phase angle of entrainment (ψ) was defined as the interval of time, or phase-angle difference (PAD), between the DLMO and mid-sleep.
Results: PAD was 40 minutes longer on average in the female subjects, $t(51) = 2.07$, $p = 0.04$. Mean PAD values (± SD) were 7.18 ± 0.99 h and 6.52 ± 1.27 h for females and males, respectively. No relationship was found between sex and diurnal preference. There were no significant differences between females and males in age, DLMO time, bedtime, or

wake time.
Conclusion: Women have a longer phase angle of entrainment than men which may reflect gender differences in intrinsic circadian period, responsiveness to environmental time cues, exposure to environmental time cues, or homeostatic sleep drive. This finding may have implications for the diagnosis and treatment of circadian disorders including advanced sleep phase syndrome, delayed sleep phase syndrome, and SAD.
Support (optional): K23RR017636-01, Sleep Research Society Foundation Gillin Award, and NARSAD Young Investigator Award (to JSE); R01 MH56874, R01 HD42125, R01 AG21826, and NARSAD Distinguished Investigator Award (to AJL); and 5 MO1 RR000334.

0185

CIRCADIAN AMBIENT LIGHT AND ACTIVITY PATTERNS IN MOTHERS AND INFANTS

Tsai S,[1] Thomas K[2]
(1) University of Washington, Seattle, WA, USA, (2) University of Washington, WA, USA

Introduction: The purpose of this study was to describe the ambient light and activity patterns of mothers and infants. While light is a major regulator of the circadian sleep rhythm in adults, little is known about entrainment to the light-dark cycle in infants.
Methods: Light levels and activity were recorded at 30-second intervals from 12 healthy first-time mothers (mean age 30.5 ± 5.1 years) and their full-term infants (mean postnatal age 50.3 ± 17.7 days) using a watch-like monitor (Actiwatch-L, Mini-Mitter Co., Bend, OR) for 7 continuous days. Mothers also recorded a diary of their own and their infants´ sleep-wake times. Cosinor parameters were derived from cosinor analysis of the log transformed light and activity data.
Results: The mesor, amplitude, acrophase (clock time) and R2 cosinor fit of mothers´ light pattern (lux) were 11.22 ± 5.18, 8.66 ± 5.37, 14:49 ± 0:50, and 0.45 ± 0.10, respectively; those of mothers´ activity pattern (count) were 16.71 ± 6.06, 7.13 ± 2.86, 16:20 ± 1:07, and 0.30 ± 0.11, respectively; those of infants´ light pattern (lux) were 5.78 ± 2.02, 6.17 ± 2.32, 14:35 ± 0:55, and 0.42 ± 0.07, respectively; those of infants´ activity pattern (count) were 10.01 ± 1.96, 3.22 ± 1.16, 15:43 ± 1:03, and 0.13 ± 0.07, respectively.
Conclusion: The level of light and activity in mothers and infants did not exhibit a strong circadian pattern. Mothers had low light exposure and babies had an even lower light exposure. Mothers´ activity level was low. The acrophase for mothers and infants was similar suggesting that the timing of the mother´s light cycle also influences the baby. Results may suggest the circadian pattern of light and activity to help improve circadian sleep pattern in infants. Such intervention may also influence maternal sleep.
Support (optional): Hester McLaw Nursing Scholarship, University of Washington School of Nursing; Virginia Henderson Research Grant and Psi Chaper-at-Large Research Grant, Sigma Theta Tau Nursing International Honor Society.

0186

EFFECT OF LESIONING THE SUPRACHIASMATIC NUCLEUS ON FRACTAL PATTERN OF HEART RATE FLUCTUATIONS

Hu K,[1] Scheer F,[1] Buijs R,[2] Shea S[3]
(1) Brigham and Women's Hospital, Boston, MA, USA, (2) Netherlands Institute for Brain Research, Netherlands, (3) Boston, MA, USA

Introduction: In mammals there is a fractal structure in heartbeat fluctuations that changes with autonomic blockade and cardiovascular pathology. We recently found that humans exhibit a circadian rhythm in this fractal structure of heartbeat fluctuations, with changes in the direction observed in cardiovascular disease at the circadian phase corresponding to ~10AM. Here we tested: (i) whether this circadian rhythm in heartbeat fluctuations also exists in a mammalian species that is nocturnally active, i.e., Wistar rats; and (ii) how this fractal structure of heartbeats changes following lesioning of the master circadian pacemaker (suprachiasmatic nucleus: SCN).
Methods: We analyzed 7 intact and 7 SCN-lesioned (SCNx) Wistar rats. Each rat was housed individually in a sound isolated and light controlled cage. Circadian phases were initially entrained by 10 recurring 24-hour LD cycles (12-hour light/12-hour dark), then the rats were studied under constant darkness (DD) for 10 more days. Heart rate was recorded every 4 minutes, and core body temperature was used as a circadian phase marker. Fractal structures of heart rate fluctuations were quantified by detrended fluctuation analysis.
Results: Control rats exhibited a robust circadian rhythm in the scaling exponent characterizing fractal structure of heart rate. The exponent had systematically 15% larger values during the biological day (inactive phase for rats) compared to during the biological night. The circadian rhythm of fractal patterns of heart rate completely disappeared in SCNx rats. These SCNx rats also had a larger mean scaling exponent compared to control rats across all circadian phases (ANOVA $p<0.0001$).
Conclusion: As with humans, in rats there exists an endogenous circadian rhythm in the fractal structure of cardiac dynamics. Lesioning the SCN abolished this circadian rhythm and brought the fractal structure closer to that observed with parasympathetic blockade, and in cardiovascular diseases in humans.
Support (optional): Supported by HL076409, HL076446, FAJL supported by Pickwick Fellowship

0187

LACK OF ENDOGENOUS CIRCADIAN RHYTHM OF PLATELET AGGREGABILITY

Scheer F,[1] Hahn M,[2] Doamekpor L,[2] Patel J,[2] Evoniuk H,[2] Kelly E,[2] Laker M,[2] Shea S[1]
(1) Medical Chronobiology Program, Division of Sleep Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA, (2) Medical Chronobiology Program, Division of Sleep Medicine, Brigham and Women's Hospital, Boston, MA, USA

Introduction: Increased blood platelet aggregability is a risk factor for adverse cardiovascular events such as myocardial infarction, sudden cardiac death and stroke. Epidemiological studies have documented an increase in adverse cardiovascular events in the morning. Therefore, we tested whether or not blood platelet aggregability has: (1) an endogenous circadian rhythm, independent of behavioral effects; (2) an effect of mental, postural and/or physical stressors, independent of circadian effects; and (3) an endogenous circadian rhythm in the magnitude of response to these three stressors
Methods: 12 healthy adults (6 female) underwent a 13 day protocol in dim light, wherein subjects slept at all phases of the circadian cycle—achieved by scheduling twelve recurring 20-hour `days´. During each 20-hour day, subjects performed a test battery consisting of a: (i) mental stressor (10-minute addition test); (ii) postural stressor (15-minute 60° head up tilt); and (iii) exercise stressor (15-minute cycling at 60% maximum heart rate). Each test was preceded by a 20-minute baseline and followed by 40 minutes recovery. Impedance aggregometry induced by exogenous collagen was performed on whole blood samples taken every 20 minute. Core body temperature was used to assess circadian phase.
Results: Mental, postural and physical stressors each significantly

increased platelet aggregability by ~10% independent of circadian phase (P always <0.01; Mixed Model ANOVA). However, there were no significant effects of circadian phase on either baseline platelet aggregability or the degree of change in platelet aggregability provoked by these three stressors.
Conclusion: These data demonstrate highly significant effects upon platelet aggregability of mental and physical stressors, yet no systematic effect upon platelet aggregability of the endogenous circadian system. Thus, behavioral factors, such as standing up, and becoming physically and mentally active likely play a more important role than endogenous circadian variations in previously observed day/night patterns in platelet aggregability.
Support (optional): NIH RO1 HL76409; K24 HL076446 in support of SAS; Pickwick Fellowship in support of FAJLS; NCRR GCRC M01 RR02635

0188

MOLECULAR AND BEHAVIORAL ONTOGENY OF THE MASKING RESPONSE IN NEONATAL RATS

Prichard J,[1] Westby L,[2] Hengen K[3]
(1) St. Paul, MN, USA, (2) University of St. Thomas, St. Paul, MN, USA, (3) University of Wisconsin-Madison, Madison, WI, USA

Introduction: In addition to entraining the circadian rhythm, light has immediate effects on sleep/wakefulness. In nocturnal animals, an acute light pulse during the dark phase abruptly decreases locomotor activity and wakefulness. This behavioral masking response, which occurs independently of the suprachiasmatic nucleus (SCN), is accompanied by c-fos expression in five nuclei of the retinorecipeint subcortical visual system. In contrast to the circadian system, very little is known about the ontogeny of the subcortical visual system that mediates acute behavioral responses to light.
Methods: To examine the molecular and behavioral maturation of the subcortical visual system, we screened Charles River F344 rats every 3 days from postnatal day 0 to p30 for changes in locomotor activity, sleep/wakefulness, and c-fos protein expression before and after a 30 minute light pulse presented during subjective night.
Results: Molecular and behavioral masking responses to acute light were first evident at p6. In response to an acute light stimulus, locomotor activity significantly decreased at p3 ($p < 0.01$) and c-fos expression in the subcortical visual system significantly increased at p6 ($p < .05$). In all cases, the magnitude of the behavioral masking response was directly proportional to the extent of light-induced c-fos staining in the subcortical visual system. Robust c-fos immunoreactivity was first observed in the lateral geniculate complex on p6 ($p < 0.05$), and by p12, c-fos immunoreactivity was also evident in select nuclei of the pretectum ($p < 0.05$).
Conclusion: Acute responses to light are first evident on p6 and continue to mature through p30, when nuclei of the subcortical visual system undergo significant developmental refinement. The early onset of these acute responses to light show that it is pertinent to understand the consequences of early common light manipulations (e.g., 24-hour lights in hospital nurseries) on the neural circuits that underlie sleep/wakefulness.

0189

CIRCADIAN RHYTHMS, STROKE TYPE, AND STROKE RISK FACTORS

Khan R,[1] Khan F,[2] Alattar M,[3] Vaughn B[1]
(1) University of North Carolina at Chapel Hill, Chapel Hill, NC, USA, (2) Surveillance Data, Inc., Plymouth Meeting, PA, USA, (3) University of North Carolina at Chapel Hill, Durham, NC, USA

Introduction: Previous research has shown that there is a circadian pattern of time of stroke onset and blood pressure elevation. However, little is known about how circadian preference is related to stroke type (i.e. ischemic vs. hemorrhagic) and to stroke risk factors.
Methods: To evaluate this, we surveyed 28 patients admitted to the UNC stroke unit, using the Early/Late Preference Scale (ELPS), Sleep Apnea Scale (SAS), Sleep Disorders Questionnaire (SDQ), Epworth Sleepiness Scale (ESS), Johns Hopkins Restless Legs Severity Scale (JHRLSS), Stanford Sleepiness Scale (SSS), Pittsburgh Sleep Quality Index (PSQI), and Insomnia Severity Index (ISI). The patients´ bedtimes, wake times, total sleep times, biometric measurements, and results of stroke tests, such as MRI, echocardiogram, and carotid ultrasound were also collected. These data were analyzed with the appropriate statistical tools, including Pearson Correlation, Student T-Test, Chi-Square, and Logistic Regression Analysis.
Results: No significant correlation was found between stroke type (i.e. ischemic vs. hemorrhagic) and circadian preference ($p=0.80$). However, significant correlations were found between later wake time and increasing BMI ($p<0.05$), later wake time and the presence of large vessel disease on MRI ($p<0.05$), and earlier bedtime and increasing degree of left ventricular hypertrophy ($p<0.05$). Trends towards significance were seen between earlier bedtime and the presence of diastolic dysfunction ($p=0.094$), earlier bedtime and the presence of aortic valve regurgitation ($p=0.096$), and earlier bedtime and the presence of aortic sclerosis ($p=0.068$).
Conclusion: This pilot study suggests that circadian factors may influence stroke risk factors. Further studies are required to further elucidate this association.

0190

PREDICTING THE DAILY PATTERN OF ASTHMA SEVERITY BASED ON RELATIVE CONTRIBUTIONS OF THE CIRCADIAN TIMING SYSTEM, THE SLEEP-WAKE CYCLE AND THE ENVIRONMENT

Shea S,[1] Scheer F,[2] Hilton M[3]
(1) Brigham & Women's Hospital, Boston, MA, USA, (2) Brigham and Women's Hospital, Boston, MA, USA, (3) Medical Chronobiology Program, Division of Sleep Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Introduction: Asthma is often worse at night. We aimed to determine whether separate circadian and sleep/wake cycle influences on pulmonary function in asthma assessed in a laboratory would simply summate to predict the daily pattern of pulmonary function observed under ambulatory settings. Any differences between laboratory and ambulatory data would provide an estimate of additional behavioral/environmental contributions to asthma in the home setting.
Methods: 13 adult asthma subjects were studied under ambulatory settings for 3 weeks and throughout a 10 day 'forced desynchrony' laboratory protocol (FD) in dim light, wherein subjects slept at all phases of the circadian cycle (by scheduling recurring artificial day lengths of 28 hours). An index of bronchoconstriction ([FEV1]) was recorded every 2-6 hours during wakefulness in both protocols, and immediately following scheduled awakenings from sleep in the FD

protocol.
Results: In the laboratory FD protocol, FEV1 was reduced attributable to sleep and reduced during the biological night attributable to the circadian pacemaker, with no interaction between these effects. Aligning circadian and sleep/wake cycle to match their normal phase relationship in the ambulatory setting, their added effects resulted in a greater day-night variation in FEV1 (8%) than predicted by either factor alone. This predicted variation was almost identical to that observed across the wake episode under ambulatory conditions where the times of most severe asthma occurred immediately upon awakening and before bedtime. However, the ambulatory data were offset by -4%, likely attributable to additional adverse behavioral and environmental factors in the ambulatory setting (e.g., increased exercise and exposure to allergens).
Conclusion: Circadian and sleep/wake cycle influences on pulmonary function determined in the laboratory predict the ambulatory pattern of pulmonary function, and reveal an additional adverse behavioral/environmental component in the ambulatory setting.
Support (optional): NIH RO1 HL064815; K24 HL076446 in support of SAS; Pickwick Fellowship in support of FAJLS; NCRR GCRC M01 RR02635

0191

SLEEP DISORDERS IN CHRONIC PEDIATRIC DEMYELINATING DISEASE

Hopkins B, Lotze T, Glaze D
Baylor College of Medicine, Houston, TX, USA

Introduction: Fatigue and sleep disorders are common in chronic adult demyelinating disease. Given the impact of sleep disorders on daytime function, it is important to determine if children with chronic demyelinating disease (CDD) such as relapsing-remitting and secondary-progressive multiple sclerosis (RRMS, SPMS), neuromyelitis optica (NMO), transverse myelitis (TM), or recurrent optic neuritis (RON) have treatable sleep disorders.
Methods: A retrospective chart review determined the frequency of fatigue, excessive daytime sleepiness (EDS), and insomnia. Demographic details including age, sex, diagnosis, medications and diagnostic evaluations were collected.
Results: Twenty-six subjects, ages 5-20 years (19 female), with CDD were identified: 12-RRMS, 1-SPMS, 7-NMO, 3-RON, and 2-TM. 8/26(31%) subjects complained of EDS and 4/26(15%) complained of insomnia. Of 21 subjects, 17(85%) endorsed fatigue. Ten subjects received these medications: 5-modafinil, 3-amantadine, 1-melatonin, and 1-zolpidem. All 5 polysomnograms performed were abnormal. The mean total sleep time was 6.4 hours (range = 4.4-7.9) with a mean sleep efficiency of 75.4% (range = 49-92%). Percent REM sleep was decreased in 4/5 subjects and increased (31.8%) in one subject. Severe periodic limb movement disorder (PLMI = 208) was noted in a single subject with SPMS. A subject with NMO and a subject with TM had obstructive sleep apnea (mean AHI = 4.7). Two subjects with RRMS complained of hypersomnia, but on Multiple Sleep Latency Testing, only one subject slept (5/5 naps) with a mean sleep latency of 7.9 minutes and REM sleep achieved.
Conclusion: Up to 85% of children with CDD experience fatigue. At least 31% endorse EDS and 15% insomnia. Polysomnographic findings indicate these children experience a variety of sleep abnormalities including insomnia, obstructive sleep apnea, idiopathic hypersomnia, and periodic limb movement disorder. Given the preponderance of fatigue and prevalence of sleep disturbances, evaluation for sleep disorders is indicated in this population.

0192

RESPIRATORY SENSATION DURING SLEEP IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

Huang J,[1] Marcus C,[1] Melendres C,[2] Karamessinis L,[1] Pepe M,[1] Samuel J,[1] Abi-Raad R,[3] Trescher W,[4] Colrain I[5]
(1) Children's Hospital of Philadelphia, Philadelphia, PA, USA, (2) Johns Hopkins University, Baltimore, MD, USA, (3) Johns Hopkins University, MD, USA, (4) Pennsylvania State University, PA, USA, (5) SRI International, Menlo Park, CA, USA

Introduction: Children with obstructive sleep apnea syndrome (OSAS) have blunted respiratory sensation which may contribute to the pathogenesis of the disease. Respiratory sensation can be tested by measuring respiratory-related evoked potentials (RREPs). RREPs are obtained by occluding the airway briefly during inspiration and measuring the resultant cortical EEG. Adults with OSAS have been shown to have a significantly smaller N550 component than controls in nonREM sleep. RREPs in children are dominated by an earlier negative component, the N350, which is also measurable in REM sleep. We hypothesize that children with OSAS have smaller N350 responses than normal children.
Methods: Nine children with OSAS and 10 controls slept wearing a mask connected to a nonrebreathing valve. Flow was measured using a pneumotachograph connected to a face mask and a differential pressure transducer. Pressure from the mask was measured by a pressure transducer. Multiple 400 ms inspiratory occlusions were performed during stage 2, slow wave (SWS) and REM sleep. EEG activity was averaged and RREPs were determined at Fz, Cz and Pz. N350 amplitude was analyzed with a site x sleep state x diagnosis ANOVA.
Results: Three OSAS patients had no obvious RREP waveforms and thus had a zero voltage input into the analysis. OSAS patients had significantly smaller N350 amplitudes than controls ($p < 0.05$). The site (largest at Fz, $p < 0.001$), and sleep state (largest in stage 2, $p < 0.01$) factors were also significant. T-tests for SWS and stage2 Fz data, excluding the subjects with aberrant responses, showed patients to be significantly smaller in both sleep states (SWS, $p<0.01$; stage 2, $p < 0.05$).
Conclusion: Children with OSAS have impaired neural processing of respiratory load information during sleep. We speculate that this may be a factor in the pathophysiology of childhood OSAS. Alternatively, it may result from chronic hypoxemia/hypercapnia or sleep disruption.
Support (optional): This study was supported by NIH grants M01-00240, U54-RR023567, R01-HL58585 and a research grant from Respironics.

0193

A COMPARISON OF THE SLEEPING PATTERNS OF HEALTHY CHILDREN FROM AN INNER CITY POPULATION TO CHILDREN FROM MIDDLE CLASS CAUCASIAN POPULATION.

Chawla A,[1] Cruz M,[2] Colleman C,[3] Adams R,[3] Grant M,[3] Kimball M,[4] Lerario M,[5] Kothare S[3]
(1) Tulane University, New Orleans, LA, USA, (2) St. Christopher's Hospital for Children, Willow Grove, PA, USA, (3) St. Christopher's Hospital for Children, PA, USA, (4) Drexel University, PA, USA, (5) University of Pennsylvania, PA, USA

Introduction: The purpose of this study is to examine the sleeping patterns of healthy children from lower socioeconomic class. Currently, the only data available on this topic is from a study conducted in predominately Caucasian, middle class 4 to 10 years old children (Owens J et al).
Methods: Parents bringing in their children for either an acute illness or well child visit were prospectively enrolled to fill out a standardized 35-item Children´s Sleep Habits Questionnaire (CSHQ; Owens et al). Children with chronic illnesses were not involved in the study. The survey examines various sleeping behaviors including bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night awakenings, parasomnias, sleep disordered breathing, and daytime sleepiness. Each category is scored, with higher scores indicating poorer sleeping patterns. The scores of these children were compared to the controls (CSHQ; Owens et al). The study also obtained a child health history and Hollingshead score to assess socioeconomic status.
Results: A total of 64 patients; 32 males and females each, were enrolled in the study. Mean age was 7.7 years; range 4 to 10 years. Fifty four were African American; the others were Hispanic. Their scores, when compared to the controls showed statistically significant higher values for Bedtime Resistance, Sleep Onset Delay, Sleep Duration, Night Awakenings, Sleep Disordered Breathing, and Daytime Sleepiness ($p<0.05$).
Conclusion: Our preliminary results show that children from a lower socioeconomic environment have higher sleep scores (indicating worse sleeping patterns) than children from middle class status. These results are not surprising but should be followed up using a larger cohort.

Excessive daytime sleepiness may have impact on daytime school performance, while sleep disordered breathing, if adequately screened for, may be treated with tonsillectomy and adenoidectomy.

0194

CAFFEINE USE, SLEEP PATTERNS, AND ACADEMIC PERFORMANCE IN MIDDLE SCHOOL STUDENTS

Canton J,[1] Patel B,[1] Quinn A,[2] Barry K,[3] Naku K,[1] Marco C,[4] Wolfson A[1]
(1) College of the Holy Cross, Dept. of Psychology, Worcester, MA, USA, (2) College of the Holy Cross, Worcester, MA, USA, (3) University of Massachusetts Medical School, Worcester, MA, USA, (4) Rhode Island College, Dept. of Psychology, Providence, RI, USA

Introduction: Caffeine is considered the most widely consumed psychoactive substance. Known to have positive and negative effects, caffeine increases alertness, decreases fine motor skills, and induces anxiety and depression. Caffeine is associated with decreased slow wave and REM sleep, shorter sleep duration, and increased night wakings. However, less is known about caffeine´s effect on young adolescents. This study examined sleep patterns, caffeine use, mood, and school behavior in middle schoolers.
Methods: As part of a longitudinal study, 7th graders (N = 51) were recruited from 2 urban middle schools. Participants completed a 7-day sleep diary that assessed caffeine use/time, bed/rise times, mood, and sleepiness. Background information was obtained through parents and academic performance through transcripts. 52% were from a minority background and 42% were from families with incomes below $40,000.
Results: Forty-five percent of the adolescents reported that they obtained less than the recommended 9 hours of sleep on school nights, 71% on weekend-nights. 32% reported consuming caffeine throughout the week (25% consumed 20 – 47 mg/day; soda > coffee/tea); however girls consumed more caffeine ($p < .05$). Adolescents used caffeine later in the day on weekends in comparison to school days ($p < .001$). Caffeine users had later school rise times and one hour delayed bedtimes on weekends (p´s < .05). Delayed school morning rise times were associated with lower GPA´s ($r = -.41$, $p < .05$); weekend caffeine use was negatively associated with daytime mood and alertness (r´s = -.32, p´s < .05); and later caffeine consumption was associated with increased absenteeism ($r = .35$, $p < .05$).
Conclusion: Young adolescents´ caffeine use and associated negative consequences are alarming. Findings indicate that young teens are using caffeine, sleeping late, and missing school. Such sleep and behavior patterns may be setting the stage for school problems as well as other types of substance use.
Support (optional): Research supported by NICHD047928

0195

THE INFLUENCE OF GENDER AND AGE ON UPPER AIRWAY LENGTH DURING DEVELOPMENT

Ronen O,[1] Malhotra A,[2] Pillar G[3]
(1) Carmel Medical Center, Haifa, Israel, (2) Brigham and Women's Hospital, MA, USA, (3) Technion- Israel Institute of Technology, Haifa, Israel

Introduction: Obstructive sleep apnea (OSA) has a strong male predominance in adults but not in children. The collapsible portion of the upper airway is longer in adult males than females (a property that can make them vulnerable to collapse during sleep). We sought to test the hypothesis that in pre-pubertal children pharyngeal airway length (AL) is equal between genders, but following puberty males have longer upper airway than females, thus explaining this change in apnea propensity.
Methods: 69 Healthy boys and girls who had undergone CT scans of their neck for other reasons were selected from the CT archives of Rambam and Carmel hospitals. The AL was measured in the midsagittal plane and was defined as the length between the lower part of the posterior hard palate and the upper limit of the hyoid bone. AL and normalized AL/body-height (AL/H) were compared between the genders in pre-pubertal (4-10 year-old) and post-pubertal (14-19 year-old) children.
Results: In pre pubertal children, AL was similar between boys and girls (43.2±5.9 vs 46.8±7.7mm, respectively). When normalized to body height, AL/H was significantly shorter in pre-pubertal boys than in girls (0.35±0.03 vs 0.38±0.04mm/cm, $p<0.05$). In contrast, post-pubertal males had longer upper airways (66.5±9.2 vs 52.2±7.0mm), and normalized AL/H (0.38±0.05 vs 0.33±0.05mm/cm) than females ($p<0.01$ in both).
Conclusion: While in pre-pubertal children boys have equal or shorter AL compared to girls, following puberty AL and AL/H are significantly greater in males than females. These data suggest that important anatomical changes at puberty occur in a gender-specific manner, which may be important in explaining the male predisposition to collapse in adults.

0196

SLEEP DISORDERED BREATHING EVENTS ARE ASSOCIATED WITH AUTONOMIC ACTIVATIONS IN CHILDREN WITH OSA

Etzioni T,[1] Suraiya S,[2] Pillar G[2]
(1) Rambam Medical Center, Haifa, Israel, (2) Technion- Israel Institute of Technology, Haifa, Israel

Introduction: It is well documented that respiratory cessations (complete or partial) in adults with obstructive sleep apnea (OSA) are associated with arousals from sleep. In children, however, blunted arousal response to respiratory stimuli with respiratory events terminated without arousals have been shown. The Watch_PAT100 device (Itamar-Medical, Caesarea, Israel) has been recently introduced as a tool to detect sleep disordered breathing events predominantly by assessing the autonomic arousals at the termination of events. It has been reported that children with SDB express increased autonomic response to sigh and cold pressor test. We have therefore sought to study children with OSA with the Watch_PAT100, to assess whether they experience autonomic activation at the termination of events. We hypothesized that they may not experience cortical arousals, but will demonstrate autonomic activation at the termination of SDB events.
Methods: Seventeen children with OSA (11m/6f) underwent simultaneous recording of in-lab polysomnography and Watch_PAT100 sleep study. PSG was blindly scored for apneas and hypopneas based on common practice for clinical sleep studies in children. WatchPAT100 was automatically scored for respiratory events based predominantly on autonomic activations.
Results: Children´s average age (±SD) was 11.8±3.2years (range 5-17). Their total sleep time was 408±40min (range 333-469min). The AHI based on PSG and Watch_PAT100 were 8.8±7.1 and 7.6±9.5, respectively ($p=0.7$). The correlation between PSG AHI and Watch_PAT100 AHI was 8.8 ($p<0.001$).
Conclusion: We conclude that utilizing autonomic activation index is an accurate tool in diagnosing sleep disordered breathing events in children. We believe that the previously reported blunted arousal response to respiratory stimuli in children with OSA is applicable for cortical arousals or arousals scored by criteria determined for adults, but not for autonomic responses.

0197

EFFECT OF INFANT FEEDING METHOD ON CHILDHOOD SLEEP-DISORDERED BREATHING

Montgomery-Downs H,[1] Gozal D[2]
(1) West Virginia University, Morgantown, WV, USA, (2) University of Louisville, KY, USA

Introduction: Childhood sleep-disordered breathing (SDB) is known to have negative consequences on cognitive development, behavior, quality of life, and utilization of healthcare resources. Early viral infections and other immune mediated responses are thought to contribute to the development of chronic inflammation of the upper airway. Removal of inflamed upper airway tissues is the frontline treatment for childhood SDB. Breastfeeding has been shown to provide immunological protection against such early exposures. We therefore sought to explore whether sleep measures would differ for children who were breast fed as infants.
Methods: Parents of children undergoing overnight polysomnography at the Kosair Children´s Hospital Sleep Medicine clinic or larger research studies filled out a brief survey about whether the child had been breast, formula, or both breast and formula fed as an infant. If breast fed, the age of weaning was also elicited. Analysis of Variance and Cohen´s d for effect size were calculated.
Results: There were 197 surveys completed. At the time of PSG, children were 6.7 (SD±2.9) years (40% female; 69% White and 30% African American). 52% were formula fed, 10% were breast fed, and 38% were both breast and formula fed as infants. The average age of weaning was 7.3 (SD±7.0) months. Sleep measures did not differ based on breast feeding <2 months. Children who had been breast fed for at least 2 months had lower apnea-hypopnea index (p=0.053, d=.30), lower snore arousal index (p=0.010, d=.57), lower respiratory arousal index (p=0.027, d=.38), and higher SpO2 Nadir (p=0.007, d=.45).
Conclusion: The findings support the notion that breastfeeding may provide long-term protection against the incidence or severity of childhood SDB. Further work will focus on controlling socioeconomic status as a possible confound and on exploring the mechanism(s) whereby infant feeding methods may affect the pathophysiology of SDB.
Support (optional): Study funded by NIH grant F32HL074591 (HM-D) and R01HL-65270 (DG).

0198

EXPLORATION OF THE RELATIONSHIP BETWEEN NOCTURNAL ENURESIS AND OBSTRUCTIVE SLEEP APNEA (OSA) IN CHILDREN

Alharbi A, Kirk V
University of Calgary, Calgary, Alberta, Canada

Introduction: Obstructive sleep apnea (OSA) in children is a disorder of breathing during sleep characterized by upper airway obstruction (either partial or complete) that disrupts normal ventilation during sleep and normal sleep patterns. Untreated OSA may result in significant morbidity and mortality. At five years of age, 15 to 25 percent of children wet the bed. Children with enuresis may be at significant risk for emotional and physical abuse. There is relationship noted between OSA and enuresis in children with prevalence rates reported to be between 26 to 34.5% in this group.
Methods: Objective: To identify the relationship between nocturnal enuresis and OSA in children undergoing laboratory polysomnography (PSG) in Alberta Children´s Hospital for suspected sleep disorders over a 7 year period.
This is a retrospective review of a computerized database containing information on all children who have had PSG performed between October 19, 1999 and October 1, 2006. All children meeting inclusion criteria of 1) otherwise healthy and 2) age 4 years and older were included.
Results: 754 (488 males, 64.7%) subjects met inclusion criteria. Median age was 11.0 years (range 4.0 – 18.0 yrs). 361 subjects (47.9%) met criteria for a diagnosis of OSA (AHI >1.5). 112 of these subjects also had enuresis (31.0%); 100 subjects with primary enuresis (27.7%) and 12 subjects (3.3%) with secondary enuresis. Overall, 193/754 (25.6%) subjects had a positive history of nocturnal enuresis - with or without OSA (152 with primary enuresis). Of those with primary enuresis, 107 subjects (70.4%) were male compared with 73.2% amongst those with secondary enuresis. 112 out of 193 subjects with enuresis also had OSA (58.0%).
Conclusion: In this select sample of healthy children being evaluated for sleep disorders, 25.6% of the overall population had nocturnal enuresis. However, the prevalence of OSA in the subgroup with enuresis was considerably higher(58%)with predominance of male and primary type of enuresis.

0199

RISK FOR SLEEP-DISORDERED BREATHING AMONG PREMATURE INFANTS AND TODDLERS

Montgomery-Downs H,[1] Ross M,[2] Polak M,[2] Ritchie S,[2] Lynch S[2]
(1) West Virginia University, Morgantown, WV, USA, (2) West Virginia University, WV, USA

Introduction: Children born prematurely are known to suffer disproportionately from the cognitive consequences of sleep-disordered breathing (SDB). We sought to determine the prevalence of SDB symptoms among infants and toddlers born prematurely.
Methods: Previous validation with polysomnography of a pediatric sleep questionnaire among older children showed that snoring reported 2 days/week was likely primary snoring while more frequent snoring (≥3 days/week) was likely SDB. Parents of patients attending a neonatal follow-up clinic at West Virginia University Hospital and Clinics completed the research questionnaire. Anthropomorphic and medical history data were obtained from medical records.
Results: 100% of patients approached agreed to participate; analyses were based on the first 71 participants. Patients were born at 31.0 (SD±3.9) weeks gestation and were 10.6 (SD±9.7) months (corrected for gestational age) at the time of study. 52% of patients were female and 83% were white. 14% of the children were reported to snore 2 days/week, 8% were reported to snore more frequently. With corrected age as a covariate, patients who were reported to snore ≥3 days/week currently weighed less than those reported to snore <2 days/week (p=.05). Groups did not differ on gender, gestational age, birth weight, or duration on ventilation or oxygen.
Conclusion: These data show that risk for SDB among infants and toddlers born prematurely may be higher than among those born full-term. Consistent with the poor growth found in children with SDB, we found that prematurely born infants and toddlers at-risk for snoring and SDB also have a lower current body weight independent of age. In light of studies indicating a disproportionate cognitive effect of SDB on children born prematurely, our findings emphasize the need for early identification and treatment of SDB among this population.

0200

THE RELATIONSHIP BETWEEN SLEEP TIME, SLEEPINESS, AND PSYCHOLOGICAL FUNCTIONING IN ADOLESENTS

Moore M,[1] Kirchner H,[2] Drotar D,[3] Johnson N,[2] Rosen C,[3] Ancoli-Israel S,[4] Susan R[2]
(1) Children's Hospital of Philadelphia, Philadelphia, PA, USA, (2) Case Western Reserve University School of Medicine, OH, USA, (3) Case Western Reserve University, Cleveland, OH, USA, (4) University of California, San Diego, San Diego, CA, USA

Introduction: Normative biological, psychological, and social changes during adolescence contribute to insufficient sleep time, irregular sleep schedules, and sleepiness. Such changes in sleep may lead to psychosocial consequences such as depressed mood and behavior problems. The aim of the current study was to examine the association between sleep time, sleepiness, and psychological functioning (e.g. symptoms of anxiety, depression, externalizing behaviors, and perceived health) in adolescents.
Methods: This cross-sectional sample, comprised of 247 adolescents (48.5% female, 54.3% ethnic minority, mean age of 13.7 years), was recruited from an ongoing community-based cohort study of sleep and health. Data were collected via 5-7 day actigraphy, the Epworth Sleepiness Scale (ESS), physical exam, and parent, teacher, and adolescent questionnaires. It was hypothesized that less mean total sleep time, more variability in sleep time, and more sleepiness would be associated with higher scores on measures of anxiety, depression, externalizing behaviors, and lower scores on a measure of perceived health.
Results: The mean ESS score was 7.9 (+/- 4.47), and scores ranged from 0-23. Higher ESS scores were associated with higher scores on measures of anxiety (p<.001) and depression (p<.01), and lower scores on a measure of perceived health (p<.001) when controlling for previously identified covariates (e.g., age, ethnicity, gender, Tanner stage, socioeconomic status, body mass index, prematurity, ADHD, vacation status, and mean total sleep time). Other relationships between sleep variables (e.g. sleep time and variability in sleep time) and psychological variables were not found. Additionally, less total sleep time and higher night-to-night variability were associated with higher ESS scores.
Conclusion: Future studies should include objective measurement of sleepiness and behavioral alertness to clarify whether the relationship between sleepiness and psychological functioning is due to sleepiness per se or to a general negative bias. In addition, clinicians should consider sleepiness when conducting psychological assessments.

0201

EXECUTIVE FUNCTION AND RISK FOR SLEEP-DISORDERED BREATHING IN PRESCHOOLERS

Karpinski A,[1] Scullin M,[2] Montgomery-Downs H[1]
(1) West Virginia University, Morgantown, WV, USA, (2) University of Texas El Paso, TX, USA

Introduction: Sleep-disordered breathing (SDB) has been linked with Executive Function (EF) impairment in adults and school-age children, possibly due to frontal lobe and hippocampal dysfunction. EF has not been included in previous studies of SDB among preschool-age children. The objective of the current study was to examine EF among preschoolers at risk for SDB.
Methods: As part of a larger study, 39 preschool children were administered EF tasks measuring working memory, inhibition, and planning. A sleep behavior questionnaire was completed by parent(s) three months retrospectively. Consistent with previous validation, sleep questionnaires were analyzed using a 17-item symptom profile for parental report of risk for sleep-disordered breathing (PR-RSDB). As a secondary method, children were categorized based on report of snoring frequency alone: Never/Rarely/Occasionally snoring indicated low risk (NRO group), Frequently/Almost Always snoring indicated risk (FA group) for SDB.
Results: Participants (N=39) were 51.6 (SD±7.0) months of age (51.3% female, 89.7% White). As expected, children´s performance on each of the EF measures was significantly correlated with age: planning (r=0.57, p<0.001), inhibition (r=0.55, p<0.001) and working memory (r=0.59, p<0.001), with higher scores indicating better performance on each task. In hierarchical regressions controlling for age, PR-RSDB was a significant predictor of deficits in each EF dimension: planning (β=-0.40, p=0.003), inhibition (β=-0.58, p<0.001), and working memory (β=-0.39, p=0.003). Compared to NRO snorers (n=33), FA snorers (n=6) performed significantly worse on planning (p=0.039), inhibition (p=0.005), and working memory (p=0.016).
Conclusion: Preschool children at-risk for SDB, as measured by parental report of both a profile of risk indicators as well as snoring frequency alone, performed significantly worse on EF measures compared to those at low risk for SDB. These data further highlight the importance of early detection of risk for SDB among the general community, as recommended by the American Academy of Pediatrics, to prevent cognitive and particularly EF impairment.

0202

PAIN, SLEEP, AND FATIGUE IN CHILDREN RECEIVING INDUCTION CHEMOTHERAPY: PRELIMINARY FINDINGS

Gedaly-Duff V,[1] Lee K,[2] Nail L,[1] Johnson K,[1] Knafl G,[1] Johnson A,[1] Stork L,[1] Anderson K,[1] Perko K,[1] Price J[1]
(1) Oregon Health & Science University, Portland, OR, USA, (2) University of California, San Francisco, San Francisco, CA, USA

Introduction: Describe sleep characteristics, fatigue, and pain in school-age children during the induction phase of chemotherapy for leukemia.
Methods: A prospective, longitudinal study of children with leukemia is describing pain, fatigue and sleep-activity using wrist actigraphy and home diaries. Data were from 6 children´s first 3 nights at home after receiving induction out-patient chemotherapy. Measures were pain in morning and evening (VAS, 1 no pain – 5 most pain), fatigue in morning and evening (VAS, 0 no fatigue - 4 very tired), and sleep characteristics were total sleep time (TST, number of minutes of sleep while in bed) and wake after sleep onset (WASO, percent awake during sleep period).
Results: Three children were between 8 and 9 years; 3 adolescents were between 11 and 16 years. Findings were averages±SD of scores per day over 3-days with ranges based on daily scores. The three younger children had morning pain scores of 1±0 (range 1), evening pain of 1±0 (range 1); morning fatigue of 1±0.9 (range 0-2), evening fatigue of 1.9±0.5 (range 1-4); TST was 468.5±52.5 minutes (range 333-624) and WASO was 14.3%±3.5 (range 4-18%). The three older children had morning pain scores of 1.3±0.6 (range 1-3), evening pain of 2.3±1.2 (range 1-4); morning fatigue of 1.2±0.5 (range 0-2), evening fatigue of 2.1±0.5 (range 1-3); TST was 565.1±61.2 minutes (range 325-671) and WASO was 14.6±8.2% (range 6-22.3).
Conclusion: While the sample is too small to compare statistical differences between younger and older children, the descriptive evidence suggests that younger children reported less pain than adolescents. Both groups reported increased fatigue in the evening. Sleep ranged between 5.5 and 11 hours with 14% disturbed sleep. Learning more about their pain, sleep disturbance and fatigue at the

induction stage of treatment will lay the foundation for developing symptom management interventions.
Support (optional): Funded by National Institutes of Health, National Institute of Nursing Research (Grant#5R01NR008570-02).

0203

ACUTE SLEEP RESTRICTION: DOES IT AFFECT SLEEP ARCHITECTURE AND SLEEP RELATED RESPIRATORY FUNCTION IN CHILDREN?

Lew J,[1] Lewin D,[2] Winnie G[1]
(1) Children's National Medical Center, Washington, DC, USA, (2) Washington, DC, USA

Introduction: This is a follow-up study for the impact of acute sleep restrictions on children´s sleep related respiratory function and sleep architecture. Our findings in the previous study suggested that sleep restriction affect sleep architecture by increasing slow wave sleep at the expense of REM sleep; sleep restriction also worsened the respiratory dysfunction of obstructive sleep apnea children but had no deleterious effects on normal children´s respirations.
Aim: In order to confirm our findings in this previous study, four more age matched children with OSAS were recruited for the study.
Methods: Overnight polysomnograms were performed in the Pediatric Sleep lab at Children´s National Medical Center in Washington DC. These children had a baseline 7- 8 hour of polysomnogram recorded and returned to the lab for sleep restriction night sleep study (sleep period 4-8 am). The sleep studies were scored according to current guidelines. The following parameters were analyzed in both the baseline and sleep restrictive nights in the two groups: Sleep efficiency, percentage of slow wave sleep, percentage of REM sleep, arousal index; respiratory disturbance index; obstructive apnea and hypopnea index in REM and NREM sleep. Data were analyzed using ANOVA and paired student t-test.
Results: Sleep Architectures: After sleep restriction, sleep efficiency increased in both groups, there was no group effects; percentage of slow wave sleep increases in both groups ($P>0.05$); percentage of REM sleep decreases in both groups ($P<0.05$), however, there were no group effects. Arousal index was not increased significantly in both groups after sleep restriction. Respiratory Functions: Respiratory disturbance index was higher in the OSAS group, however, not statistically significant, no change was noted in the comparison group. There was also no difference in respiratory disturbance index between REM and NREM sleep in the OSAS patients.
Conclusion: This study confirms our previous study´s findings about sleep architectures: Acute sleep restriction increased slow wave sleep, with decreased REM sleep; However, it is to our surprise that some of the severe OSAS children in this study have less disordered breathings in the sleep restricted night. Normal children´s breathing functions were not affected by sleep restriction. The significance of this study is its clinical relevance about adequate sleep in school age children 6-10 year old who have obstructive sleep apnea.
Support (optional): NKH K01001958

0204

IMPACT OF 5 NIGHTS OF SLEEP RESTRICTION ON HEALTHY ADOLESCENTS´ BEHAVIORS

Beebe D,[1] Schaffner L,[2] Ridel S,[3] McNally K,[4] Grampp K,[3] Tlustos S,[4] Raouf A[2]
(1) University of Cincinnati, Cincinnati, OH, USA, (2) Children's Hospital Medical Center of Cincinnati, OH, USA, (3) Xavier University, OH, USA, (4) University of Cincinnati, OH, USA

Introduction: Adolescents are at high risk for obtaining inadequate sleep, and correlational studies have associated inadequate sleep during adolescence with poor behavioral and academic outcomes. Although such correlational studies are important, we cannot rely solely on them, as these yield associations that may have hidden confounding factors. Complementary experimental findings are needed to more clearly establish the presence and directionality of causation. Unfortunately, aside from sleepiness, no behavioral effect of experimental sleep restriction has been reported in any pediatric sample with a mean age older than 13.5. Here we document the impact of 5 consecutive nights of experimental sleep restriction on the behaviors of adolescents, as reported by the teens themselves and their parents.
Methods: Nineteen healthy adolescents aged 13.9 - 16.9 years completed a three-week experimental protocol. The first week assessed baseline functioning and validated the behavioral outcome measures. In counterbalanced order, participants then completed a short-sleep week (SS: Monday-Friday nights limited to 6.5 hours time in bed) and an extended sleep week (ES: 10 hours lights-out time in bed Monday-Friday nights). All participants´ sleep occurred at home, monitored with a daily sleep diary and objective actigraphy. Behavioral functioning was assessed using questionnaires obtained from parents and participants on the Saturday mornings following each week.
Results: All participants had markedly less sleep in the SS condition than the ES condition (average nightly gap 2.5 hours, $p < .001$). Parents reported that their teens displayed markedly greater sleepiness, inattention, anger/oppositionality, behavior regulation problems, and metacognitive problems in the SS condition than ES condition ($p < .01$). Teens reported the same symptoms, but the gaps between conditions were smaller and reached $p<.01$ only in sleepiness and attention problems.
Conclusion: Complementing large-sample correlational findings, this small-sample experimental study supports a causal relationship between inadequate sleep during adolescents and daytime behavioral morbidity.
Support (optional): Grants #K23 HL075369 and M01 RR 08084 from the National Institutes of Health, plus pilot funding from the Cincinnati Children's Division of Behavioral Medicine and Clinical Psychology

0205

FEASIBILITY AND SAFETY OF AN AT-HOME MULTI-NIGHT SLEEP RESTRICTION PROTOCOL FOR ADOLESCENTS

Beebe D,[1] Fallone G,[2] Godiwala N,[3] Flanigan M,[4] Martin D,[5] Amin R[6]
(1) University of Cincinnati, Cincinnati, OH, USA, (2) Forest Institute of Professional Psychology, MO, USA, (3) University of North Carolina, NC, USA, (4) Ohio University, OH, USA, (5) Miami University of Ohio, OH, USA, (6) Children's Hospital Medical Center of Cincinnati, OH, USA

Introduction: Adolescents are at high risk for obtaining inadequate sleep, and correlational studies have associated inadequate sleep during adolescence with poor functional outcomes. Few experimental sleep restriction trials have been used with adolescents, however, in part because of significant challenges to their feasibility. The aim of this presentation is to document the feasibility and ethics of a multi-night, at-home experimental sleep restriction protocol for use with adolescents.
Methods: Twenty healthy adolescents aged 13.9 - 16.9 years participated in a within-subjects, counterbalanced cross-over experiment during a summer break from school. The three-week protocol included a baseline week, followed in random order by a short-sleep week (SS; Monday-Friday nights limited to 6.5 hours time in bed) and an extended sleep week (ES; 10 hours lights-out time in bed Monday-Friday nights). All participant sleep occurred at home. Each participant completed a sleep diary and wore an actigraph nightly throughout the study. These

were reviewed with participants and parents on the Saturdays at the end of each study week, when participants also completed questionnaires about caffeine use, napping, accidents and injuries.
Results: One participant dropped out of the study, but each of the remaining 19 displayed markedly less sleep in the SS condition than the ES condition (average nightly gap ~2.5 hours, $p < .001$). Sleep diary and actigraphy findings were similar. Consistent with predictions, participants had shorter sleep latencies, more difficulty awakening, and better sleep efficiency in the SS than the ES condition ($p < .01$). There were no reported sleepiness-related accidents or injuries. A few participants broke directives with respect to driving, napping, and caffeine use; most could have been identified as problematic at the baseline assessment.
Conclusion: These data suggest that a multi-night, at-home sleep manipulation protocol for use with adolescents is feasible and can be conducted safely.
Support (optional): Grants #K23 HL075369 and M01 RR 08084 from the National Institutes of Health, as well as pilot funding from the Cincinnati Children's Division of Behavioral Medicine and Clinical Psychology.

0206

SLEEPINESS AND FATIGUE IN ADOLESCENTS

Chung S,[1] Vetsis E,[2] Shapiro C[2]
(1) University Health Network, Toronto, Ontario, Canada, (2) University Health Network, Ontario, Canada

Introduction: Adolescents in have short sleep length and commonly report daytime sleepiness. Aim: To investigate excessive daytime sleepiness (EDS) and fatigue among adolescents in high school.
Methods: Demographics of 96 students from Grades 9-12 (14-18 yrs) were collected and they were surveyed about sleep, daytime sleepiness and fatigue.
Results: These adolescents slept for 7.5 ± 1.2 hours on school nights. 60% reported EDS during school and, of these, 14% stated it was daily problem. Overall, 33% of students admitted to falling asleep in class and 28% reported taking naps at school. Sleep length in those with EDS (7.2 ± 1.2 hrs) was significantly ($p<0.005$) shorter than those without EDS (7.9 ± 1.1 hours). Adolescents with EDS were significantly ($p<0.02$) older (16.4 ± 1.5 years) versus those without EDS (15.7 ± 1.3 years) and more girls (71%) than boys (55%) reported having EDS. Regularity of bedtime was not related to complaints of EDS. Fatigue (very low energy levels) in the morning was endorsed by 46% of adolescents. Those reporting fatigue slept significantly ($p<0.04$) less time (7.0 ± 0.9 hrs) than those with normal energy levels (7.8 ± 1.2 hrs). There was no difference in age, gender distribution or grade point average in those reporting fatigue versus normal energy levels. However, an irregular bedtime schedule was twice more common in those reporting fatigue.
Conclusion: Symptoms of EDS and fatigue are common in high school adolescents. Those with EDS and fatigue have a shorter sleep time. EDS was related to older age and female gender. Fatigue was related to an irregular bedtime schedule.

0207

DO GENDER DIFFERENCES EXIST IN PRE-PUBERTAL AND ADOLESCENT CHILDREN WITH OBSTRUCTIVE SLEEP APNEA?

Won C, Guilleminault C
Stanford University, Stanford, CA, USA

Introduction: Gender differences in the prevalence, severity, and clinical presentation of obstructive sleep apnea (OSA) have been well-described in adults. We explored whether gender differences in clinical and polysomnographic features also exist in pre-pubertal and adolescent children with OSA.
Methods: We analyzed nocturnal polysomnographies of 1,079 children referred to the Stanford Sleep Disorders Center from 1996-2006 for symptoms consistent with obstructive sleep apnea. Studies during this period were conducted with the same equipment, and scored by the same team of scorers. Children were identified as pre-pubertal (age 2-12 years) or adolescent (age 13-18 years). Obstructive sleep apnea was diagnosed in children with apnea-hypopnea index (AHI)>1.
Results: OSA was diagnosed equally among the genders in pre-pubertal (21% of 495 boys, 20% of 299 girls), and adolescent children (17% of 181 boys, 23% of 104 girls). There were no gender differences in age, BMI, AHI, and sleep stages among pre-pubertal children with or without OSA, and adolescents without OSA. Among adolescents with OSA, however, boys had significantly less total sleep time (388±81 vs 419±78 mins), greater stage 1 sleep (7±6 vs 5±4%), and less stage 2 sleep (56±13 vs 60±10%). When comparing pre-pubertal to adolescent children, adolescent children had significantly greater BMI (26±9 vs 21±10 kg/m2), shorter total sleep time (378±79 vs 443±81 min), less REM periods (3±1vs 3.8±2), greater stage 2 (57±12 vs 49±13%), and less stage 3 or 4 sleep (22±13 vs 34±14%).
Conclusion: Gender differences in children were only reflected in adolescents with OSA, where boys despite having similar BMI and disease severity, manifested greater sleep architecture disturbances. The greater BMI, prevalence and severity of OSA reported in adult men with OSA was not observed in children in this study.

0208

SLEEPING IN THE HOSPITAL: PRELIMINARY DATA

Potasz C,[1] Varela M,[1] Varela M,[1] Ferraz P,[2] Modenesi L,[2] Feliciano R,[1] Carvalho L,[1] Prado L,[1] Prado G[1]
(1) Federal University of São Paulo, São Paulo, Brazil, (2) Children's Hospital Candido Fontoura, São Paulo, Brazil

Introduction: Hospitalization means a rupture in the child´s daily activities and represents a stressful experience requiring adaptation. It may cause eating and sleeping disorders, as well as endocrine reactions like a rise in cortisol levels (CL), disturbing internal homeostasis. Nevertheless the hospitalized child still needs to play, and being able to do so in the hospital may have important roles during this period. We present preliminary data of a study designed to evaluate the influence of playing in the levels of stress and sleep during hospitalization.
Methods: 26 children, 4 to 14 years old, hospitalized for pneumonia were evaluated. Trained researchers made sleep logs. CL was measured in 24 hour urine, on the first and seventh days of hospitalization. Children in one ward formed the Playing group (PG), and those in another formed the Non playing group (NPG). Hospitalization in different wards followed hospital routines and the researchers didn´t have any influence on it.
Results: The NPG (n=12) slept less at night (516.9±16.2 minutes) and showed higher CL (842.5±633.7µ/24) than did PG (n=14) with 547.3±20.6 minutes (p=0.13) and CL 321.4±168.2 µ/24 (p=0.36). NPG napped more times (0.63±0.51) and longer (58.8±49.1 minutes) than PG (0.40±0.28, p= 0.15; 51.6± 38.4 minutes, p=0.56).
Conclusion: These preliminary data suggest that playing seems to be a good tool for lowering stress and improving sleep in hospitalized children, but additional data must be added as the study continues.
Support (optional): Center of Multidisciplinary Studies Candido Fontoura

0209

EXCESSIVE DAYTIME SLEEPINESS, SLEEP-DISORDERED BREATHING AND ADHD IN OBESE CHILDREN

Cortese S,[1] Konofal E,[2] Mouren M,[2] Dalla Bernardina B,[3] Lecendreux M[3]
(1) Child psychopathology Unit, Robert Debré Hospital, Paris, France, (2) * Child Psychopathology Unit. *, France, (3) Italy

Introduction: Recent evidence suggests a possible association between obesity and symptoms of attention-deficit/hyperactivity disorder (ADHD). The mechanisms underlying this comorbidity are still unclear. One unexplored possibility is that obesity contribute to ADHD symptoms via Sleep-Disordered Breathing (SDB) and consequent Excessive Daytime Sleepiness (EDS). The aim of this study was to assess the relationship between symptoms of sleep disorders (including SDB), EDS and ADHD in a clinical sample of obese children and adolescents.
Methods: Forty-five obese subjects (age range: 10-16 years). The parents filled out the Sleep Disturbance Scale for Children (SDSC) and the Conners Parents Rating Scale-Revised (Short version) (CPRS-R:S).
Results: SDB and EDS scores on the SDSC were significantly correlated with the ADHD index on the CPRS-R:S (respectively, r= 0.313, p=0.036 and r=0.334, p=0.025). After controlling for EDS, SDB was no more significantly associated with ADHD symptoms, while, after taking into account the association between SDB and ADHD symptoms, EDS was still significantly associated with ADHD symptoms (p=0.038) in our regression model.
Conclusion: This is the first study that assesses the relationship between symptoms of SDB, EDS, and ADHD in a sample of obese subjects. According to our results, obese children with significant SDB and EDS might be at higher risk for ADHD symptoms, suggesting to systematically screening for ADHD in obese children with EDS and SDB. EDS, more than SDB per se, might specifically contribute to ADHD. However, since our cross-sectional study does not permit to infer causality, further studies are needed to confirm our hypothesis.
Support (optional): No financial relationship to declare

0210

POLYSOMNOGRAPHIC CHARACTERISTICS IN REGRESSED AND NONREGRESSED AUTISTIC CHILDREN

Giannotti F,[1] Cortesi F,[1] Vagnoni C,[1] Sebastiani T,[1] Cerquiglini A,[2] Bernabei P[2]
(1) University of Rome La Sapienza, Rome, Italy, (2) University of Rome La Sapienza, Italy

Introduction: Autism is a neurodevelopmental disorder, that, in about 30% of children, appears after an apparently "normal"development, as a loss of acquired abilities. Regression typically takes place between 1-3 yr. Autistic children frequently experience sleep disorders. In a previous study we found a higher incidence of parentally-reported sleep problems in regressed than nonregressed
Aim of the study was to compare video-EEG-polysomnographic data of regressed and nonregressed autistic children without coexistent pathologies.
Methods: Children with EEG abnormalities, epilepsy and profound mental retardation were excluded. We compared polysomnographic findings of 22 nonregressed (mean age 6,1 yr) with 14 regressed (mean age 5,8 yr) and 24 TD children matched for chronological age and gender.
Results: Anova results showed significant differences in almost all PSG data. Post-hoc contrast analyses showed that regressed had longer sleep latency (58 vs 42 vs 12 mins), lower sleep efficiency (76% vs 83% vs 94%), increased WASO (22 vs 14 vs 5 min), longer REM latency than nonregressed and, both than TD ($p < .001$). It is to be noted that TST was shorter, as well as the relative duration of REM and SWS, while stage I and II, were increased in regressed group, although these differences did not reach a level of significance because of large variance. None of the patient met PSG criteria for the diagnosis of OSA or PLM disorders.
Conclusion: Our findings suggested that, even though it is clear that sleep problems were highly prevalent in both groups, regressed showed more disrupted sleep pattern than nonregressed. Although the biological basis and possible casual relationships of these associations remain to be explained, they may point to different subgroups of patients. Even though the etiology of this frequent comorbidity remains unknown, our findings pointed to a potential interesting complex relationship between sleep and developmental regression.

0211

AN EPIDEMIOLOGIC STUDY OF SELF-REPORTED SLEEP PROBLEMS AND DAYTIME SLEEPINESS AMONG ADOLESCENTS IN NORTH TAIWAN

Huang Y,[1] Gau S,[2] Guilleminault C[3]
(1) Chang Gung Memorial Hospital, Taoyaung, Taiwan, (2) Taiwan, (3) Stanford University, Stanford, CA, USA

Introduction: This study was designed as a cross-sectional, community based study. The goals were to understand the prevalence of sleep problems and the associations of daytime sleepiness among Taiwanese adolescents; and to compare the adolescent´s sleep problems with the study conducted 10 years ago.
Methods: The considered schools involve the North Taiwan district. The classes to approach were selected randomly from schools in Lin-Kou area, and included elementary grade 6, junior high school and senior high school students. All 13-18 y/o adolescent from these classes were asked to participate. A self-reported sleep questionnaire was distributed to 2005 adolescents, in their respective school classes. 1939 completed questionnaires were returned. The response rate was 96.7%.
Results: There were 1906 valid questionnaires It involved 37.7% male and 62.3 % female. The mean of sleep time per weekday was 7.35+ 1.23 hrs, and 9.38+1.62 hrs on week-end days. Nocturnal time sleep on weekdays decreased significantly with increasing grade (mean nocturnal ST=6.87+1.14 for senior high school). About 47.3 % high school students reported presence of daytime sleepiness, and here was a trend toward reporting greater daytime sleepiness increased with higher school years/ grades. Daytime sleepiness in elementary school students is correlated with parasomnia. Daytime sleepiness in high school students is correlated with symptoms of sleep breathing problem , shorter night time sleep and increase intake of caffeinated beverages in the daytime.
Comparing the study to result of a study performed 10 years ago on junior high school students in the same Taiwan school district, there was no change in report of insomnia but report of parasomnia is significantly higher than 10 years ago.
Conclusion: Daytime sleepiness in high school students correlated with SDB, nasal allergy and caffeinated beverages intake. Sleep problems for Taiwanese adolescents have not changed significantly compared to those 10 years ago. Compared to other Far-East Asian countries, the youth in Taiwan report more sleep problems.

0212

A LARGE COMMUNITY BASED STUDY OF NEUROCOGNITIVE FUNCTIONING IN SNORING CHILDREN

Crabtree V, Sans Capdevila O, Witcher L, Gozal D
University of Louisville, Louisville, KY, USA

Introduction: Reduced global intellectual functioning has consistently been reported in children with sleep-disordered breathing (SDB). However, findings on the effect of SDB on specific areas of neurocognitive functioning have been mixed. This study sought to examine these relationships in a large community-recruited sample of children.
Methods: Parents of children ages 5-8 years (Mean age = 6.6 ± 1.0) enrolled in the Jefferson County (Kentucky) Public Schools were mailed questionnaires regarding their children´s sleep. Of the responders, 785 children (56% males) underwent nocturnal polysomnography and morning neurocognitive assessments that included the Differential Ability Scales (DAS), NEPSY, Clinical Evaluation of Language Fundamentals (CELF), Peabody Picture Vocabulary Test-II (PPVT-II), and Expressive Vocabulary Test (EVT).
Results: General Linear Model was used to determine relationships between respiratory and neurocognitive variables. The NEPSY Language and Visuospatial subscales were significantly related to apnea-hypopnea index (AHI), nadir SpO2, sleep pressure score (SPS), and obstructive apnea index (OAI) (r^2 = .07, $p < .001$ for Language and r^2 = .02, $p < .05$ for Visuospatial). The DAS Verbal and Nonverbal subscales and General Conceptual Ability, CELF Working Memory subscale, PPVT-II, and EVT were also significantly related to all respiratory variables (r^2 = .07, $p < .001$ for all). Although BMI z-scores did not independently contribute to the model, there were significant interactions between BMI z-scores and AHI, respiratory arousal index, SPS, and OAI in predicting neurocognitive scores.
Conclusion: To our knowledge, this is the largest community-based cohort of children in this age group to be assessed with attended nocturnal polysomnography and extensive neurocognitive measures. Higher AHI, SPS, and OAI, and lower nadir SpO2 were significantly related to almost all assessed areas of neurocognitive function, with the exception of the DAS Spatial subscale. Furthermore, while obesity did not independently affect neurocognitive functioning, BMI z-scores interacted with sleep-related respiratory disturbance to further affect neurocognitive scores.
Support (optional): This study was supported by NIH Grant #R01 HL-65270

0213

OBJECTIVE QUANTIFICATION OF SLEEP DURATION IN HEALTHY CHILDREN

Crabtree V, Dayyat E, Molfese D, Gozal D
University of Louisville, Louisville, KY, USA

Introduction: Most studies that have assessed children´s sleep duration have relied on parental reports, while the few that have used actigraphy in pre-adolescent children have not excluded primary sleep disorders with polysomnography.
Methods: As part of an ongoing study, 99 children ages 4 to 8 years (39% male; mean age = 6.64 ± 1.2 years) who had parental reports as non-snorers were assessed by overnight polysomnography. After normal sleep was confirmed, sleep duration was assessed by having children wear an actigraph on their non-dominant wrists for 7 nights with parents maintaining a concurrent sleep log.
Results: Mean total sleep time was 8 hours 17 minutes ± 36 minutes. Average sleep onset time was 9:52 pm with an average rise time of 7:37 am. Children were separated into four age categories (4-5, 6, 7, and 8 years), and a 4 X 2 ANOVA indicated significant main effects of both gender ($F = 17.41$, $p < .001$) and age ($F = 8.33$, $p < .001$), with a significant interaction in relation to sleep onset time ($F = 4.41$, $p = .001$). Six-year-olds initiated sleep later than 8-year-olds, and girls initiated sleep later than boys. Interaction effects indicated that while 4-5 year-old girls initiated sleep later than boys, 7-year-old boys were falling asleep later than girls.
Conclusion: To our knowledge, this is the largest sample of children with normal sleep in this age group to have actigraphically-recorded sleep duration. Although total sleep time has been reported to decrease as a function of age, we did not find supportive evidence. Furthermore, most children slept substantially less each night than is currently recommended or has been previously reported by parental report or actigraphy. This study provides rather compelling evidence that a large proportion of children appears to be receiving inadequate amounts of sleep.
Support (optional): Supported by NIH Grant # RO1 HL 070911-01

0214

SLEEP HYGIENE AND BEHAVIOR PROBLEMS IN SNORING CHILDREN

Witcher L, Gozal D, Crabtree V
University of Louisville, Louisville, KY, USA

Introduction: Several studies have examined the effects of sleep-disordered breathing, sleep restriction, dyssomnias, and parasomnias on daytime behavior in children. However, the potential relationship(s) between sleep hygiene and children´s daytime behavior have not been fully examined. The primary goal of this study was to investigate the relationship between poor sleep hygiene and problematic behaviors in snoring children.
Methods: Parents of 52 5- 8-year-old children (22 females; mean age = 6.98 ± 0.7 years) who were reported to snore "frequently" to "almost always" participated. As part of a larger, ongoing study, children underwent nocturnal polysomnography, and parents were asked to complete the Children´s Sleep Hygiene Scale (CSHS) and the Conners´ Parent Rating Scales-Revised (CPRS-R).
Results: Strong negative correlations between the CSHS overall sleep hygiene score and CPRS-R total externalizing behaviors ($r = -.51$; $p < .001$) emerged. The CSHS Total was also negatively correlated with the CPRS-R cognitive/inattention problems ($r = -.36$, $p < .01$), hyperactivity ($r = -.46$; $p < .01$), perfectionism ($r = -.29$, $p < .05$), ADHD Index ($r = -.50$; $p < .001$), restlessness and impulsivity ($r = -.45$; $p=.001$), emotional lability ($r = -.30$, $p < .05$), Global Index ($r = -.43$; $p < .01$), DSM-IV inattentive ($r = -.39$, $p < .01$), DSM-IV hyperactivity-impulsivity ($r = -.42$, $p < .01$), and DSM-IV total scores ($r = -.51$, $p < .001$). The CSHS physiological, cognitive, emotional, environmental, and bedtime routine subscales were also significantly negatively correlated with externalizing behaviors on the CPRS-R (p-values from < .001 to .04).
Conclusion: Parental reports indicate poorer sleep hygiene is associated with both internalizing and externalizing behavior problems, specifically those associated with ADHD symptoms. While no causation can be inferred, an overlap between daytime behavior problems, poor sleep hygiene, and potentially problematic bedtime behaviors in snoring children may exist and deserves further study.
Support (optional): This study was supported by NIH Grant #R01 HL-65270

0215

OBSTRUCTIVE SLEEP APNEA AND ENDOTHELIAL FUNCTION IN SCHOOL-AGED NON-OBESE CHILDREN: EFFECT OF ADENOTONSILLECTOMY

Gozal D, Kheirandish-Gozal L, Serpero L, Sans Capdevila O, Dayyat E
University of Louisville, Louisville, KY, USA

Introduction: Obstructive sleep apnea (OSA) in children is associated with increased cardiovascular morbidity such as systemic and pulmonary hypertension. However, it remains unclear whether endothelial dysfunction occurs in pediatric OSA, and whether it is reversible upon effective treatment.
Methods: Consecutive non-obese children (ages 6-11 years) who were polysomnographically diagnosed with OSA and age-, gender-, ethnicity-, and BMI-matched control children underwent blood draw the next morning for soluble CD40 ligand (sCD40L), ADMA and nitrotyrosine levels, as well as 2 30 sec cuff occlusion tests for assessment of endothelial function. These tests were repeated 4-6 months after adenotonsillectomy (T&A).
Results: OSA children showed blunted reperfusion kinetics following release of occlusion, which completely normalized in 18 of 26 patients after T&A. All 8 children in whom no improvements occurred had a strong family history of cardiovascular disease (vs. 4 of 18; $p<0.001$). Plasma nitrotyrosine and ADMA levels were similar in OSA and controls. However, sCD40L levels were higher in OSA, and were reduced after treatment, particularly in those with normalized hyperemic responses.
Conclusion: Postocclusive hyperemia is consistently blunted in children with OSA and such altered endothelial function is reversible 4-6 months after treatment, particularly if a family history of cardiovascular disease is not present. Although no evidence for either nitric oxide dependent oxidative/nitrosative stress or for the increased presence of the circulating NO synthase inhibitor ADMA were found in children with OSA, sCD40L levels were increased in OSA and overall reflected changes in endothelial function with treatment.
Support (optional): NIH grant R01HL-65270 (DG), The Children´s Foundation Endowment for Sleep Research, and the Commonwealth of Kentucky Challenge for Excellence Trust Fund.

0216

SLEEP PATTERNS IN CO-SLEEPING AND SOLITARY SLEEPING PRESCHOOL CHILDREN

Ward T,[1] Gay C,[2] Lee K[2]
(1) University of Washington, Seattle, WA, USA, (2) University of California, San Francisco, San Francisco, CA, USA

Introduction: The purpose of this study was to compare sleep patterns by actigraphy in co-sleeping and solitary sleeping 3-to 5- year-old children.
Methods: Data was collected from 53 preschool children. Wrist actigraphy was used to estimate sleep and nap patterns for 3 consecutive weekdays (Tuesday, Wednesday, and Thursday). Parents used sleep diaries to code the time and location of their child´s sleep. The Sadeh algorithm was used to estimate sleep measures. Co-sleeping was defined as sleeping in the same bed with a parent or sibling for at least half the duration of the night for 2 of the 3 nights.
Results: Forty-seven (n=23) of the children were White, 32% multi-ethnic, 15% Chinese, 4% African-American, 4% Latino/ Hispanic American, 2% Korean-American, and 2% Native American. Mean age of the children was 46.5+ 7.7SD months, 57% (n= 31) were male and 39% (n=21) co-slept. Family and child characteristics did not differ between co-sleeping and solitary sleeping children. Night time sleep did not differ ($t(49) = .732$, $p=.47$) between co-sleeping (542+ 34.0SD) and solitary sleeping children (552+50.7 SD). Daytime nap durations were 71 minutes for co-sleeping children compared to 57 minutes for solitary sleeping children. The number of night awakenings did not differ ($t(49) = -.487$, $p=.63$) between co-sleeping (1.7+.93SD) and solitary (1.6+.98SD) sleeping children. No differences were found for night activity between co-sleeping (20+4.6SD) and solitary sleeping (23+6.5SD) children. Bedtimes by actigraphy differed between co-sleeping children (21:31+0:24SD) than solitary sleeping (21:10+0:38SD) children.
Conclusion: We found a high prevalence of co-sleeping in our families regardless of socioeconomic status, race, and household space. Co-sleeping and solitary sleeping children did not differ on most of the actigraph sleep measures except bedtimes. Additional studies with objective measures are needed to gain a better understanding of co-sleepers and solitary sleeper´s patterns in preschool children.
Support (optional): NIH Grant #R01 NR05345, KA Lee, P.I. & Graduate Student Association, University of California, San Francisco

0217

DEVELOPMENT OF A CLASSROOM AID FOR TEACHING CHILDREN THE ASSOCIATION BETWEEN AGE, BEDTIME, SLEEP LENGTH AND WAKE-UP TIME: THE SLEEP SLIDE-RULE

Lushington K,[1] Kennedy D,[2] Martin J[2]
(1) University of South Australia, Adelaide, South Australia, Australia, (2) Adelaide University, South Australia, Australia

Introduction: Over the past decade, children have been going to bed later and sleeping less. This decline can be partly attributed to a general lack of awareness in the community concerning sleep need in children and how this varies across age. As part of a broader public health strategy addressing sleep, health and learning in children it was thought instructive to develop a classroom tool to illustrate the relationship between age and sleep need.
Methods: Based on the principle of an old fashioned slide-rule, a demonstration Sleep Slide-Rule unit was manufactured for use in the classroom. The Sleep Slide-Rule consisted of a top bar to indicate bedtime, a movable centre rule with a key to indicate sleep need for the age bands 3-5y; 5-12y and 12-18y (as per recommended guidelines) and a bottom bar displaying the appropriate wake-up time range according to age. The aid was trialled as part of a lesson plan on sleep in a cohort of Year 3 (9-10y) and Year 4 (10-11y) students. Feedback was collected from focus group report.
Results: Responses from teachers and children indicated that the Sleep Slide-Rule concept was instructive and functional. Examples of responses include: “You need between 10-11 hours of sleep”, “You need to change your bedtime if you are getting up early”, “We now know what `school night´ means”, “I need a lot more sleep than I normally get”, “I didn´t know you needed so much sleep”, “You don´t need as much sleep when you are older”, “Bedtime and going to sleep time are different” and “Sleep is really important to you as a human being”.
Conclusion: The Sleep Slide-Rule was found to improve children's understanding of the relationship between age and sleep need and, moreover, proved to be an effective teaching aid in the classroom setting.

0218

BEHAVIORAL SLEEP QUALITY IN CHILDREN OF REFUGEE AND NON-REFUGEE FAMILIES, A COMPARATIVE STUDY

Darchia N,[1] Gvilia I,[1] Eliozishvili M,[2] Oniani N,[2] Maisuradze L,[3] Lortkipanidze N,[4] Rukhadze I,[4] Naneishvili M,[4] Oniani T[4]
(1) I.Beritashvili Institute of Physiology, Tbilisi, Georgia, Tbilisi, Georgia, (2) I.Beritashvili Institute of Physiology, Tbilisi, Georgia, Georgia, (3) I.Beritashvili Institute of physiology, Tbilisi, Georgia, (4) Georgia

Introduction: Family environment is an important predictor of sleep quality in children. This work was aimed to evaluate sleep habits and sleep quality in children who are not refugees themselves but who grew up in refugee families adapting to life in Tbilisi after escaping from Abkhazia, and compare it to the sleep of children of non-refugee families. We addressed the question: how much the family status may affect sleep of children during their early maturation.
Methods: 60 children (7 to 11 years old) were studied in each group. Children completed Epworth sleepiness scale, Child Depression Inventory (CDI) and were interviewed regarding the main sleep-wake characteristics. General information about sleep behavior in children was collected from their parents as well. Parents were asked to evaluate children´s behavioral sleep quality and fill 15 items questionnaire that was generated based upon the relevant literature. Parents were administrated the Perceived Stress Scale (PSS). Chi-square analysis and ANOVA with repeated measures were performed.
Results: Total sleep time was nearly identical in both groups of children. Significant difference between sleep time on week and weekend nights was found only for children from refugee families; they slept 1.2h more on weekend nights ($p<0.05$). Non-refugee parents reported better sleep hygiene and quality compared to the other group. Children of refugee families were rated as having problems with going to bed and maintaining sleep, and they had higher rate of sleepiness during the day (51% vs. 34%; $p<0.001$). Significant difference in the mean total CDI scores between non-refugee and refugee groups were also revealed (7.4 vs. 9.7). Mean score for PSS was higher for refuge parents (23.9 vs. 18.7; $p<0.05$) appraising life situations as more unpredictable and stressful.
Conclusion: Findings of this study suggest that stressful family situation is a risk factor for developing behavioral problems and sleep disturbances in children.
Support (optional): Research supported by ESRS-Sanofi-Synthelabo research grant

0219

SLEEP ARCHITECTURE IN ASPERGER SYNDROME

Bruni O,[1] Vittori E,[2] Novelli L,[2] Vignati M,[3] Ferri R,[4] Curatolo P[3]
(1) University of Rome La Sapienza, Rome, Italy, (2) University of Rome La Sapienza, Italy, (3) University of Rome Tor Vergata, Italy, (4) Oasi Institute, Troina (EN), Italy

Introduction: Asperger syndrome (AS) is a pervasive developmental disorder characterized by altered social interactions, restricted interests and repetitive and stereotyped behavior as in autism but, contrary to the latter, does not show significant delay in language, psychomotor and cognitive skills. There are few studies on sleep patterns in children with AS, and no studies attempted to analyze sleep microstructure. The aim of this study is evaluate the sleep macrostructure and microstructure in children with AS.
Methods: Ten children with AS (mean age 14.4 years), 13 with autism (AD; mean age 9.4) and 12 normal controls (mean age 12.6) were enrolled and underwent standard polysomnographic recording. AS subjects filled out a two-weeks sleep diary and were assessed by means of the Wechsler Intelligence Scale (WISC-R) and the Pediatric Daytime Sleepiness Scale. Sleep microstructure was evaluated through the analysis of the cyclic alternating pattern (CAP).
Results: Children with AS showed no differences in macrostructural parameters, but an increase of periodic limb movements (PLMs) with a PLM index > 5 in all but one. Several differences have been found on CAP parameters: mainly an increase of CAP rate % in Slow Wave Sleep (SWS) (63.3 vs. 33.9 in AD; $p < 0.01$) and in the A1% phases (80.5 vs. 65.1 in AD; $p < 0.001$) and in A1 mean duration (9.5 vs. 4.9 in AD; $p < 0.001$). We found a positive correlation in AS children between CAP rate in SWS and A1 index with Verbal IQ and A1 mean duration with total IQ.
Conclusion: The analysis of CAP revealed an increase of the slow oscillations (%A1 phases) as a typical feature of AS vs. AD and mental retardation children that, on the contrary, had low level of A1. This finding and the high correlation between A1 and IQ in AS children might support the hypothesis of the importance of NREM sleep and of slow oscillations in the processes of learning and memory.

0220

EFFECT IN MEASURED SLEEP EFFICIENCY OF CHILDREN WITH AUTISTIC SPECTRUM DISORDER AFTER INITIATION OF A STANDARDIZED MANAGEMENT PROTOCOL

McNair A, Splaingard D, Iris K, Beasley S, Wynn J, Hayes J, Dzodzomenyo S, Splaingard M
Columbus Children's Hospital, Columbus, OH, USA

Introduction: Children with autistic spectrum disorders (ASD) often have significant sleep problems, but there is limited data regarding polysomnographic findings in these children. In addition, children with ASD often do not tolerate disruptions in their schedules or new environments, which can be challenging when they are involved in an overnight polysomnographic study. There can be problems in performing the sleep studies of children with ASD.
Methods: All children with ASD who underwent sleep studies at The Sleep Disorders Center at Children´s Hospital between 2/04 and 11/06 were included in this study. Beginning in 2/1/06, a standardized tailored protocol for children with autism (STP) was developed with the assistance of a psychological consultant. The protocol includes a tour of the lab and desensitization techniques and was instituted for children with autism prior to their sleep study. The family was also asked to bring items of comfort (e. g. videos, music, etc.) to help the child adapt to the demands of the new environment.
Results: Sixty-six children with ASD are included in this study. The study included 10 females and 56 males with a mean age of 8 years. 47 children underwent overnight polysomnographic studies prior to initiation of the STP intervention. 19 children underwent sleep study after the STP intervention. Sleep efficiency (SE) was compared in the two groups. There was no difference between SE in No STP group (n=47; mean=76.0%, 15.2 SD) and the STP group (n=19; Mean=80.7%, 14.0 SD) as assessed by a Student t-test (p=0.26).
Conclusion: No statistically significant difference in sleep efficiency was noted between the STP group and No STP group. Future study might include comparing parents´ perception of the hook-up process and their satisfaction with the sleep study night. Specific limitations and clinical implications will be discussed.

0221

SENSORY MODULATION AS A CONTRIBUTING FACTOR IN THE RELATIONSHIP BETWEEN SLEEP AND BEHAVIOR IN CHILDREN

Shochat T,[1] Tzischinsky O,[2] Engel-Yeger B[1]
(1) University of Haifa, Haifa, Israel, (2) Emek Yezreel Academic College, Emek Yezreel, Israel

Introduction: Investigations on the relationship between sleep and behavioral disturbances in children have yielded inconsistent results, and lack a conceptual framework defining causality and contributing factors. Our objective was to assess the contribution of sensory modulation in the relationship between sleep and behavior in school children.
Methods: Cross sectional questionnaire based design. Participants: A convenience sample of 56 parents of elementary school children (mean age: 8.6±2.0, 27 girls). Tools: The Children´s Sleep Habits Questionnaire (CSHQ, Owens *et al.*, 2000), was used for sleep assessment, with higher scores indicating higher sleep disturbance. The Connors Parent´s Rating Scale (CPRS, Connors, 1989) was used to assess behavior, with higher scores indicating more severe behavioral problems. The Short Sensory Profile (SSP, McIntosh *et al.*, 1999), was used to assess sensory sensitivity level, with lower scores indicating increased sensitivity. Procedures: Questionnaires were disseminated and collected a few days later. Pearson correlations were computed between global scores, partial correlation was computed between the CSHQ and the CPRS controlling for the SSP, stepwise linear regression was used to assess contributions of specific sensory modalities on sleep and behavior.
Results: Correlations between the CSHQ and the CPRS was r=0.47 (p<0.001), between CSHQ and SSP was r=-0.41 (p=0.002), and between CPRS and SSP was r=-0.52 (p<0.001). Partial correlation between CSHQ and CPRS controlling for SSP was r=0.33 (p=0.013). Significant predictors of sleep disturbance included vestibular (movement) sensitivity and auditory filtering accounting for 25% of the variance (F(2,53)=8.82, p<0.001); significant predictors of behavioral disturbance included sensation seeking and proprioceptive (energy) level accounting for 35% of the variance (F(2,53)=14.06, p<0.001).
Conclusion: Further investigations may shed light on the mechanisms underlying the relationships found between all three constructs. Sensory profiles of children suspected of sleep disturbance and/or behavioral disorders should be routinely assessed.

0222

MATURATION OF SLEEP HOMEOSTASIS BETWEEN AGES 9 AND 15, A LONGITUDINAL STUDY

Darchia N,[1] Campbell I,[2] Higgins L,[2] Trinidad J,[2] Feinberg I[2]
(1) I.Beritashvili Institute of Physiology, Tbilisi, Georgia, Tbilisi, Georgia, (2) University of California, Davis, Davis, CA, USA

Introduction: The decline in slow wave (delta) EEG activity across the night reflects the rate or dynamics of sleep homeostasis. We use longitudinal data to evaluate adolescent maturational changes in the homeostatic sleep process by determining whether the across night decline in standardized slow wave activity changes between ages 9 and 15.
Methods: Longitudinal data are from 6 semiannual at-home EEG recordings in two cohorts: C9 (n=31), initially age 9 and C12 (n=38), initially age 12. For each of the first five NREM periods, EEG power density (power/min) in the 1-4 Hz (delta) band was calculated for all artifact free epochs. The decline across the night in standardized delta power density is described by three parameters in the process S declining exponential function: tau – the time constant of the decline, SWA_A – the asymptote of slow wave activity, and SWA_0 – the initial slow wave activity minus the asymptote. We used SAS procedure NLMIXED to determine whether these parameters changed with age.
Results: In C9 none of the three process S parameters changed significantly between ages 9 and 12 years. In C12, SWA_0 significantly (p=0.01) changed with age, declining from 294% at age 12 at a rate of 14.5% per year. However, neither tau nor SWA_A changed (p=0.31 and p=0.65 respectively) across the 12 to 15 year age range.
Conclusion: The decline in SWA_0 in C12, but not in C9, indicates that homeostatic regulation is changing at a time in adolescence when raw (non-standardized) delta power density is declining rapidly. We propose that both changes are linked to adolescent brain maturational processes driven by synaptic pruning. Synaptic pruning reduces waking brain metabolic rate, which in turn reduces the need for the homeostatic recovery of slow wave sleep.
Support (optional): PHS Grant R01 MH62521

0223

SLEEP DISORDERS AND OBJECTIVE SCHOOL PERFORMANCE

Carvalho L,[1] Prado L,[1] Ferreira V,[1] Ruotulo F,[1] Torres I,[2] Biscuola F,[2] Juliano M,[2] Potasz C,[2] Prado G[2]
(1) Federal University of Sao Paulo, Sao Paulo, Brazil, (2) Federal University of Sao Paulo, Brazil

Introduction: The neuropsychological conditions are very important in the learning process. The sleep disorders (SD) are positively associated with cognitive dysfunction. We studied the objective school performance of children with SD comparing to children without sleep disorders (NSD).
Methods: We distributed 5400 Sleep Disturbance Scale for Children (Bruni, 1996) adapted for Brazilian Portuguese to 7- to 10-year-old children from elementary public schools of Sao Paulo City, Brazil, without any genetic syndrome. From 2975 returned questionnaires completed by parents, 2384 (1224 girls – 51%) had a teachers´ report about children´s objective performance, Mathematics and Portuguese grades (ranged from 0 to 10). We compared boys and girls, with SD and NSD, and insufficient grade (<5) and sufficient grade (≥5).
Results: We found 439 children with SD (18%) and there were more boys with SD (20%) than girls (17%, p<0.05). We observed 765 children with insufficient grade (32%), and there were more SD children (40%) than NSD children (25%, p<0.05). There was no grade difference comparing boys and girls with SD, but there are more NSD boys with insufficient grades (33%) than NSD girls (28%, p<0.05). Among boys, there were more SD boys with insufficient grade (43%) than NSD boys (33%, p<0.05). Among girls, there were more SD girls with insufficient grade (36%) than NSD girls (28%, p<0.05).
Conclusion: SD impaired the objective school performance of children. The SD made equally bad the performance of boys and girls that was different in children without SD.
Support (optional): Supported by FAPESP 02/02145-1.

0224

ASSESSMENT FOR SEVERITY OF SLEEP-DISORDERED BREATHING IN CHILDREN

Hara Y,[1] Noda A,[2] Nakata S,[3] Miyata S,[4] Honda K,[5] Minoshima M,[4] Sugiura M,[4] Nakashima T,[3] Koike Y[2]
(1) Nagoya University Graduate School of Medicine, Pathophysiology Laboratory Sciences, Nagoya, Japan, (2) Nagoya University School of Health Sciences, Nagoya, Japan, (3) Nagoya University Graduate School of Medicine Department of Head and Neck and Sensory Organ Medicine, Japan, (4) Nagoya University Graduate School of Medicine,

Pathophysiology Laboratory Sciences, Japan, (5) Nagoya University School of Health Sciences, Japan

Introduction: The clinical picture of sleep disordered breathing (SDB) differs between children and adults. Children appears to have clinical sequlae associated with milder forms of SDB than adults i.e. with fewer and shorter obstructive apneas. The purpose of this study is to examine the differences in polysomnographic findings between children and adults and to consider about severity of SDB in children.
Methods: We studied 15 adults and 15 children with SDB (adults; age 45.3 ± 8.4 years children; 6.7 ± 3.9 years mean ± SD) and all patients underwent polysomnography (PSG). Correlation between ΔSpo_2 and apnea-hypopnea durations were investigated by Piason correlation analysis. ΔSpo_2 was defined as subtraction of baseline Spo_2 and lowest Spo_2 in one apnea or hypopnea event. We calculated each of the apnea-hypopnea index (AHI) to compare cessation of airflow through the mouth and nose for ≥10 seconds (criteria 1) with absence of airflow for at least 2 breaths(criteria 2).
Results: In both children and adults, ΔSpo_2 was significantly correlated with durations of apnea/hypopnea (children; $r=0.75$, $p<0.001$. adults ; $r=0.70$, $p<0.001$). Mean ΔSpo_2 with short obstructive apnea of ≤ 2 respiratory cycles in children was significantly higher than those in adults(3.5 ± 1.4 vs 1.3 ± 0.5 %, $p<0.05$). In children, the AHI which calculated by criteria 2 was significantly higher than criteria 1 (6.5 ± 4.9 vs. 10.9 ± 9.4 /h, $p < 0.05$), but there are no significant differences between the two criterias in adults.
Conclusion: The changes of Spo_2 to duration of apnea/hypopnea significantly differ between children and adults. Our findings suggest that AHI as well as consideration of the Spo_2 on PSG would be more important for evaluating the severity of SDB in children.

0225

IMPROVEMENT OF OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS) IN CHILDREN AFTER TREATMENT OF GASTROESOPHAGEAL REFLUX (GER) WITH OMEPRAZOLE

Rizzi D, Cecinati V, Tesse R, De Sario V, Lorè M, Tranchino V, Armenio L, Brunetti L
University of Bari, Bari, Italy

Introduction: Recent studies have documented that apnoeas and/or apparent life-threatening events frequently coexist with GER episodes. Data on the association between nocturnal GER and OSAS are not available in children. The aim of the study was to investigate whether a treatment with an omeprazole may reduce the occurrence of sleep apnoea attacks in children.
Methods: Three children (age 0.5y, 2.4y, 3.9y) referred to our Department with chronic cough, severe snoring, sleep disruption, apnoeas, failure to thrive, but without gastrointestinal symptoms, performed a combined 24-h pH monitoring and nocturnal polysomnography (NP). The following data were recorded: Reflux Index (RI), obstructive apnoeas (OA) or central apnoeas (CA), hypopnoeas, *f*Ýarousal, oxygen desaturation, temporal relation between respiratory events and GER (related if occurring within 60 sec).
Results: All children had OSAS (AHI 3.5, 6.5, 3.2) and GER (RI: 12.4%, 30.5%, 5.4%) mainly nocturnal (RI: 18.8%, 38.2%, 11.1%). The NP detected 3 CA in two children, and one was preceded by GER; 17 OA in two children, and one of them had 8 out of 12 OA (67%) episodes preceded by GER; 81 hypopnoeas, 41 preceded by GER; 48 *f*Ýarousals, 13 (27%) preceded by GER. All children were treated with omeprazole (1mg/Kg, daily) for 3 months. All children presented clinical improvement of sleep disorders during the period of treatment.
Conclusion: Our findings suggest that GER episodes may play a role in worsening OSA attacks.

0226

UROLOGISTS´ ATTITUDE TO NOCTURNAL ENURESIS

Shahid A,[1] Chung S,[1] Shapiro C[2]
(1) University Health Network, Toronto, Ontario, Canada, (2) Youthdale Child and Adolescent Sleep Clinic, Ontario, Canada

Introduction: The reported incidence of nocturnal enuresis is 3% for boys and 2% for girls at age 10 years. It persists in about 1% of adolescents. Nocturnal enuresis is more common in children and adolescents with sleep disordered breathing and parasomnias, and also in those diagnosed with ADHD. The aim of this study is to investigate the attitude and experience of urologists in managing nocturnal enuresis and if they are aware of the link between this complaint and sleep problems in children and adolescents.
Methods: A survey was emailed to 48 urologists from Ontario and was followed up with fax for those urologists who did not respond to the emailed survey.
Results: Only a minority of the urologist responded to the survey. Of those responding, two-thirds saw patients with nocturnal enuresis and, on average, would see 5 patients under the age of 20 years per month with this problem. The majority of the patients seen are boys. The urologists reported that less than 20% of their pediatric nocturnal enuresis patients had significant neurodevelopmental problems and that an organic cause was found in only approximately 20% of the patients. The urologists did not refer any of their pediatric patients for sleep evaluation. The reasons given were that they were not previously aware of such a facility and/or they did not perceive a sleep evaluation to be necessary. None of the the urologists indicated that they wanted further information on this topic.
Conclusion: Awareness of the link between pediatric sleep disorders and nocturnal enuresis amongst this group of urologist appears very limited. Pursuing non-urological assessment and treatment seems to be of low priority in this group of specialists.

0227

BEHAVIORAL SCALES IN 5-7 YEAR OLD CHILDREN AND OBSTRUCTIVE SLEEP APNEA

Sans Capdevila O,[1] McLaughlin Crabtree V,[2] Witcher L,[2] Gozal D[2]
(1) University of Louisville, Louisville, KY, USA, (2) University of Louisville, KY, USA

Introduction: A relatively large number of studies suggest that children with snoring or sleep disordered breathing (SDB) are at increased risk for, and display higher levels of behavioral and cognitive problems. A wide range of behavioral problems have been reported in these children, including somatic complaints, anxiety, depression, aggression, oppositional behavior, inattention and hyperactivity. However, most of these studies were limited in size or included a wide age range. We here examine potential relationships between SDB severity and problem behaviors in a large sample of community recruited 5-7 year-old children.
Methods: Participants were 747 children (mean age: 6.65±0.51, 55% boys), selected from the Louisville public school system. Neuropsychological evaluation was performed in all participants the morning after the PSG. Parents also completed the Child Behavior Checklist (CBCL) and the Conners´ Parenting Rating Scales-Revised (CPRS-R) at the time of the neuropsychological evaluation.
Results: Group comparisons were used to test the hypothesis that the group with obstructive AHI of ≥5 (n=72) would display higher subscale scores on the CBCL and CPRS-R, compared to children with AHI < 5

(n=675). The group with AHI≥5 had significantly higher CPRS-R subscales scores for Oppositional (t = 2.91, p=0.03), ADHD index (t = 2.14, p=0.03), Hyperactive-impulsive (t = 2.22, p=0.03) and the total DSM-IV Behavioral Problems (t = 2.09, p=0.04). No significant differences were found between groups on any of the CBCL measures.
Conclusion: Sleep disordered breathing defined by an AHI≥5 is associated with more behavioral problems (hyperactivity, impulsivity and inattentiveness) when compared to the group of children with an AHI < 5, in otherwise healthy children. Furthermore, the CPRS-R appears to be more sensitive to the effects of sleep-disordered breathing on daytime behavior in children when compared to the CBCL.
Support (optional): NIH grant HL 65270

0228

THE IMPACT OF SLEEP ON CHILDREN´S EXECUTIVE FUNCTIONING

McNamara J,[1] McCrae C,[2] Berg W[1]
(1) University of Florida, Gainesville, FL, USA, (2) Gainesville, FL, USA

Introduction: Approximately 25 % of children experience sleep disturbance (Mindell, 1997). Exploring the relationship between sleep and cognition in children is important, because people with insomnia perform worse than good sleepers on attention and concentration tasks (Bastien, et al, 2003). Additionally, Steenari and colleagues (2003) found that sleep affects working memory in school age children. Furthermore, Pilcher and Huffcutt (1996) found that people who slept less had poorer reaction times. The Tower of London (TOL) task has been used to investigate aspects of problem solving, requires complex strategy use (Byrd & Berg, 2000), and assesses several components of executive functioning including inhibition and working memory (Shallice, 1982). This study examined the relationship between sleep and executive functioning in kindergarteners.
Methods: Children (n=27; mean age=5.66 years; SD=0.56) were given 30 TOL problems (ranging from 3- to 7-move problems). Parents were asked to complete 2 weeks of sleep diaries for their child. TOL variables examined were proportion of problems solved and efficiency of solution attempt. Sleep variables examined were napping, bed/waketimes, total wake time, and total sleep time.
Results: Parents reported that on average, their children´s sleep efficiency was 96.2 percent (SD=.03), total sleep time was 596.33 minutes (SD=53.35), and total wake time was 23.29 minutes (SD=16.77). The number of minutes children spent napping per day negatively impacted the number of problems solved, $F(1,23) = 4.849$, $p < .05$, R-squared=.174. Additionally, the later a child went to bed at night negatively impacted move efficiency, $F(1,26)=4.967$, $p < .05$, R-squared=.166.
Conclusion: Children who spend more time napping or who go to bed later at night may perform more poorly on complex executive functioning tasks. Implications are: 1-children must get sufficient sleep at night in order to perform well in school, and 2-napping is not a substitute for lost nocturnal sleep.

0229

PREVALENCE OF ENURESIS IN 5-7 YEAR-OLD CHILDREN AT RISK FOR OBSTRUCTIVE SLEEP APNEA (OSA) IS INDEPENDENT FROM THE SEVERITY OF RESPIRATORY DISTURBANCE

Sans Capdevila O,[1] McLaughlin Crabtree V,[2] Kheirandish-Gozal L,[1] Gozal D[1]
(1) University of Louisville, Louisville, KY, USA, (2) University of Louisville, KY, USA

Introduction: Both habitual snoring and OSA have been associated with nocturnal enuresis in children. Furthermore, effective treatment of OSA has been reported to improve or resolve underlying nocturnal enuresis in many of these children. However, it remains unclear whether the severity of respiratory disturbance influences the prevalence of enuresis.
Methods: Questionnaires collected from parental surveys of 5-7 year-old children attending the Jefferson County Public Schools in Louisville, KY during the period 2000-2006 were retrospectively reviewed for the presence of habitual snoring (HS > 3 nights/week) and enuresis (>1 night/week). In addition, the presence of enuresis was also assessed in a cohort of 378 with HS who underwent overnight polysomnographic evaluation
Results: There were 17,646 surveys completed (50.6% boys; 18.3% AA). 1,976 of these children (11.2%) were HS (53% boys; 25.2% AA). 531 HS had also enuresis (26.9%) with a predominant representation of males (472 boys; 87.5%). Among the 15,670 non-snoring children (NS), enuresis was reported in 1,821 children (11.6%; $p<0.00001$; OR: 2.79; CI: 2.50-3.13) of which 88.8% were boys. However, the frequency of enuresis among 378 children with HS was not correlated with the magnitude of respiratory disturbance during sleep as derived from the obstructive AHI, lowest SaO2, or Respiratory arousal index). Indeed, enuresis was reported in 33 of 149 HS children with AHI>2/hrTST (53% boys) as compared with 36 HS children with enuresis (62% boys) and AHI <2/hr TST (p-not significant).
Conclusion: The findings support the notion that habitual snoring is associated with a significant increase in the prevalence of nocturnal enuresis. However, the prevalence of enuresis is not modified by the severity of respiratory disturbance during sleep. Taken together, we postulate that even mild increases in sleep pressure due to HS may raise the arousal threshold and promote enuresis in particularly prone children.
Support (optional): NIH grant R01HL-65270 (DG), The Children´s Foundation Endowment for Sleep Research, and the Commonwealth of Kentucky Challenge for Excellence Trust Fund.

0230

PRACTICAL TIPS FOR CONDUCTING SUCCESSFUL ACTIGRAPHY RESEARCH IN CHILDREN WITH AUTISM SPECTRUM DISORDERS

Adkins K,[1] Goldman S,[1] Crowe C,[2] Malow B[2]
(1) Vanderbilt University, Nashville, TN, USA, (2) Vanderbilt University, TN, USA

Introduction: Sleep in children with autism spectrum disorders (ASD) is a topic of growing interest, with obtaining objective data an important component of the overall research. As an alternative to polysomnography (PSG), we have been incorporating actigraphy into our research designs.
Methods: Children ages 4 to 10 years with ASD are recruited into several ongoing studies, which include: (1) comparison of sleep parameters in children who are described by parents as either "good" sleepers or "poor" sleepers, (2) trial of supplemental melatonin for children who exhibit prolonged sleep latency, and (3) trial of parental education classes to assist parents in helping their children become better sleepers. Actigraphy data are collected in conjunction with PSG, sleep diaries, the Children's Sleep Habits Questionnaire, and questionnaires assessing behavior.
Results: Each family was given desensitization games, and picture books using a 'social story' approach to help prepare the child for the sleep and actigraphy experience. To ensure that actigraphy data are

collected accurately the study coordinator meets with the primary parent for an education session prior to the scheduled date for actigraphy use. An explanation for completion of the diary forms and use of the actigraphy device event marker was provided using sample diary forms and hands- on experience. The parent was given a scenario and asked to demonstrate how to complete the diary forms and use the actigraphy device event marker.
Conclusion: Presently, 28 children with ASD have successfully completed at least 7 nights of actigraphy. We attribute our success to our education supports using 'social story' booklets, face to face parental education and hands-on opportunity with the study coordinator.
Support (optional): Vanderbilt University Interdisciplinary Discovery Award, General Clinical Research Center MO1 RR00095, National Alliance of Autism Research/Autism Speaks Organization for Autism Research

0231

THE ADOLESCENT INCREASE IN DAYTIME SLEEPINESS IS STRONGLY RELATED TO THE DECLINE IN SLOW WAVE EEG ACTIVITY

Campbell I, Higgins L, Trinidad J, Feinberg I
University of California, Davis, Davis, CA, USA

Introduction: The increase in adolescent daytime sleepiness is commonly attributed to a changing sleep schedule that decreases adolescents´ nighttime sleep duration. However, in a study with sleep schedule controlled, Carskadon et al found that more mature adolescents were sleepier than younger subjects despite having the same sleep duration. We propose that adolescent daytime sleepiness is due in part to their declining intensity of waking brain activity. NREM slow wave EEG (delta) activity is a correlate of waking brain activity. We used longitudinal data to determine whether increasing subjective daytime sleepiness is related to declining delta EEG independently of sleep schedule changes.
Methods: Longitudinal data are from the first 6 semiannual recordings in two cohorts: C9 (n=31), initially age 9, and C12 (n=38), initially age 12. Subjects were studied in their homes on their habitual sleep schedules with ambulatory recorders. EEG power density (power/min) in the 1-4 Hz (delta) band was calculated for all artifact free epochs in the first 5 hours of NREM. Subjects rated sleepiness on a modified Epworth Sleepiness Scale. Habitual sleep schedule was both self-reported and determined from actigraphy.
Results: Sleepiness in C9 was only related to age. In C12, subjective daytime sleepiness was significantly ($p<0.01$) related to age, bedtime, time in bed, and delta power density. However, it was not related to rise time, NREM duration, REM duration or total sleep time. With sleep schedule measures controlled, sleepiness was strongly ($p<0.0001$) related to delta power density.
Conclusion: The data support our hypothesis that increasing sleepiness in adolescence is related to declining delta power density independently of sleep schedule changes. We believe that the delta decline is a correlate of adolescent brain maturation driven by synaptic pruning. This pruning decreases the intensity of waking brain activity, thereby decreasing arousal level and allowing the emergence of daytime sleepiness.
Support (optional): PHS grant RO1 MH62521

0232

THE CLEVELAND ADOLESCENT SLEEPINESS QUESTIONNAIRE: A NEW MEASURE TO ASSESS EXCESSIVE DAYTIME SLEEPINESS IN ADOLESCENTS

Spilsbury J,[1] Drotar D,[2] Rosen C,[1] Susan R[2]
(1) Case Western Reserve University School of Medicine, Cleveland, OH, USA, (2) Case Western Reserve University School of Medicine, OH, USA

Introduction: Excessive daytime sleepiness occurs among alarming numbers of adolescents and is linked to a variety of behavioral and cognitive problems. The purpose of this study was to develop and validate a brief, easily comprehensible instrument to measure adolescent daytime sleepiness that avoids some of the potential limitations of existing measures.
Methods: The study design was a cross-sectional analysis. Participants consisted of (a) a subsample of 411 adolescents 11-17 years of age recruited from area schools, churches, and "control" participants in a sleep disordered breathing cohort study; and (b) a second subsample of 62 adolescents with diagnosed sleep disordered breathing also participating in the sleep disordered breathing study. Participants completed the CASQ along with two other available measures of daytime sleepiness and other sleep parameters (sleep duration on school nights, sleep duration on non-school nights, and sleep debt, defined as non-school night sleep duration minus school-night sleep duration). Demographic information was obtained from a caregiver-completed questionnaire. The CASQ was developed using exploratory factor analysis, followed by confirmatory factor analysis using structural equation modeling techniques.
Results: Goodness-of-fit measures for the final 16-item scale structure ranged from good to excellent. The CASQ´s internal consistency was good ($\alpha = .89$). Correlations between the CASQ, two other measures of daytime sleepiness, and sleep parameters gave preliminary evidence of the CASQ´s construct validity.
Conclusion: The CASQ shows promise as a valid measure of daytime sleepiness in adolescents.
Support (optional): NIH Grants 5T32HD041923, RR02326402, HL070916

0233

CYCLIC ALTERNATING PATTERN (CAP) AND COGNITIVE FUNCTIONING IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA (OSA)

Kheirandish-Gozal L,[1] Sans Capdevila O,[1] McLaughlin Crabtree V,[2] Miano S,[3] Ferri R,[4] Bruni O,[5] Gozal D[1]
(1) University of Louisville, Louisville, KY, USA, (2) University of Louisville, KY, USA, (3) Rome, Italy, (4) Oasi Institute, Troina (EN), Italy, (5) University of Rome La Sapienza, Rome, Italy

Introduction: We have previously shown that sleep microstructure, analyzed as CAP, is altered in children with OSA. Furthermore, a substantial body of evidence indicates that children with OSA are at higher risk for neurobehavioral dysfunction. However, not all children with OSA display cognitive deficits, suggesting that differences in sleep microstructure among children with OSA may account for the variance in their cognitive phenotype.
Methods: 16 children with OSA were divided into 2 groups based on their general conceptual ability (GCA) as derived from the Differential Ability Scales battery, but were matched according to age, gender, ethnicity, BMI, and obstructive AHI. Their overnight NPSG were then blindly analyzed for NREM sleep microstructure (i.e., CAP).
Results: Mean age for the 2 groups was 7.0±0.2 years, 50% were

males, 37.5% were AA, and their mean BMI was 17.9±0.9 kg/m2. Their mean AHI was 4.1±2.3/hrTST. The GCA was <85 for 8 of these children and >100 for their matched counterparts. There were no significant differences in sleep macrostructure, such that total sleep time, sleep latency, and overall distribution of NREM and REM sleep were similar in the 2 groups. As previously reported for children with OSA, the NREM sleep microstructure in these 2 sub-groups differed from CAP rates in normal controls, with reduced CAP A1 and increased CAP A3 in the children with OSA. However, there were no significant differences in CAP rates or other CAP-derived measures in children with lower GCA when compared to those with normal GCA.
Conclusion: The variance in general conceptual ability (GCA) induced by OSA in children can not be solely explained on the basis of alterations in NREM sleep microstructure. While it is possible that increased sample size may reveal differences in CAP structure across children with or without neurocognitive alterations and OSA, we postulate that other mechanisms, i.e., intermittent hypoxia, may play a more substantial role. Alternatively, CAP alterations in OSA children may lead to more specific functional deficits, e.g., executive dysfunction.
Support (optional): Supported by National Institutes of Health HL-65270

0234

POLICIES, PRACTICES AND PROVISIONS FOR PARENTS SLEEPING OVERNIGHT WITH A HOSPITALIZED CHILD

Stremler R,[1] Wong L,[2] Parshuram C[3]
(1) University of Toronto, Toronto, Ontario, Canada, (2) University of Western Ontario, Ontario, Canada, (3) The Hospital for Sick Children (SickKids), Ontario, Canada

Introduction: This study describes, for the first time in the literature, practices, policies, and provisions for parents sleeping overnight with their hospitalized child.
Methods: A descriptive, cross-sectional design was used. Telephone surveys were completed with senior administrative staff at US and Canadian pediatric hospitals. Included hospitals had >50 acute care beds and >2 wards. Survey questions were based on literature and clinical experience. Data were analyzed with descriptive statistics.
Results: From July-September 2006, 184 of 268 hospitals were contacted. 15 hospitals were ineligible, 35 did not respond, and 134 interviews were completed (73% response rate). Hospitals had a median of 107 beds and 4 units. 134 (100%) general pediatric units allowed parents to sleep overnight; only 85 (66%) PICUs and 22 (18%) NICUs allowed parents to stay. 83 (62%) hospitals limited overnight visitors at the bedside to one, 46 (34%) hospitals to two visitors, and only 5 (4%) hospitals allowed >3 people to stay. Only 11 (8%) hospitals routinely allowed siblings to sleep overnight. 56 (42%) hospitals allowed parent-child bed-sharing. Overnight stays by parents were routinely limited based on number of patients in the room in 23 (17%) hospitals, and acuity of the child in 26 (19%) hospitals. Although 133 (99%) hospitals provided a bed for the parent at the child´s bedside, for parents not allowed at the bedside, only 62 (46%) hospitals provided a bed elsewhere, with limited access. 133 (99%) hospitals reported parental involvement in their child´s care at night, with 52 (39%) stating this was an expectation. 132 (99%) hospitals made provisions to improve sleep for parents, including use of music, reduced lighting and noise, and minimal visits to the room.
Conclusion: In general, parents are given the opportunity to stay at the bedside overnight, but barriers exist that limit opportunities for sleep during their child´s hospitalization.

0235

IN VITRO TONSILLAR TISSUE PROLIFERATION IN CHILDREN WITH TONSILLAR HYPERTROPHY: EFFECT OF ZILEUTON

Dayyat E,[1] Serpero L,[2] Kheirandish-Gozal L,[2] Goldman J,[1] Veling M,[1] Gozal D[2]
(1) Devision of Pediatric sleep Medicine , University of Louisville, Louisville, KY, USA, (2) University of Louisville, Louisville, KY, USA

Introduction: The leukotriene receptor (LR) antagonist montelukast appears to be effective in reducing of severity of respiratory disturbances during sleep in children with mild OSAS. However, the biological activity of this compound is restricted to the LR1, and therefore 5-lipoxygenase inhibitors (LPI) which operate upstream of the receptors in blocking leukotriene formation, could be potentially more effective in controlling lympadenoid tissue proliferation within the upper airway. We therefore examined the effect of zileuton, an orally administered LPI, on cellular proliferation of tonsils harvested from either children with polysomnographically-established OSAS undergoing tonsillectomy and adenoidectomy or from those with recurrent tonsillar infections.
Methods: Whole tonsil cell cultures were either maintained in normal medium (CO) or stimulated with a combination of lipopolysacharide and concanavalin A (STIM), in the presence or absence of zileuton at final concentrations of 10-4 to 10-6M, and then assessed for [3H]-thymidine incorporation for assessment of proliferation. Supernatants were also assessed for several inflammatory cytokines.
Results: STIM significantly increased proliferation rates in tonsillar cultures compared to CO (404±69 vs. 146±113 cpm, $p<0.0001$; n=15). Zileuton significantly reduced CO and STIM cellular proliferation rates, particularly at the highest drug concentration. Furthermore, TNFalpha, IL-6, and IL-12 concentrations in the STIM supernatants were reduced by zileuton at 10-4 M while no changes occurred in IL-8 and IL-10 levels.
Conclusion: Leukotriene pathways mediate both intrinsic and stimulus-induced proliferative signaling in pediatric tonsillar tissues from patients with either OSAS or recurrent infections. Targeted pharmacological approaches to disruption of leukotriene pathways may provide non-surgical alternatives for prevention and treatment of children with conditions associated with adenotonsillar hypertrophy, such as OSAS.
Support (optional): The Children´s Foundation Endowment for Sleep Research, and the Commonwealth of Kentucky Challenge for Excellence Trust Fund.

0236

SLEEP ESTIMATES IN YOUNG CHILDREN: PARENTAL VERSUS ACTIGRAPHIC ASSESSMENTS

Dayyat E,[1] Sans Capdevila O,[2] Gozal D,[2] Molfese D,[2] McLaughlin Crabtree V[3]
(1) Division of Pediatric Sleep Medicine , University of Louisville, Louisville, KY, USA, (2) University of Louisville, Louisville, KY, USA, (3) University of Louisville, KY, USA

Introduction: Actigraphy has now been well validated against polysomnography (PSG) in healthy adults. Although not as accurate as PSG for determining particular components of sleep, actigraphic recordings may be preferable for certain sleep assessments due to their ability to record over long time periods and their improved reliability over subjective sleep logs. However, the validity of using actigraphy as opposed to parental report for documenting some sleep parameters with children is based on very limited data.
Methods: As part of an ongoing study, we assessed 92 children (58%

female) ages 4-8 years (Mean = 6.6 + 1.2), who were reported by their parents to be non-snorers. Children with normal PSG were asked to wear an actigraph on their non-dominant wrist, and parents were instructed to maintain a concurrent sleep log over the course of one week. Sleep log reports and actigraphically-derived variables were compared using paired t tests.
Results: Parents reported bedtimes that were significantly earlier than actigraphic sleep onset (~ 22-41 minutes) across all 7 nights (p- < .01). Parental reports of rise times were significantly later than the actual children´s rise times (8-13 minutes) in 3 of 7 mornings (p-values < .05), with the other 4 mornings showing concordance.
Conclusion: The discrepancies between parental estimated bedtimes and actual sleep onsets may reflect either inaccurate reporting or alternatively longer sleep onset latencies. The more accurate reports on rise times were most likely due to parents waking their children for school. Thus, actigraphy may provide a more valid tool for assessing sleep in healthy children rather than relying solely on parental reports.
Support (optional): NIH Grant # RO1 HL 070911

0237

PREVALENCE OF RECURRENT OTITIS MEDIA IN 5-7 YEAR-OLD CHILDREN AT RISK FOR OBSTRUCTIVE SLEEP APNEA (OSA)

Gozal D,[1] Sans Capdevila O,[1] Kheirandish-Gozal L,[1] Dayyat E,[2] Kheirandish E[3]
(1) University of Louisville, Louisville, KY, USA, (2) Division of Pediatric Sleep Medicine , University of Louisville, Louisville, KY, USA, (3) Tehran, Iran

Introduction: The pathophysiology of both OSA and recurrent otitis media (ROM) is intimately associated with the presence of adenotonsillar hypertrophy in children. However, it remains unclear whether habitually snoring children have a higher prevalence of ROM and whether they require tympanostomy tube placement more frequently.
Methods: Questionnaires collected from parental surveys of 5-7 year-old children attending the Jefferson County Public Schools in Louisville, KY during the period 2000-2006 were retrospectively reviewed for the presence of habitual snoring (HS; > 3 nights/week), ROM (>6 OM episodes), and the need for tympanostomy tubes insertion.
Results: There were 16,321 surveys with complete datasets (51.2% boys; 18.6% AA with a mean age of 6.2±0.7 years). 1,844 of these children (11.3 %) were HS (53% boys; 25.9% AA). Of these, 827 HS had also a positive history of ROM (44.8%) with a slight predominance in males (55%). In addition, 636 of these children underwent placement of tympanostomy tubes (i.e., 34.4% of all HS and 76.9% of ROM). Among the 14,477 non-snoring children (NS), ROM was reported in 4,247 NS children (29.3%; p<0.000001; OR: 1.95; CI: 1.77-2.16) of which 57.6% were boys, and 1,969 NS with ROM underwent tympanostomy tube placement (i.e., 46.3% of those with ROM and 13.6% of all non snoring children). Thus, the risk for tympanostomy tube placement was also greater among HS compared to NS children (p<0.00001; OR: 2.19; CI: 1.98-2.43).
Conclusion: The findings support the notion that habitual snoring is associated with a significant increase in the prevalence of recurrent otitis media and the need for tympanostomy tube placement. Further studies aiming to assess the prevalence of obstructive sleep apnea among children with ROM are needed.
Support (optional): NIH grant R01HL-65270 (DG), The Children´s Foundation Endowment for Sleep Research, and the Commonwealth of Kentucky Challenge for Excellence Trust Fund.

0238

INCIDENCE AND REMISSION OF SLEEP RELATED SYMPTOMS IN CHILDREN

Goodwin J,[1] Silva Torres G,[2] Kaemingk K,[3] Sherrill D,[1] Morgan W,[1] Fregosi R,[1] Quan S[1]
(1) University of Arizona, Tucson, AZ, USA, (2) Arizona State University, AZ, USA, (3) University of Arizona, AZ, USA

Introduction: There are few reports of the incidence and remission rates of symptoms associated with sleep in children, such as loud snoring (SN), excessive daytime sleepiness (EDS), witnessed apnea (WITAP), and insomnia (INSOM).
Methods: Parents of 503 Tucson elementary school children allowed home polysomnograms on their 6-11 year-old children. Approximately 5 years later, 216 of these children completed a subsequent home polysomnogram visit. On both occasions parents were asked to report the frequency of symptoms associated with sleep in their child. The symptom was defined as present if the parent reported it occurred "frequently" or "almost always". EDS was defined as being sleepy in the daytime, falling asleep at school or while watching television. WITAP was defined as stopping breathing, struggling to breathe, or having to shake the child awake while sleeping. SN was present if the parent reported their child snored loudly. INSOM was present if the child currently experienced trouble falling asleep, staying asleep, or waking too early.
Results: The mean age at first assessment was 8.7 years (range 6-12) while mean age at second assessment was 13.7 (10-17). The mean time between assessments was 4.7 years (3.5-6.2). There were 52.3% males and 47.7% females. Ethnicity was 68% Caucasian and 32% Hispanic. The incidence rates for key symptoms of sleep disturbance were: SN 2.7%, EDS 13.1%, WITAP 0.4%, and INSOM 17.0%. Remission rates were 58.8%, 66.7%, 77.0%, and 59.7% respectively. The percent of children who were unchanged between assessments was 88.4%, 78.7%, 95.0%, and 71.8%. This represents 81.9%, 73.6%, 93.5%, and 61.1% answering “no” both times, and 7.0%, 5.1%, 1.4%, and 10.7% who answered “yes” both times.
Conclusion: In children, the incidence of nocturnal sleep apnea symptoms is relatively low, but the incidence of daytime symptoms are high. Remission rates of all symptoms were high.
Support (optional): HL 62373

0239

SLEEP DISORDERED BREATHING IN INFANTS WITH PIERRE-ROBIN SEQUENCE

Phromchairak J, Simakajornboon N
Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

Introduction: Previous studies have shown high prevalence of obstructive sleep apnea in infants with Pierre Robin sequence. A recent study has suggested that a prenatal brainstem dysfunction may play a role in pathophysiology of sleep disordered breathing and other abnormalities in some cases of Pierre Robin sequence. However, there is limited information on central apnea and the effect of apnea on sleep architecture in this population.
Methods: A retrospective review of polysomnogram was conducted at the Sleep Disorders Center, Cincinnati Children´s Hospital Medical Center. Infants with Pierre Robin sequence and age matched control were included into the study. All infants underwent multi-channels polysomnographic recordings. Any infants with significant identified neurological disorders or inadequate study were excluded from the study.

Results: 32 infants met the criteria for entry into analysis; 17 infants with Pierre Robin sequence [P] and 15 controls [C]. The average age for infants with Pierre Robin sequence was 1.8 ± 1.6 months (1-6 months). 15 of 17 infants with Pierre Robin sequence (88.2%) had obstructive apnea (obstructive index > 3/hr). 6 of 17 patients (35.3%) had central sleep apnea (central apnea index > 5/hr). 4 of 17 patients (23.5%) had nocturnal hypoventilation (EtpCO2 > 50 torr, >15% TST). Infants with Pierre Robin had significant changes in sleep architecture with a decrease in sleep efficiency (67.5±10.1% [P] vs 79.3±6.1% [C], P<0.05) and a decrease in the percentage of active sleep (37.0±13.0% [P] vs 54.8±7.1% [C], P<0.05). There was a significant correlation between sleep efficiency (SE) and the severity of apnea (RDI) (r=-0.50, p<0.05).
Conclusion: It is concluded that both obstructive and central apnea are common in infants with Pierre Robin sequence. Sleep disordered breathing leads to significant alteration in sleep architecture. It is speculated that brainstem dysfunction may underlie pathophysiologic mechanism of central apnea in this population.
Support (optional): Supported by the Cincinnati Children´s Hospital Research Foundation and King Bhumibol Royal Thai Air Forces Hospital Educaion Fund.

0240

SLEEP DISORDERED BREATHING IN CHILDREN WITH DOWN SYNDROME

Quennell N, Thomas V, Kirk V
Alberta Children's Hospital, Calgary, Alberta, Canada

Introduction: To study characteristics and treatment of sleep diordered breathing in children with Down Syndrome referred to a tertiary level Pediatric Sleep Service.
Methods: A retrospective review of children 0 to 18 yrs with overnight polysomnographic study (PSG) and diagnosis of Down Syndrome between December 1999 and August 2006. Data regarding demographics, PSG results incorporating diagnostic (Dx) and treatment (Tx) were entered into an Excel database.
Results: 172 children met criteria (mean age 6.71 years), (84 male, 88 female). The diagnostic PSG established 148 of 172 (85.5 %) had sleep disordered breathing defined as an AHI of 1.5 or greater. 144 were diagnosed with obstructive sleep apnea, 9 obstructive hypoventilation, and 19 were normal. Body sizes were grouped by observation; 48 normal weight, 57 thin, 37, mildly obese, 8 moderately obese, 4 severely obese, 18 not rated. Initial PSG (means shown): AHI 17.5, SaO2 (Minimum 81.0%, Mean 94.5%), ETCO2 (Maximum 54.6 mmHg, Mean 47.3), Sleep Efficiency 81.3%. 114 underwent surgical treatment, 100 adenotonsillectomy, 13 adenoidectomy, 1 tonsillectomy. Post operative PSG: AHI 15.9, SaO2 (Minimum 81.0%, Mean 94.4%), ETCO2 (Maximum 54.4 mmHg, Mean 49.0), Sleep Efficiency 81.9%. 99 required CPAP or BIPAP, 90 CPAP for obstructive sleep apnea and 9 BIPAP for obstructive hypoventilation. 63 underwent Tx PSGs and treatment re-evaluated every 6 months to 2 years. 9 % had sufficient improvement with time to discontinue CPAP. 36 are pending Tx PSGs due to compliance issues or on the PSG waitlist. CPAP or BIPAP treatment PSG: AHI 3.6, median 0, SaO2(Minimum 90.7%, Mean 95.7%), ETCO2 (Maximum 49.5 mmHg, Mean 45.2), Sleep Efficiency 82.6%.
Conclusion: Children with Down Syndrome referred for evaluation to the Pediatric Sleep Service have significant sleep disordered breathing. Adenotonsillectomy seldom provided sufficient treatment alone with the vast majority of children needing subsequent treatment with CPAP or BIPAP.
Support (optional): Marcus CL, Keens TG, Bautista DB, von Pechmann WS, Ward SL. Obstructive sleep apnea in children with Down Syndrome. Pediatrics 1991; 88:132-139 Dyken ME, Lin-Dyken DC, Poulton S, Zimmerman MB, Sedars E. Prospective polysomnographic analysis of obstructive sleep apnea in down syndrome. Arch Pediatr Adolesc Med 2003;157:655-660 Donnelly LF, Shott SR, LaRose CR, Chini BA, Amin RS. Causes of persistent obstuctive sleep apnea despite previous tonsillectomy and adenoidectomy in children with down syndrome as depicted on static and dynamic cine MRI. AJR 2004; 183:175-181

0241

SLEEP-DISORDERED BREATHING IN CHILDREN REFERRED FOR TYMPANOSTOMY TUBE INSERTION

Tauman R,[1] Derowe A,[2] Sivan Y[2]
(1) Tel-Aviv University, Tel Aviv, Israel, (2) Tel-Aviv University, Israel

Introduction: Adenoidal hypertrophy is a pathophysiologic factor of eustachian tube dysfunction. The latter may lead to chronic persistent middle ear effusion, recurrent otitis media and conductive hearing loss that are all treated by tympanostomy tube insertion (TTI). Adenoidal hyperthrophy is also the major underlying mechanism of sleep-disordered breathing (SDB) in children. Since adenoidal hypertrophy is a common pathophysiologic factor for both eustachian tube dysfunction and SDB, co-morbidity of these two disorders is anticipated. Therefore, our objective was to investigate whether children referred for isolated TTI are at increased risk for snoring and SDB.
Methods: Children who underwent isolated TTI between 1995 and 2003 were studied. In addition age- gender- and relBMI- matched children who did not undergo TTI were recruited as controls. Parents of all children completed a questionnaire that included demographic information and data regarding SDB symptoms and adenotonsillectomy at any time post TTI.
Results: 112 children (51% male) were studied. The mean age was 9.4±3.0 years and the mean relBMI was 105.3±22.8. Of these, 64 had isolated TTI (study group) and 48 were controls. The mean age at the time of TTI was 4.3±2.2 years and the mean time from the procedure to completing the questionnaire was 4.8±1.0 years. Significant increased frequencies of snoring and of adenotonsillectomy were found in the study group compared with the control group (27% vs. 10%, p=0.03 and 18.8% vs. 4.2%, p=0.02, respectively). The odds ratios for snoring and for adenotonsillectomy in children who underwent TTI compared to controls were 3.1 (95% CI: 1.1-9.2) and 5.3 (95% CI: 1.1-25.0), respectively. For the study group, there were no significant differences in age, age of TTI, gender, and relBMI between children who snored at any time after surgery compared to children who did not snore.
Conclusion: This study suggests that children referred for tube insertion are at increased risk for SDB. Although this increased risk may not justify routine adenoidectomy during TTI in non-snoring children, we suggest that a scheduled clinical and polysomnographic follow-up of these children is warranted.

0242

REM SLEEP ANALYSES DURING PUBERTY BY FFT

Kauati A,[1] Lopes M,[1] Guilleminault C,[2] Roizenblatt S,[3] Poyares D,[3] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Stanford University, Stanford, CA, USA, (3) Univ Fed Sao Paulo, Sao Paulo, Brazil

Introduction: Brain Maturation is associated with EEG changes during rapid eye movement (REM) sleep. There is higher delta power during sleep in the first decade in humans. After that changes in sleep EEG

might be related to puberty period. Most studies assessed EEG during wakefulness and NREM sleep. We sought to evaluate possible changes in REM sleep EEG spectral analysis across puberty.
Methods: Twenty healthy children were studied. They were divided into two groups: early puberty (n=10, mean age=10±0.9, ranging from 8 to 12) and late puberty (n=10, mean age= 14.8±0.9, ranging from 13 to 16). Polysomnography was performed in 2 nights, one for adaptation purpose. The Tanner scales were obtained and exclusion criteria were the presence of sleep and daytime complaints at least 14 days before recruitment. FFT was performed in C3-A2 derivation across all night, and during REM sleep. The FFT was calculated in 4s Hanning windows and the mean of delta (0.5-2.0 Hz), delta 2 (2.0-4.0 Hz), theta (4.0-8.0 Hz), alpha (8.0 - 12.0 Hz), sigma (12.0-16.0 Hz) and beta (16.0 - 20.0 Hz) were obtained.
Results: We found differences in EEG activities during REM sleep between two groups (U-test, $p<0.05$). The delta 2 (U-test, $p=0.02$) and theta power were higher in early puberty group (U-test $p=0.04$). The delta power correlated negatively with the duration in minutes of stage 1 ($rs=-0.46$ $p<0.05$), and the wake time after sleep onset ($rs=-0.48$, $p<0.05$) and correlated positively with sleep efficiency ($rs=0.45$, $p<0.05$). Theta power during REM sleep also correlated positively with stage 4 ($rs=0.45$, $p<0.05$).
Conclusion: The present results suggest that there are changes in REM sleep EEG across puberty, and it may relate to puberty brain maturation.
Support (optional): AFIP, FAPESP/CEPID

0243

SLEEP AND SLEEP BEHAVIOURS IN A SAMPLE OF FRENCH ADOLESCENT POPULATION

Viot-Blanc V,[1] Muzet A,[2] Krieger J,[3] Davenne D,[4] Levy P[3]
(1) Hôpital Lariboisière, Paris, France, (2) Institut National du Sommeil et de la Vigilance, Strasbourg, AE (Europe), Germany, (3) Institut National du Sommeil et de la Vigilance, AE (Europe), (4) Institut National du Sommeil et de la vVgilance, AE (Europe)

Introduction: While the NSF "Sleep in America" poll provided much information about sleep in young Americans, there was no data about the usual sleep schedule, the prevalence of sleep and sleepiness complaints in French adolescents.
Methods: A telephone survey was performed in a representative sample of 502 adolescents aged from 15 to 19 in February 2005 (quota method). Age, sex, familial, social and occupational status, sleep and sleepiness complaints, sleep duration, sleep schedule, sleep needs, daytime functioning impairment as well as consequences on daily life were collected and analysed. An Epworth Sleepiness Scale was also completed by each subject.
Results: The mean sleep duration of the sample before a weekday was 7h45 min, 78% sleeping 8hrs or less. During week-ends or holidays the mean sleep duration was 9h10 min, 50% sleeping 10 hrs or more. The usual bedtime shifted from 22h43 to 00h18 from weekdays to WE or holidays and usual wake time from 6h46 to 10h21. A majority (55%) wished to start work or school at least one hour later. The mean sleep need was 9h 02min. The individual sleep debt (difference between sleep need and sleep duration before weekdays) was 1h17min, 78% having a sleep debt of more than 1hr. Insomnia problems were rated as frequent in 19%. Peaks of severe stress, anxiety or blues were experienced frequently by 11% and occasionally by 23%. Drug intake against stress, anxiety or in order to improve sleep was present on a daily basis in 2%, occasionally in 8%, and seldom in 8%. EDS was frequent: 30% had an ESS>10, 55% complained of sleepiness or fatigue more than once a week during daytime and 65% upon awakening. Sleepy adolescents (ESS> 10) vs. non-sleepy had a slightly greater sleep debt (1h33 vs.1h10), they suffered also more often from stress, anxiety or blues, (44% vs. 33%) take more often drugs for stress, anxiety or sleep on a daily basis (6% vs1%) and have more absenteeism (3.4 vs. 2.1 days off) (all $p<0.05$).
Conclusion: Nearly 4 on 5 French adolescents from 15 to 19 are sleep deprived, they have sleep recovery on week-ends and holidays with a large delay of wake time. Insomnia, stress, anxiety, blues, and related drug consumption are not uncommon problems. These aspects are associated with excessive sleepiness which is present in 30% of the sample. Educational measures should target this population in order to prevent poorly adapted behaviours.
Support (optional): Survey performed by SOFRES and Institut National du Sommeil et de la Vigilance

0244

SLEEP LOSS IN SECONDARY SCHOOL STUDENTS IN HONG KONG

Wong T, Chan J
Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong SAR, China

Introduction: Sleep loss in adolescents is a recognized major global health issue. This is related to both intrinsic biological factors and extrinsic modifiable social factors. Adolescents of age 10 to 17 years have an average sleep requirement of 9 hours. However, recent data showed a consistent pattern of sleep loss of at least 1 hour in American and Asian adolescents.
Methods: We performed a questionnaire study in 2 secondary schools (1 ranked among the top, 1 ranked above average) in Hong Kong, using a Chinese version of the School Sleep Habits Survey Questionnaire.
Results: Of the 456 questionnaires completed, 26 were excluded because of presence of significant medical illness or incomplete data. We analyzed 430 questionnaires from students studying Form 1 to Form 7 (mean age 12.6 to 18.7 years). During school nights, the mean sleep durations decreased from Form 1 to Form 7 ($p<0.001$), with mean sleep durations of 7.8, 7.4, 7.1, 7.0, 6.9, 6.4, and 6.5 hours respectively. Compared with the 9 hours sleep requirement, the estimated sleep loss ranged from 1.2 to 2.6 hours. Bedtime was progressively delayed from Form 1 (mean 22:53) to Form 7 (mean 00:21), whereas rise time remained unchanged at around 07:00. During non-school nights, the mean sleep durations were similar across all Forms, ranging from 8.9 to 9.2 hours ($p=0.53$). These were much longer than the sleep durations during school nights, suggesting a significant sleep loss during the school nights.
Conclusion: Secondary school students in Hong Kong suffered from significant sleep loss, which was worse towards higher Forms. The sleep loss was related to progressively delayed bedtime during the school days. The degree of sleep loss was slightly worse than that reported in the Sleep in America poll.

0245

AFFERENT RESPIRATORY PROCESSING IN CHILDREN WITH CONGENITAL CENTRAL HYPOVENTILATION SYNDROME

Huang J,[1] Colrain I,[2] Bandla P,[3] Schwartz M,[1] Pepe M,[1] Samuel J,[1] Panitch H,[3] Bradford R,[3] Mosse Y,[3] Marcus C[1]
(1) Children's Hospital of Philadelphia, Philadelphia, PA, USA, (2) SRI International, Menlo Park, CA, USA, (3) Children's Hospital of Philadelphia, PA, USA

Introduction: Congenital central hypoventilation syndrome (CCHS) is characterized by generally adequate ventilation during wakefulness but

alveolar hypoventilation during sleep, to the point where patients need mechanical ventilation. Respiratory mechanoreception has not been studied in CCHS during sleep. Respiratory sensation can be tested by measuring respiratory-related evoked potentials (RREPs); RREPs are thought to be mediated in part by mechanoreceptors. RREPs are obtained by occluding the airway briefly during inspiration and measuring the resultant cortical EEG. In children sleep RREPs are dominated by an N350 component. We therefore hypothesized that children with CCHS have abnormal respiratory mechanoreception during sleep as reflected by a smaller N350 component.
Methods: Eight subjects with CCHS and 12 controls slept with a nonrebreathing valve connected to either a facemask or a tracheostomy tube. Flow was measured using a pneumotachograph and a differential pressure transducer. Pressure from the mask or tracheostomy was measured by a pressure transducer. Multiple, 400 ms inspiratory occlusions were performed during stage 2, slow wave (SWS) and REM sleep. EEG activity was averaged and RREPs were determined for each sleep stage at Fz, Cz and Pz. N350 amplitude was analyzed with a site x sleep state x diagnosis ANOVA.
Results: RREPs were produced by all patients and controls. Patients with CCHS had significantly smaller N350 amplitudes than controls ($p < 0.05$). The site (largest at Fz, $p < 0.001$), and sleep state (largest in stage 2, $p < 0.001$) factors were also significant. None of the interaction terms was significant.
Conclusion: While subjects with CCHS have a significantly smaller N350 than controls, they nevertheless demonstrate a robust RREP response during sleep. Previous studies raised the speculation that patients with CCHS have functional chemoreceptors but have abnormal central integration of chemoreceptor input. This study supports the presence of intact mechanoreception, but leaves open the possibility of abnormal central integration of respiratory afferents.
Support (optional): This study was supported by NIH grants M01-00240, U54-RR023567, R01-HL58585 and a research grant from Respironics.

0246

NEUROPHYSIOLOGIC ASSESSMENT OF BRAIN MATURATION: PRELIMINARY RESULTS OF A SIX-WEEK TRIAL OF SKIN CONTACT WITH PRETERM INFANTS

Scher M,[1] Kaffashi F,[1] Johnson M,[2] Ludington-Hoe S,[1] Holditch-Davis D,[3] Loparo K[1]
(1) Case Western Reserve University, Cleveland, OH, USA, (2) Case Western Reserve University, OH, USA, (3) University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Introduction: Skin-to-skin contact (SSC) promotes physiological stability and improves developmental care. Validation of this practice using neurophysiologic studies (EEG) compared brain maturation between SSC and non-SSC cohorts.
Methods: Sixteen EEG studies (8 infants) at 32 and 40 weeks. Each child received six weeks of SSC compared with two non-SSC cohorts (T-test comparisons $p<.05$). Seven linear physiologic measures (a dysmaturity index) (1,2) (REMs, arousals, quiet sleep percentage, sleep cycle length, spectral beta power, spectral EEG correlation, and spectral respiratory regularity), using Mahalanobis Distance which calculates differences in the preterm vector to the center of the cluster of fullterm infants at the same corrected age. Non-linear analyses were approximate and sample entropy.
Results: Fewer REMs ($p=.0001$), more quiet sleep ($p=.0005$), increased respiratory regularity ($p=.0077$), longer cycles ($p=.0148$), and less spectral beta ($p=.0259$) for SSC compared with fullterm non-SSC cohorts. Fewer REMs ($p=.00006$), greater arousals ($p=.0002$), more quiet sleep ($p=.0005$), and greater spectral beta ($p=.0136$) for SSC compared with a non-SSC preterm cohort at term.
Five regions had greater complexity on sample entropy (C4-O2, T4-O2, T4-C4, C3-Cz, and C4-Cz), while only the right hemisphere was more complex for SSC than both fullterm and preterm cohorts at corrected term ages (C4-O2, T4-C4, C4-Cz). Left posterior hemisphere was less complex for the SSC group (T3-C3, C3-O1, T3-O1).
Conclusion: Linear and non-linear signal measures detect altered region-specific brain maturation with SSC. Earlier findings reported fewer arousals and more quiet sleep after a single SSC session at 32 weeks gestation (3). Computational analyses of neonatal state represent phenotypic markers of developmental neural plasticity.
1. Scher MS: Pediatr Neurol 16:287-295, 1997.
2. Scher MS, Jones BL, Steppe DA, et al: Clin Neurophysiol 114:875-882, 2003.
3. Ludington-Hoe SM, Johnson MW, Morgan K, et al: Pediatrics 117:e909-923, 2006.
Support (optional): NS01110, NS26793, RR0084, NS34508, NR01894, NR04926

0247

ADOLESCENT ALCOHOL USE ASSOCIATED WITH GENERAL PRODUCTIVITY AND ACTIVITY LEVEL DUE TO SLEEPINESS

Stone K,[1] Acebo C,[2] Carskadon M[3]
(1) Brown University, Providence, RI, USA, (2) Brown University, RI, USA, (3) Brown Medical School, Department of Psychiatry and Human Behavior; E.P. Bradley Sleep and Chronobiology Research Lab, Providence, RI, USA

Introduction: This study investigates alcohol use as a predictor of sleepiness among adolescents, an association few studies have explored.
Methods: 49 high school students (at least 10 from each grade, 61% female) completed weekly questionnaires for 4 months regarding how many days they used alcohol as well as whether their use was during one or multiple parts of the day. From this questionnaire adolescents were categorized as either alcohol-using or non-using, and frequency of alcohol use was calculated. Daytime functioning was assessed once with the Functional Outcomes of Sleep Questionnaire (FOSQ). FOSQ general productivity was measured by rating how much difficulty participants had due to sleepiness with activities such as concentrating and eating. FOSQ activity level was measured by rating general level of activity, how affected relationships had been by sleepiness, and how much difficulty adolescents had with activities such as keeping pace with peers. FOSQ social outcome was measured by how much difficulty adolescents had visiting with others due to sleepiness.
Results: According to independent samples t-test, alcohol using adolescents reported more impairment due to sleepiness with regard to general productivity than non-alcohol-using adolescents, $t(45) = 2.9$, $p = .006$. Using hierarchical regression analysis, alcohol use was a significant predictor of activity level due to sleepiness ($\hat{a} = -.029$, $p = .033$) after accounting for social outcome. Higher reported levels of alcohol use and lower levels of social difficulty predicted lower levels of activity due to sleepiness. There were no significant interactions between gender or grade and alcohol use.
Conclusion: The data suggest that adolescent alcohol use may contribute to daytime sleepiness and warrant further investigation of associations between alcohol use and sleeping patterns. Causation cannot be inferred from this study. Future studies should manipulate alcohol use in adolescents to assess its direct effects on sleeping patterns and daytime consequences.

0248

SLEEP IN CHILDREN WITH PRENATAL COCAINE EXPOSURE

Stone K,[1] High P,[2] Lester B[2]
(1) Brown University, Providence, RI, USA, (2) Brown University, RI, USA

Introduction: Little is known about the effects of prenatal cocaine exposure (PCE) on sleep. We investigated whether mother-report of sleep deficits were more prevalent in PCE children compared to controls.
Methods: Using data collected for the Maternal Lifestyle Study (MLS) – a longitudinal, multi-site investigation of the effects of PCE – we investigated children´s sleep in the Providence cohort of the MLS (n = 108-159; no race or gender differences between groups) as reported by mothers at various time points with the Child Behavior Checklist, a general health questionnaire, and the Family Interest Interview. Sleep-related items assessed by these measures include nightmares and fatigue in addition to the following: sleeping less/more than most kids, talking/crying/walking in sleep, having trouble falling/staying asleep, not wanting to sleep alone, resisting bedtime, and being diagnosed with a sleep disorder.
Results: According to mother-report, at 2.5 years of age the PCE group protested going to bed significantly longer (p = .009) and woke up calling for attention significantly more often (p = .006) than did the unexposed group. At 7 years of age mothers reported that children in the exposed group were more likely to talk/walk in sleep than children in the unexposed group (p = .028). At 9 years of age mothers of children in the exposed group reported those children sleeping less than most children significantly more frequently than did mothers in the unexposed group (p = .015). At 10 years of age children in the exposed group were significantly more likely to be diagnosed with a sleep disorder than children in the unexposed group (p = .011) according to maternal report.
Conclusion: Results suggest sleep problems associated with PCE. Possibly, some of the behavior and cognitive effects reported in children with PCE are mediated by sleep problems.
Support (optional): This work was funded under a cooperative agreement (U-10) by NICHD and NIDA through the NICHD NICU Research Network.

0249

CYCLIC ALTERNATING PATTERN EXPRESSION DURING NREM SLEEP ACROSS PUBERTY.

Lopes M,[1] Guilleminault C,[2] Roizenblatt S,[3] Poyares D,[3] Tufik S[4]
(1) Sao Paulo, Brazil, (2) Stanford University, Stanford, CA, USA, (3) Univ Fed Sao Paulo, Sao Paulo, Brazil, (4) Universidade Federal de São Paulo, São Paulo, Brazil

Introduction: It has been reported a reduction in delta EEG power in post-pubertal adolescents with Tanner Scale = 4/5 compared to Tanner Scale = 2/3 children. Since delta is a fundamental frequency band included in cyclic alternanting pattern (CAP) A phases, we hypothesized that there are differences between peripubertal and post-pubertal healthy children in the expression of phasic events of CAP during NREM sleep.
Methods: 21 healthy children (10 subjects (5 boys; 10.0 ± 0.9 years), ranging from 8 to 12 years old with Tanner scale 2 or 3, and 11 subjects (6 boys; 14.4 ± 1.0), ranging from 13 to 16 years old with Tanner scale 4 or 5) were analyzed by standard polysomnogram after adaptation night in sleep laboratory. The sleep was scoring according to standard criteria and CAP analyses.
Results: Comparing peripubertal and post-pubertal period by Mann-Whitney U-test significant differences were found: CAP rate (61.5 ± 10.2% vs 46.6 ± 5.5%, p=0.005), CAP cycle (545.6 ± 129 vs 391.6 ± 58.4, p=0.002), sequence time in seconds (456.3 ± 62.4 vs 333.5 ± 65.4, p=0.0003), duration of CAP cycle (25.1 ± 1.7 vs 27.7 ± 2.1, p=0.006) and duration of phase B (17.5 ± 0.8 vs 19.7 ± 1.6, p=0.004). However, the duration of phase A CAP in minutes was not different between groups (7.6 ± 0.8 vs 8.0 ± 1.3). The subtypes of CAP were not significantly different: subtype A1 (85.3 ± 2.8% vs 79.1 ± 10.7%), CAP A2 plus A3 subtypes (21% ± 10.7) vs 14.7 ± 2.8%).
Conclusion: There is an increase in CAP phasic events in NREM sleep during early pubertal period and an increase in the duration of phase B of CAP (background EEG activity) in post-pubertal adolescents. The present results suggest that there is a higher stability of older adolescents compared to peripubertal age, as seen by increase in the time of phase B of CAP in NREM sleep.
Support (optional): Supported by AFIP.

0250

THE CLINICAL MANIFESTATION OF SLEEP-DISORDERED BREATHING IN CHILDREN AND ADOLESCENT

Kim J, Won C, Guilleminault C
Stanford University, Stanford, CA, USA

Introduction: Sleep-disordered breathing (SDB) in children is associated with several sleep and daytime symptoms. We investigated the clinical symptoms and their frequency associated with the reports of chronic snoring with or without witnessed sleep apnea.
Methods: A retrospective study of children up to 18 years of age referred to Stanford sleep clinic was done. All subjects had clinical interviews and examinations, filled in Pediatric Sleep Questionnaires and underwent overnight polysomnograms.
Results: A total of 189 patients' charts were reviewed (M:F=108:81, mean age:9.0 ± 4.4 years). Children were subdivided in preschool (n=41), pre-adolescent (n=91) and adolescent (n=51) groups. For each age group, from preschool up to adolescent, they presented the following associated problems: Daytime fatigue (30%, 50%, 71.1%, p=0.002), excessive daytime sleepiness (38.7%, 59.2%, 80.4%, p=0.001), sleep-onset insomnia (40%, 21.6%, 48.1%, p =0.006), nocturnal sleep disruption (85.3%, 69.5%, 70.6%, p =0.195), sweating during sleep (46.9%, 56.6%, 37.5%, p =0.114), sleep talking (54.5%, 50.7%, 27.7%, p=0.019), sleep terror (51.5%, 28%, 19.1%, p=0.007), sleep walking (9.4%, 24%, 12.8%, p=0.112), enuresis (40.7%, 31.9%, 20.5%, p=0.172), bruxism during sleep (50%, 49.3%, 23.9%, p=0.013), nightmare (12.5%, 19.7%, 21.3%, p=0.586), attention deficit-hyperactivity (13.8%, 29.4%, 40.9%, p=0.046), morning headache (9.7%, 12%, 19.1%, p=0.416) and delayed sleep phase syndrome (0%, 4.1%, 30.6%, p<0.0001). PSG findings showed similar mean apnea-hypopnea indices (mean ± SD: 16.4 ± 16.8, 10.3 ± 13.3, 16.2 ± 22.9; p=0.120) and mean respiratory disturbance indices (16.6 ± 15.7, 11.1 ± 12.2, 16.3 ± 21.8; p=0.089) between three groups.
Conclusion: Children referred for chronic snoring present florid symptomatology that did not lead to consultation and remained untreated. SDB-associated sleep problems and daytime dysfunctions change with age despite persistence of similar apnea-hypopnea index and respiratory disturbance index in all three age groups.

0251

SPONTANEOUS BREATHING IN CHILDREN WITH CONGENITAL CENTRAL HYPOVENTILATION SYNDROME IN REM VS. NON REM SLEEP

Marcus C,[1] Schwartz M,[1] Bandla P,[2] Samuel J,[1] Pepe M,[1] Panitch H,[2] Bradford R,[2] Ian C,[3] Mosse Y,[2] Huang J[1]

(1) Children's Hospital of Philadelphia, Philadelphia, PA, USA, (2) Children's Hospital of Philadelphia, PA, USA, (3) Stanford Research Institute International, Menlo Park, CA, USA

Introduction: Congenital central hypoventilation syndrome (CCHS) is a rare condition characterized by generally adequate ventilation during wakefulness but alveolar hypoventilation during sleep, to the point where patients need mechanical ventilation. The early literature suggested that hypoventilation in children with CCHS was less severe during rapid eye movement (REM) than nonREM sleep. This conclusion was drawn from a few case reports and has not been tested rigorously. We hypothesized that there would be no difference in terms of hypoventilation between REM and nonREM sleep in children with CCHS.
Methods: Nine subjects with CCHS, aged 4 months to 20 years, were studied during sleep while being mechanically ventilated on their home settings. Spontaneous ventilation during REM and nonREM sleep was evaluated briefly by disconnecting the ventilator under controlled circumstances. Once the end-tidal PCO2 rose to more than 60 mm Hg or SaO2 dropped to less than 85%, patients were placed back on their ventilators.
Results: Arousal occurred in 56% of REM trials vs. 32% of nonREM trials (NS). Central apnea occurred in 25% of REM vs. 68% of nonREM trials (p=0.026). The average minute ventilation (VE) during the challenge was 30±26% (mean ± SD) of baseline in REM vs. 12±17% in nonREM (p=0.036).
Conclusion: 1. Children with CCHS have hypoventilation and central apnea when breathing spontaneously during sleep. However, patients who are usually adequately ventilated during sleep frequently arouse in response to gas exchange abnormalities. 2. The hypoventilation in CCHS is more severe during nonREM than REM sleep.
Support (optional): This study was supported by NIH grants M01-00240, U54-RR023567, R01-HL58585 and a research grant from Respironics.

0252

LEVETIRACETAM (LEV) AS A POSSIBLE TREATMENT FOR RLS IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD) CHILDREN

Silvestri R,[1] Arico' I,[2] Gagliano A,[3] Calarese T,[3] Condurso R,[4] Gervasi G,[4] Mento G[2]
(1) Sleep Medicine Center Messina Italy, Messina, Sicily, Italy, (2) Sleep Medicine Center Messina Medical School, Italy, (3) Messina Medical School, Italy, (4) Sleep Medicine Center, Messina Medical School, Italy

Introduction: To assess the efficacy of LEV for the treatment of RLS and co-morbid sleep disorders in ADHD children referred to a Sleep Clinic for “restless” nocturnal sleep.
LEV has been reported to stabilize sleep structure and continuity in normal volunteers as well as in epileptic patients (Bell et al 2002, Cicolin A et al, 2006). Preliminary evidence suggested its efficacy for RLS treatment (Della Marca et al 2006, Lacey et al 2004). The drug shares also antimyoclonic and antiepileptic effects. Therefore its use in children with sub-clinical (IEDs) or clinical epileptic discharges often co-morbid with ADHD as well as sleep related movement disorders (SRMD) could represent an optimal choice.
Methods: 7 male ADHD children (mean age 7.7y, range 5-11y) diagnosed with RLS (mean IRLS-RS: 22.3) after all night video-PSG showing the presence of co-morbid seizures in 1, IEDs in 5, disorders of arousals in 5, other SRMD in all (2 bruxism, 6 PLMS, 1 SRRD), were assigned LEV treatment bid (750-1000mg) to be re-evaluated after 6 months therapy. Reassessment included: IRLS rating scale, a structure sleep interview (parents and child) behavioural scale (ADHDRS, CTRS, CPRS, SNAP-IV: H, I, O). All of these measures had been previously assessed at baseline.
Results: Upon re-evaluation IRLS rating was significantly improved (mean IRLS-RS: 6.4; $p<0.05$), along with seizures and DOA disappearance, improved quality of sleep as rated by children and parents, IEDs reduction (>50%), with a trend for improvement in behavioural rating scales scoring (CPRS and SNAP IV: H, I, O).
Conclusion: LEV could represent an optimal choice to be proposed as an olistic treatment for ADHD related sleep and epileptic disorders.

0253

DOCUMENTED HOME MONITORING OF OXYGENATION IN INFANTS

Gelinas J, Davis G, Arlegui C, Cote A
McGill University, Montreal, Quebec, Canada

Introduction: Infant home cardiorespiratory monitors have been used for decades but do not give information on the oxygenation status during events. Pulse oximeters with low false alarm rates are now available but with no standards for alarm adjustment. The objectives of the study were to determine whether oximeters are good alternatives to cardiorespiratory monitors and whether the alarm levels chosen were safe and limited the number of alarms for non-significant events.
Methods: Retrospective review of all recorded data on monitored infants (n=29) between 2002-2006. Audible alarm: SpO2 <85% for ≥10s. Significant events defined as SpO2 <85% for ≥10s (80% for <1month).
Results: Most common reasons for monitoring: --airway obstruction (choanal stenosis, craniofacial malformation), --ALTE, --hypotonia/neuromuscular disease. Monitoring used for up to 25 months. Compliance to monitor use was 99% (median, range: 49%-100%). We had 13,517 hours of valid data available for analysis. 2735 significant events occurred in 21 patients (range 1-766) with several of those signaling a need for intervention. Four patients were readmitted to the hospital on the basis of increasing alarm number. Clinical deterioration usually followed (rather than preceding) the increased alarm number. Parents reported less than 1 alarm/night on average (confirmed on recordings). The number of false alarms decreased significantly after the first 2 weeks. Significant events were at 0.3 alarm/night (median). With the software used, we could determine that if the alarm had been set for drops of 10% point in SpO2 (no delay), there would have been 10 alarms/night; for a drop of 15% point, there would have been 3 alarms/night.
Conclusion: New generation pulse oximeters are a possible alternative to cardiorespiratory monitors and could be superior in cases of airway obstruction. Care should be taken in setting up the audible alarm, balancing the need to identify events and avoid alarms for very brief events.

0254

RACE DIFFERENCES IN OXYGEN SATURATION AND SLEEP QUALITY AMONG OVERWEIGHT CHILDREN

Davis C,[1] Blanchard A,[1] Pogula A,[1] Waller J,[1] Chervin R[2]
(1) Medical College of Georgia, Augusta, GA, USA, (2) University of Michigan, Ann Arbor, MI, USA

Introduction: Greater prevalence and severity of sleep-disordered breathing (SDB) in black than white children may be due to more severe overweight in blacks.
Methods: Unattended overnight home sleep studies in 35 healthy

overweight children recruited from local schools (BMI ≥85th percentile, BMI z-score mean±SD=2.0±0.4; age 9.5±1.1, range 7-11 yrs; 49% female, 43% black) used oximetry to assess oxygen desaturation (3402, Smiths Medical PM, Inc., Waukesha WI) and wrist actigraphy to assess sleep fragmentation (MicroMini-Motionlogger, Ambulatory Monitoring, Inc., Ardsley NY). Desaturation events were defined as a drop in O_2 saturation ≥2% for ≥10 sec. Records were scored by a pulmonologist. Oximetry data (nadir O_2%, desaturation index, % time <93% saturation) was categorized due to skew. Actigraphy data included sleep efficiency, activity counts, wake after sleep onset (WASO), and activity index. Sex and race differences were tested with t-test or chi-square. Multiple regression tested possible explanations of differences.
Results: Every child showed desaturations >2/hr. All 6 children with >3% time <93% saturation were black. Blacks were more overweight (BMI z-score 2.3±0.4 vs. 1.8±0.4, p=.01) and more had nadir O_2<85% (11/13 vs. 7/19, p=.007) compared to whites. Blacks had worse sleep efficiency (83±10 vs. 90±7%, p=.004), higher activity counts (23±12 vs. 16±9/min, p=.02), and more WASO (80±47 vs. 50±37 min, p=.01). Race differences on actigraphy were not explained by differences in BMI z-score, allergies, asthma, ADHD or age. Excluding 6 children (5 white) with history of tonsilloadenoidectomy reduced race differences on nadir O_2 <85% (p=.07), sleep efficiency (p=.02), and activity counts/min (p=.06) but did not affect WASO results.
Conclusion: Overweight children show substantial abnormalities in oxygen saturation and sleep quality, which may be due to SDB. Blacks show more sleep fragmentation and severe desaturations than whites. Worse sleep quality among black vs. white overweight children is not explained by BMI.
Support (optional): NIH R01 DK60692, R01 DK70922, and Medical College of Georgia Research Institute

0255

TRIDIMENSIONAL AND BIDIMENSIONAL ASSESMENT OF PHARYNGEAL AIRWAYS IN CHILDREN: A PILOT STUDY

Lentini-Oliveira D, Carvalho F, Villela C, Paschoal G, Morais J, Sugaya H, Machado M, Silva J, Prado G
Federal University of Sao Paulo, Sorocaba, Brazil

Introduction: Cephalometric data can be used to diagnose airway narrowing but they have limitations in localizing the exactly sites of obstruction. Recently, three-dimensional instruments as computadorized tomographies (CT), with high resolution and low radiation dose, have been used to study craniofacial structures. Our objective was to compare data from three-dimensional and two-dimensional models of airway assessment.
Methods: A cross-sectional study was conducted with computadorized tomographies: cone beam (Newton 3G with patient in bed) of ten children (8 males and 2 females) aged from 4 years and 9 months to 13 years and 2 months. The following data was compared: 1. Three-dimensional model – areas of: PAS (pharyngeal transversal section of B-Go line extended to airway); SPAS (smaller pharyngeal transversal section above PAS); IPAS (smaller pharyngeal transversal section below PAS); 2. Two-dimensional model: linear measures in cephalograms obtained from three-dimensional CT of: PAS (B-Go line extended to airways); SPAS (smaller linear measure above PAS); IPAS (smaller linear measure below PAS).The softwares used were: In Vesalius (slices and image manipulation) and Magics 9.51 (volume). The correlation Spearman rank was used to compare the groups. The significance level was 0.05.
Results: There was no significant correlation between three-dimensional and two-dimensional models (p>0.05). It suggests that linear measures are not correlated with the area measures; and it is possible that the airway obstruction sites are not being adequately identified.
Conclusion: There is some statistic evidence about lack of similarity between two-dimensional and three-dimensional measures (p>0.05). More trials with adequate sample size are necessary to define the best model of airways assessment.

0256

PREDICTIONS OF MATURATIONAL CHANGE USING COMPUTATIONAL ANALYSES OF NEONATAL SLEEP

Scher M,[1] Janjarasjitt S,[2] Johnson M,[2] Loparo K[2]
(1) Rainbow Babies and Children's Hospital, Cleveland, OH, USA, (2) Case Western Reserve University, Cleveland, OH, USA

Introduction: Computational neurophysiologic studies of neonatal EEG sleep are sensitive markers of functional brain maturation.
Methods: EEG recordings were studied for three groups of neonatal cohorts (18 neonates): fullterm and preterm infants at 40-41 weeks, and preterm infants at 31-32 weeks. There were six data sets for each group. EEG time series (FP1-C3) using 2000 two minute epochs during active (AS) and quiet (QS) sleep. Surrogate time series were also analyzed for each epoch. Correlation dimension (D2) was used as a time-series measure of complexity, classifying two forms of complexity as deterministic vs. stochastic.
Results: D2 was more significant in AS than QS for both fullterm cohorts. Lower D2 (less complexity) was noted for the healthy preterm cohort at corrected fullterm age when compared to fullterm group. Surrogate datasets for D2 provided a measure of nonlinear determinism in the EEG that distinguished the fullterm and preterm cohorts during AS and QS. D2 increased with maturity from 31-32 weeks to 40-41 weeks. It was also observed that QS epochs for the preterm and fullterm cohorts at term and all epochs of the preterm at 31-32 weeks were statistically different from their surrogates as measured by D2, suggesting that along with maturity emerged a change in both D2-complexity of the EEG and also the form of complexity. As the brain matured the strong nonlinear determinism detected at 31-32 weeks gives expressed stochastic features, especially during AS.
Conclusion: These preliminary findings together with our published results (1) support the concept of physiologic dysmaturity for a healthy preterm cohort, representing altered neurodevelopment due to conditions of prematurity. Computational analyses of neonatal EEG sleep state serve as phenotypic markers of developmental neural plasticity.

1. Scher MS, Waisanen H, Loparo K, Johnson MW: J Clin Neurophysiol. 2005 Jun;22(3):159-65.
Support (optional): NS01110, NS26793, RR0084, NS34508

0257

MODAFINIL IS WELL TOLERATED IN CHILDREN AND ADOLESCENTS WITH EXCESSIVE SLEEPINESS AND OBSTRUCTIVE SLEEP APNEA: A 6-WEEK DOUBLE-BLIND STUDY

Owens J,[1] Bogan R,[2] Lankford A,[3] Sheldon S[4]
(1) Rhode Island Hospital, Providence, RI, USA, (2) SleepMed, Columbia, SC, USA, (3) Sleep Disorders Center of Georgia, Atlanta, GA, USA, (4) Northwestern University, IL, USA

Introduction: Excessive sleepiness (ES) contributes to psychosocial and academic difficulties in children and adolescents with obstructive sleep apnea (OSA). The efficacy, safety, and tolerability of modafinil, a wake-promoting agent, was evaluated in a group of children and adolescents with residual ES associated with nCPAP-treated OSA.
Methods: In a double-blind, multicenter study, patients aged 6–16 years

with ES and OSA were randomized to receive modafinil 100, 200, or 400 mg/day or placebo in the morning for 6 weeks. Efficacy parameters included the Multiple Sleep Latency Test and Clinical Global Impression of Change. Safety and tolerability were assessed by monitoring adverse events (AEs), vital signs, and the Child Behavior Checklist for Ages 6–18 (CBCL/6–18).
Results: 26 patients were randomized (modafinil, n=19; placebo, n=7). Patients had a mean±SD age of 10.2±2.9 years and 15 (58%) were boys. Due to the limited number of patients who enrolled in this study, inferential statistics were not performed. On average, mean change in sleep latency was higher for patients receiving modafinil vs placebo. Five patients receiving modafinil were very much improved vs none in the placebo group. Decreased appetite (modafinil, 3/19 patients; placebo, 0/7 patients) and insomnia (modafinil, 2/19 patients; placebo, 0/7 patients) occurred in >1 patient in any modafinil group. Mean±SD changes from baseline at final visit for modafinil vs placebo were heart rate: –1.7±11.5 vs +0.7±9.2 bpm; systolic BP: –0.8±12.5 vs +3.4±22.8 mmHg; and diastolic BP: +1.5±8.3 vs +6.6±14.7 mmHg. Mean change from baseline at final visit in CBCL/6–18 total score for modafinil vs placebo was –4.2±7.8 vs –15.8±22.7, respectively.
Conclusion: Modafinil is well tolerated in a small group of children and adolescents with ES associated with OSA. Conclusions regarding the efficacy of modafinil in the studied population cannot be made due to the small sample size.
Support (optional): Cephalon, Inc.

0258

RELATIONSHIP BETWEEN INFANT SLEEP AND MATERNAL DEPRESSIVE SYMPTOMS

Gardiner A, Gay C, Lee K
University of California, San Francisco, San Francisco, CA, USA

Introduction: Although both depression and pregnancy are associated with poor sleep quality, few studies have looked at infant sleep and its relationship to maternal depressive symptoms.
Methods: Data were collected from a sample of 40 mother-infant pairs 24 hours before the infant´s first immunization, when the infants were 60±10 days old. Ankle actigraphy was used to assess infant quiet sleep time, active sleep time, and number of wakes. Wrist actigraphy was used to assess mothers´ total sleep time (TST) and wake after sleep onset (WASO). Mothers completed the Center for Epidemiologic Studies - Depression Scale (CES-D), and the standard cutoff of 16 was used to classify those at high and low risk of depression.
Results: The infants of mothers at high (n=12) and low depression risk (n=28) differed in 24-hr quiet sleep time (p=.040) and number of wakes (p=.044). The infants of mothers at high risk for depression had less quiet sleep (236±94 mins) and more wakes (23±7) than those of mothers at low risk for depression (300±84 mins and 19±5 wakes). Infants in the two groups did not differ in active sleep time, although infants´ active sleep time was correlated with mothers´ CES-D score (r=.399). Infant quiet sleep was correlated with the mother´s TST (r=.517) and WASO (r=-.492), but maternal sleep was unrelated to CES-D scores. Infants in the two groups did not differ in age, gender, or total (sum of active and quiet) sleep.
Conclusion: In this sample, mothers at high risk for depression had infants with less quiet sleep and more awakenings. Since it is unclear from this correlational study whether the mother´s psychological status influences the infant´s sleep pattern or infant sleep influences a mother´s depressive symptom experience, further longitudinal research is needed to better understand the nature and pattern of this relationship.
Support (optional): NIH Grant #R01 NR05345, KA Lee, P.I.

0259

PARENTAL RESPONSIVENESS TO CHILDREN'S SLEEP SIGNALS

Ramos K
American Academy of Sleep Medicine, Fresno, CA, USA

Introduction: It has been firmly established that the quality of the infant's attachment to a primary caregiver predicts numerous important outcomes in the infant's life. Ainsworth (1978) demonstrated that the quality of attachment is a product of the caregiver's responsiveness to the child's expressed needs. However, more recent studies (DeWolff & VanIjzendoorn, 1997) have reported smaller relationships between responsivness and attachment, leaving attachment experts to speculate about the limitations of current methods of measuring responsiveness. Responsiveness to sleep-related signals is an unexamined construct that may be crucial to the formation of attachment quality, as transitions in and out of sleep are both very frequent in infancy, and thought to trigger the attachment system. This research reports the psychometric properties of a questionnaire specifically designed to measure sleep-related parental responsiveness, and correlates of it.
Methods: A survey was designed to assess parental response to sleep-related signals based on Ainsworth's components of sensitive responsiveness: awareness of signals, accurate interpretation of them, prompt and appropriate response, and rhythmicity. Once the items achieved face validity, it was posted online. Parents of infants 12 months and younger were invited, via message boards and email listservs devoted to parenting, to complete the online survey. Responses (n=333) were tabulated electronically. Virtually all (98.8%) respondents were women who self-identified as the child´s mother and primary caregiver. Babies were an average of 7 months old.
Results: Cronbach´s alpha was 0.82.A forced four factor principal components analysis produced four factors that explained 45% of the variance and resembled Ainsworth´s concepts. The total responsiveness score was directly correlated with the active comforting subscale of the Parental Interactive Bedtime Behavior Scale (Morrell & Cortina-Borja, 2002) ($r = 0.517$; $p<0.0001$) and inversely correlated with the autonomy-promoting subscale ($r = -0.305$; $p<0.0001$). It was weakly, but positively correlated with the social comforting subscale ($r = 0.120$; $p<0.041$). Total responsiveness was lowest among those who had successfully used a cry-it-out form of sleep training, intermediate for those who had tried unsuccessfully to cry-it-out, and highest among those who had never used cry-it-out ($F(2,331)=3.87$, $p=.022$). In addition, total responsiveness scores were lowest among parents with solitary sleeping children, intermediate among reactive cosleepers, and highest among intentional cosleepers ($F(2,331)=3.69$, $p=.012$).
Conclusion: This is a valid and reliable tool that can be used to provide valuableinformation about parenting approaches to infant sleep.

0260

HEART RATE AND SATURATION CHANGES DURING SPONTANEOUS AROUSALS IN FUTURE VICTIMS OF SUDDEN INFANT DEATH SYNDROME (SIDS)

Kato I,[1] Scaillet S,[2] Groswasser J,[2] Togari H,[1] Kahn A,[2] Lin J,[3] Franco P[4]
(1) Nagoya City University Medical School, Japan, (2) University Children´s Hospital, Free University of Brussels, Belgium, (3) INSERM U628, France, (4) Pediatric Sleep Unit, Hôpital Debrousse, Lyon, France

Introduction: Compared to control infants, victims of SIDS have fewer cortical arousals and more frequent subcortical activations suggesting an incomplete arousal process (Kato *et al.* Am J Respir Crit Care Med 2003). This study was undertaken to determine the heart rate and

saturation changes before and during arousals in SIDS infants.
Methods: Sixteen infants died of SIDS some days or weeks after their night-time sleep was recorded polysomnographically in a sleep laboratory. Their sleep recordings were compared with those of control infants matched for gender, gestational age and age at recording. Arousals were differentiated into subcortical activation or cortical arousal, according to the presence of autonomic and/or EEG changes. Oxygen saturation was recorded continuously by a transcutaneous sensor. Median values of blood oxygen saturation were calculated for 10 sec. periods before each spontaneous arousal. Basal heart rate values and heart rate changes during each spontaneous arousal were compared between SIDS victims and control infants.
Results: In REM sleep, oxygen saturation values preceding cortical arousals ($p < .001$) and subcortical activations ($p=.013$) were lower in SIDS victims than in control infants.
Changes in heart rates during all arousals were lower in SIDS victims in REM sleep ($p< .001$). No differences were found in NREM sleep. Heart rate changes during cortical arousals were lower in SIDS victims during REM sleep ($p< .001$). There was no significant difference during NREM sleep.
Conclusion: The lower oxygen saturation values found in SIDS victims before cortical arousals and subcortical activations in REM sleep suggest an abnormal breathing control during sleep in these infants and could explain the increased frequency of subcortical activations. The smaller heart rate changes found during arousals in SIDS victims in REM sleep could suggest some structural lesions preventing the progression of arousal sequence in SIDS victims.

0261

PSYCHOSOCIAL CORRELATES OF PARENT-INFANT BED-SHARING

Gay C, Gardiner A, Lee K
University of California, San Francisco, San Francisco, CA, USA

Introduction: Research has compared sleep and fatigue in bed-sharing and room-sharing parents, but psychosocial differences among parents choosing different sleeping arrangements have not been examined. This study evaluates whether sleeping arrangements are associated with depressive symptoms, perceived stress, relationship satisfaction, and parental adjustment among new parents.
Methods: Data were collected from 76 couples during their last month of pregnancy and at one, two, and three months postpartum. Parents used 48-hour sleep logs to record times and locations of their infant´s sleep; parents were classified at each assessment as bed-sharers, room-sharers, or solitary-sleepers based on where their infant usually slept midnight - 6:00am. Parents also completed the Center for Epidemiological Studies – Depression Scale, Perceived Stress Scale, Relationship Satisfaction Questionnaire, a maternal adjustment scale (also modified for fathers), and a rating of infant temperament.
Results: Bed-sharing was common at 1 month postpartum (45%), but less so at 3 months (28%). In most cases of bed-sharing (83%), the infant shared a bed with both parents, although some fathers slept separately. Parents´ sleeping arrangement had little association with psychosocial measures in the first two postpartum months. However, at 3 months postpartum, bed-sharing mothers reported less relationship satisfaction and poorer maternal adjustment than room-sharing mothers, and bed-sharing fathers reported more stress than room-sharing fathers. Furthermore, parents who shared a bed with their infant at 3 months postpartum reported more distress at prior assessments. Mothers reporting more depressive symptoms or poorer maternal adjustment in the first 2 postpartum months and fathers reporting more stress, more depressive symptoms, less relationship satisfaction, or poorer parental adjustment early in the postpartum period were more likely to bed-share at 3 months. Sleeping arrangement was unrelated to infant temperament.
Conclusion: Bed-sharing beyond the first few postpartum months was associated with greater parental distress, although bed-sharing may be the result rather than the cause of such distress.
Support (optional): NIH Grant #R01 NR05345, KA Lee, P.I.

0262

SEX DIFFERENCES IN SLEEP AND FATIGUE IN A PEDIATRIC ONCOLOGY POPULATION

Sanford S,[1] Okuma J,[2] Tong X,[2] Srivastava D,[2] West N,[2] Hinds P[2]
(1) St. Jude Children's Research Hospital, Memphis, TN, USA, (2) St. Jude Children's Research Hospital, TN, USA

Introduction: There is evidence to support sex differences in sleep and fatigue across the lifespan. Females tend to report more fatigue than males in normative samples and survivors of childhood cancer. There is evidence that girls sleep more than boys while boys have more fragmented sleep. Data presented here were collected with primary aims of establishing the relations between dexamethasone exposure and adverse effects on sleep and fatigue in pediatric patients with acute lymphoblastic leukemia (ALL). This secondary analysis was completed in hopes of elucidating the relation of sex on sleep and fatigue in this population.
Methods: Participants included 100 children with low (n=37) or standard (n=63) risk ALL (62 boys; 38 girls.) Age ranged from 5 to 18 years (M=9.24; SD=3.23). Activity levels were measured with wrist actigraphy worn for 10 consecutive days (5 days pre-dexamethasone, 5 days on dexamethasone.) Dexamethasone dosage was dependent on risk group. On 4 occasions fatigue scales (parent and child/adolsecent report) and sleep diaries (parent report) were completed.
Results: Wilcoxon-Mann-Whitney tests, stratified by risk group, were used to compare sleep variables by sex for week one (pre-dexamethasone) and two (on dexamethasone.) With the exception of the lowest risk group, boys had significantly more nocturnal awakenings than girls across weeks ($p<.05$). There was a trend for boys to have greater wake time after sleep onset than girls ($p=.065$) and for boys to have lower sleep efficiency scores than girls ($p=.052$). Girls had significantly higher duration of daytime napping than boys ($p<.05$) in week two. There were no sex differences in fatigue.
Conclusion: Results suggest that boys receiving treatment for ALL have slightly more disturbed nighttime sleep than do girls although girls tend to nap more in the day. This pattern is more pronounced after administration of dexamethasone. The relations of sex and sleep to fatigue remain unclear and require further investigation.

0263

THE EFFECT OF EXTERNAL MOTION ON THE CORRESPONDENCE BETWEEN INFANT ACTIGRAPHY AND SLEEP-WAKE DIARY

Thomas K, Burr R, Tsai S
University of Washington School of Nursing, Seattle, WA, USA

Introduction: Actigraphy is increasingly accepted as a measure of infant sleep yet few studies have assessed the possible influence of animate (caregiver) and inanimate external motion on actigraph recording. Measures of correspondence between actigraphy and mother-recorded sleep wake diary were calculated with and without excluding periods of external motion.
Methods: Activity (Actiwatch, MiniMitter, Bend, OR), was continually recorded at 15 second epochs over 4 to 7 days in thirty-one healthy term gestation infants, postnatal age 4 to 10 weeks. Actigraphs were worn on

the ankle. Diaries completed by mothers included infant sleep-wake state recorded in 15 minute epochs. Actigraphy was transformed to log units and aggregated into 15 minute blocks by computing the mean. Correspondence between actigraphy and diary was examined using area under the curve (AUC) derived from receiver-operator function, correlation (r), and logistic regression coefficient (B) and classification percent correct (% correct). Values were compared using paired t-test.
Results: External motion comprised approximately 40% of total recording time across infants. Correspondence between diary and actigraphy calculated with and without external motion differed significantly (t(30), p < .000): AUC (0.843 vs. 0.896), r (0.470 vs. 0.588), B (1.091 vs. 1.565) and % correct (77.5% vs. 86.3%).
Conclusion: External motion is a predominant experience for infants. Characterization of infant 24-hour sleep pattern using actigraphy should include control for external motion.
Support (optional): NINR RO3 NR009038, Hester McLaw Scholarship, Sigma Theta Tau International and Psi Chapter Research Grants

0264

EFFECTS OF A CONSISTENT BEDTIME ROUTINE ON INFANT SLEEP

Mindell J,[1] Luedtke K,[2] Wiegand B,[2] Friscia D,[2] Telofski L[2]
(1) Saint Joseph's University; Children's Hospital of Philadelphia, Philadelphia, PA, USA, (2) Johnson & Johnson Consumer Products Company, Division of Johnson & Johnson Consumer Companies, Inc., Skillman, NJ, USA

Introduction: Establishment of a consistent bedtime routine is often recommended to parents of infants, especially those with sleep difficulties, however little research has been done to understand the benefits of such a routine. The purpose of this study was to examine the effects of a consistent bedtime routine on infant sleep.
Methods: 58 mothers (ages 18-49 years) and their infants (ages 7-18 months; mean =11.9 months; 29 males) participated in a 3-week study. The first week of the study served as a baseline during which the mothers were instructed to follow their usual bedtime routine. In the second and third weeks, mothers were instructed to conduct a specific 30-minute bedtime routine, including a warm bath, massage, and quiet bedtime activities (e.g., reading). All mothers maintained a daily infant sleep diary and completed the Brief Infant Sleep Questionnaire (BISQ) on a weekly basis.
Results: Significant reductions in problematic sleep behaviors were noted two weeks after the institution of the nighttime routine, according to the BISQ. Improvements were seen in latency to sleep onset (22.04 vs 13.83 minutes; -37%) and number (2.07 vs 1.29 times, -37%) and duration of night wakings (36.2 vs 18.45 minutes; -49%), p < .05. Longest continuous sleep period increased by 23%, from 7.12 hours to 8.78 hours, p < .05. In addition, there was a 71% decrease in the number of mothers who rated their infant´s sleep as problematic, p < .05.
Conclusion: These results suggest that instituting a consistent bedtime routine, in and of itself, is beneficial in improving multiple aspects of infant sleep, especially wakefulness after sleep onset and longest continuous sleep period.
Support (optional): This study was supported by Johnson & Johnson Consumer Products Company, Division of Johnson & Johnson Consumer Companies, Inc.

0265

POLYSOMNOGRAPHY OF CHILDREN WITH SLEEP DISORDERED BREATHING PRESENTS ASSOCIATION TO THEIR CRANIOFACIAL MORPHOLOGY

Juliano M,[1] Machado M,[1] Prado L,[1] Carvalho L,[2] Carvalho F,[3] Lentini-Oliveira D,[4] Macedo C,[5] Zortea F,[2] Sugaya H,[6] Prado G[7]
(1) Federal University of Sao Paulo, Sao Paulo, Brazil, (2) Federal University of sao Paulo, Sao Paulo, Brazil, (3) Universidade federal de Sao Paulo, Osasco, Sao Paulo, Brazil, (4) Federal University of Sao Paulo, AA, Brazil, (5) UNIFESP, Brazil, (6) Federal University of Sao Paulo, Sorocaba, Brazil, (7) Federal University of São Paulo, São paulo, Brazil

Introduction: Children with adenotonsillar hypertrophy are predisposed to sleep disordered breathing, as Obstructive Sleep Apnea Syndrome, due to the condition of many respiratory obstructions that it promotes, leading them to be oral breathers. Studies have shown that the modified craniofacial morphology can be a predisponent factor for sleep disordered breathing. Lateral radiography is a common approach to recognize this feature. The aim of this study is to verify if there is association between the polysomnographic data and the cephalometric measures of children with sleep disordered breathing and with oral breathing, including the nasopharynx airway space measures.
Methods: We analyzed polysomnographies and cephalograms of 26 children (14 oral breathing children - OB; 12 nasal breathing children - NB) aged 7 to 14 years from Neuro-Sono outpatient clinic, Unifesp, Sao Paulo, Brazil. The polysomnography variables were: sleep efficiency, sleep latency, AHI, SaO2, arousal index and snoring. The evaluated cephalometric measures were: SNA, SNB, ANB, NS.PlO, NS.GoGn, 1.NA, 1.NB, SPAS, PAS, MPH and C3H. Statistical analysis was based on the Qui-Square Test.
Results: Oral breathing children showed greater snoring association with cephalometric measures than nasal breathing children, as follow: snoring and ANB (OB-92%, NB-8%, p<0,05); snoring and NS.PlO (OB-100%, NB-14%, p<0,05); snoring and NS.GoGn (OB- 64%, NB-16%, p<0,01); snoring and SPAS (OB- 78%, NB- 8%, p<0.001); sleep efficiency and SPAS (OB- 64%, NB- 8%, p<0,01); arousal and ANB (OB- 71%, NB- 25%, p< 0,05); arousal and SPAS (OB- 64%, NB- 8%, p< 0,05).
Conclusion: Our study showed association between polysomnographic data and cephalometric measures of oral breathing children. Snoring was the most important variable associated with craniofacial morphology, suggesting that measures like SPAS, ANB, NS.PlO, NS.GoGn should be considered in the approach of oral breathing children referred to orthodontic evaluation.

0266

BODY POSITION AND OBSTRUCTIVE SLEEP APNEA IN EIGHT TO TWELVE MONTH OLD INFANTS

Rathi N, Fatakia A, Weinstock Y, Haque S, Castriotta R, Pereira K
University of Texas Health Science Center at Houston, Houston, TX, USA

Introduction: The supine position is associated with an increased risk of obstructive sleep apnea (OSA) in adults, but limited information exists about positional risk in children and little is known about infants under one year of age. A reduction in sudden infant death syndrome incidence has been attributed to the preferential positioning of supine rather than prone sleep in infants. The purpose of this study is to evaluate children 8-12 months of age for effects of body position on OSA.
Methods: Consecutive nocturnal polysomnograms (NPSGs) of 50

children ages 8 to12 months old referred to the sleep disorders center between January 1, 2003 and June 1, 2006 for possible sleep disordered breathing were retrospectively reviewed. 46% of the patients were female, and the mean age was 9.5 months. Total obstructive apnea-hypopnea index (OAHI), OAHI by body position, and REM and non-REM sleep OAHI were recorded.
Results: There were no significant differences between the mean non-supine OAHI (2.0 +/- SE 0.72), supine OAHI (2.5 +/- 0.77), prone OAHI (2.9 +/- 1.03), left lateral decubitus OAHI (1.1 +/- 0.87), or the right lateral decubitus OAHI (2.5 +/- 1.07), p=0.71. Children spent an average of 50% of their total sleep time supine. OSA was significantly worse in REM sleep (OAHI 4.3 +/- 7.3) than in non-REM sleep (OAHI 1.4 +/- 3.9), p=0.015. Mean time in REM sleep was 30% (range 5% to 42%).
Conclusion: There was no significant effect of body position on sleep disordered breathing in 8 to12 month old infants, although REM sleep was associated with a significant worsening of OSA.

0267

SLEEP IN THE FIRST THREE YEARS: NORMATIVE U.S. DATA

Sadeh A,[1] Mindell J,[2] Luedtke K,[3] Wiegand B[3]
(1) Tel-Aviv University, Tel Aviv, Israel, (2) Saint Joseph's University; Children's Hospital of Philadelphia, Philadelphia, PA, USA, (3) Johnson & Johnson Consumer Products Company, Division of Johnson & Johnson Consumer Companies, Inc., Skillman, NJ, USA

Introduction: There are little data available on sleep in infants and toddlers in the United States. The two primary aims of this study were to (1) characterize normal sleep patterns in a large sample of children ages 0 to 3 and (2) assess the relationship between sleep ecology and sleep behaviors.
Methods: Parents of 5004 infants and toddlers (48.2% girls) completed an expanded online version of the Brief Infant Sleep Questionnaire that included questions about sleep patterns and sleep-related behaviors. Respondents completed the survey at BabyCenter.com (online website for parents of young children) and received no remuneration. The respondents were primarily mothers (97.2%), Caucasian (79.7%), ages 25-34 (61.0%), and educated (67.5% had some college education).
Results: Total sleep times decreased from a mean of 13.27 hours in 0-2 month olds to 10.87 hours in 24-36 month olds (p<.0001). The primary changes were a decrease in daytime sleep (p<.0001) and a shift in the night to day sleep ratio (p<.0001). Longest nighttime sleep episode increased from 4.99 hours (0-2 months) to 9.01 hours at 24-36 months (p<.0001). 24.94% of parents perceived their child as experiencing a sleep problem, with sleep problems peaking between 6-11 months. Utilizing an investigator-developed algorithm, which included total sleep time, latency to sleep onset, and night wakings, 19.50% of the children were classified as having poor sleep. The factors that most predicted sleep problems were sleeping arrangement and parental interventions.
Conclusion: The results provide a normative base for sleep patterns and sleep behaviors for young children in the United States, enabling age-based comparisons to identify sleep problems. In addition, the identification of risk factors for sleep problems, including sleeping arrangements and parental behaviors, provide the basis for prevention and intervention recommendations.
Support (optional): This study was supported by Johnson & Johnson Consumer Products Company, Division of Johnson & Johnson Consumer Companies, Inc.

0268

PARENTING AND INFANT SLEEP: BEHAVIOR AND PATTERNS OF ADAPTATION IN MOTHERS VS. FATHERS

Teti D, Countermine M, Mayer G
Pennsylvania State University, University Park, PA, USA

Introduction: Chronic infant sleep disruption can place families in turmoil (Mindell, 1999). Importantly, most studies of parent behavior and adaptation target mothers, without considering that fathers´ behavior and reactions to their infants´ sleep have import for family stress levels. The present study systematically compares mothers´ and fathers´ behavior and adaptation to infant sleep disruption.
Methods: To date, data on nine middle-class families with infants 12 months and under have been collected as part of an ongoing investigation of infants between 1 and 24 months of age (projected N = 40 by conference time). Parents complete a sleep diary and established measures of parental cognitions about infant sleep. We are also making infra-red digital video and actigraph recordings of parent-infant behavior during bedtimes and night wakings.
Results: Infant bedtime and night waking routines were more likely to be done by mothers than by fathers, although some fathers were actively involved. Frequency of infant night wakings (sleep diary) was significantly associated with parental perceptions that the infant has sleeping difficulties, but only among mothers ($p < .05$), not fathers ($p = .58$). Interestingly, if infants had difficulty settling to sleep at bedtime, mothers (but not fathers) were significantly likely to see that as a function of the infant not getting enough food during bedtime ($p < .05$). Fathers, by contrast, tended to react to such behavior with anxieties about the infant´s physical well-being ($p < .07$).
Conclusion: These results are limited primarily to families of very young infants and represent but a small sampling of significant findings in this emergent data set. We plan on having the full complement of data (N = 40) to analyze by conference time, to present analyses of video data and actigraph recordings, and to assess the moderating role of infant age.

0269

BEHAVIORAL PROBLEMS CORELATE WITH SLEEP SYMPTOMS IN CHILDREN

Kohrman M,[1] Vanderbilt T[2]
(1) University of Chicago, Chicago, IL, USA, (2) University of Chicago, IL, USA

Introduction: As part of an ongoing study of sleep problems in children we evaluated behavioral symptoms in children with neurologic disease and those referred for polysomnography.
Methods: A 111 item questionnaire was administered to 462 pediatric neurology patients(55% M,45% F). The control group consisted of 185 children recruited from general pediatric clinics with a similar distribution. The sleep disordered breathing group consisted of children referred to sleep lab with snoring and apnea defined as an AHI greater than 5. Patients ranged in age from 5 to 17 years old, with an average age of 10. Children under age 5 were excluded. Behavioral measures consisted of 11 questions assessing daytime, school and home, attention, acting out, sleep related anxiety, and or learning disability. These were related to five measures, of symptoms of sleep problems, excessive daytime sleepiness, restlessness, insomnia, and parasomnia.
Results: We found that behavioral scores ranged from 2.9 in control group to 14 in the ADHD subgroup, children with apnea 9.5, children with PSG and no apnea 4.5, headache 7.5 and epilepsy 8.6. These groups were significantly different (Kruskla –Walish) p<0.05. In addition behavioral scores correlated (Pearson R) with EDS 0.647,

parasomnia 0.305, restlessness 0.408, and insomnia 0.456(p< 0.001for all measures).
Conclusion: Behavioral symptoms were more common in children with sleep apnea than all groups including children with epilepsy and headache. The only subgroup of neurology patients with greater behavioral problems were children with ADHD. In addition the behavioral score correlated with increasing symptoms of excessive daytime sleepiness, restlessness during sleep, insomnia and parasomnias.

0270

PEDIATRIC POLYSOMNOGRAM DURATION AFFECTS MEASURED SLEEP PARAMETERS

Winnie G,[1] Massolo A,[2] Huntley E,[3] Lewin D[4]
(1) Children's National Medical Center, Washington, DC, USA, (2) University of Rome La Sapienza, Rome, Italy, (3) Children's National Medical Center, Washington, Washington, DC, USA, (4) Washington, DC, USA

Introduction: Children require at least 9 hours of sleep per night, but clinical polysomnograms (PSGs) are often shorter. We hypothesized short PSGs may produce misleading data.
Methods: PSGs at least 9.0 hours long in children age 1 to 17 years performed 01/10/05 to 6/30/05 and scored by one individual were retrospectively analyzed. Apnea-Hypopnea Index (AHI), arousal index, and sleep stages were calculated with Lights On set at either 9 or 6 hours after Lights Out. Studies were also divided into 4 groups based on AHI at 9 hours: Group 0 AHI 0.0-0.9/hour, MILD 1.0-4.9, MOD 5.0-9.9, and SEVERE >10.0. Comparisons were made by ANOVA.
Results: 33 studies met criteria, 9 in Group 0, 9 MILD, 7 MOD and 8 SEVERE. For the whole group, there was higher percent stage 2 and lower percent stage 4 (22.4 vs 28.9%, p<0.000) at 9 vs 6 hours; within AHI groups, these differences were observed for MILD and MOD groups. There were more minutes REM at 9 hours (39.6 vs 19.1 minutes, p<0.000 for the whole group, and p<0.000 for MILD and MOD). There were no differences in arousal index or AHI. Compared with 9 hour study length, 6 hour studies misclassified 3 Group 0 children as MILD, one MOD as MILD, 2 MOD as SEVERE, and one SEVERE as MOD.
Conclusion: Shortened PSG length of 6 instead of 9 hours was associated with decreased percent stage 2, increased percent stage 4 and fewer REM minutes in children referred for evaluation of sleep disorders. 7 of 33 studies had different severity classification at 9 vs 6 hrs of recording time; such differences may cause errors in clinical decisions. Larger groups and better assessment of individual variability are needed to determine optimal PSG length in children.
Support (optional): None

0271

CULTURALLY-BASED INFANT SLEEP DIFFERENCES: SLEEP IN THE UNITED STATES VERSUS UNITED KINGDOM

Mindell J,[1] Sadeh A,[2] Luedtke K,[3] Wiegand B[3]
(1) Saint Joseph's University; Children's Hospital of Philadelphia, Philadelphia, PA, USA, (2) Ramat Aviv, Israel, (3) Johnson & Johnson Consumer Products Company, Division of Johnson & Johnson Consumer Companies, Inc., Skillman, NJ, USA

Introduction: There are little data available comparing sleep in infants and toddlers cross-culturally. The primary aim of this study was to characterize normal sleep patterns in a large sample of children ages 0 to 3 in the United States versus the United Kingdom.
Methods: Parents of 5807 infants and toddlers (5004 US; 803 UK) completed an expanded version of the Brief Infant Sleep Questionnaire, which included questions about sleep patterns and sleep-related behaviors, online at BabyCenter.com or BabyCentre.co.uk. Because of the large sample size and the multiple analyses, findings were considered significant if p < .001.
Results: US infants had later bedtimes (8:51 PM) than UK infants (7:54) and shorter nighttime sleep (8.76 vs 9.47 hours), but longer daytime sleep (3.15 vs 2.60 hours), p<.0001. There were no significant differences, though, in total sleep time (11.91 vs. 12.07), p>.001. No differences were found for number of night wakings (1.06 vs 1.16), and wake after sleep onset (22.2 vs 25.2 minutes), p>.001. However, UK infants were more likely to fall asleep independently at bedtime and less likely to feed to sleep, p<.0001. The same percentage of parents in the US and UK believed that their child had a sleep problem (24.7%).
Conclusion: Overall, young children in the US go to bed almost an hour later at night than those in the UK, getting less total nighttime sleep, but compensating with more sleep during the day. No differences were found in latency to sleep onset, night wakings, or parental perception of sleep problems, however UK babies are more likely to fall asleep independently at bedtime. These results indicate that in spite of differences in the sleep schedules and sleep habits of infants and toddlers in the US and UK, there are no overall differences in problematic sleep behaviors and sleep quality.
Support (optional): This study was supported by Johnson & Johnson Consumer Products Company, Division of Johnson & Johnson Consumer Companies, Inc.

0272

CHARACTERISTICS OF SLEEP HABITS IN PEDIATRIC PATIENTS PRESENTING WITH HYPERTENSION: INTERIM ANALYSIS OF A PILOT STUDY

Smith K, Feig D, Glaze D
Baylor College of Medicine, Houston, TX, USA

Introduction: Ten to 40% of children and adolescents in the general population have significant sleep problems and 1-3% have sleep disordered breathing. The Fourth Task Force on High Blood Pressure in Children and Adolescents recommends screening children with hypertension for sleeping disorders. The objective of this pilot study is to characterize the sleep habits of pediatric patients referred for initial evaluation of high blood pressure.
Methods: The parents of 80 consecutive patients 3 to 18 years of age evaluated in the Hypertension Clinic between January 1st and November 1st, 2006 completed the Children´s Sleep Habits Questionnaire (CSHQ) and the Pediatric Sleep Questionnaire (PSQ). Results from children with hypertension (pre-hypertension, essential hypertension & secondary hypertension) and normotensive patients (white coat hypertension) were compared.
Results: Thirteen of 16 patients (81%) with pre-hypertension were identified by the CSHQ as having abnormal sleep domains (CSHQ score > 40) as compared to twenty-four of 35 patients (69%) with essential hypertension, eight of 11 patients (73%) with secondary hypertension, and twelve of 18 normotensive patients (67%). The mean CSHQ total score was highest with pre-hypertension (46) and lowest for normotensive patients (41), (p=0.6). The percentage of obese patients (BMI > 95th%) was similar in all four groups (63%, 58%, 73%, & 61% respectively). Controlling for BMI % predicted, age, and race revealed a trend towards a higher CSHQ sleep disordered breathing subscale score in the pre-hypertension group compared to the normotensive group (p=0.2). The PSQ also showed a trend towards a higher prevalence of sleep disordered breathing in patients with pre-hypertension (47%) compared to normotensive patients (17%) (p=0.13).

Conclusion: This interim analysis suggests the prevalence of sleep disordered breathing may be higher in patients with pre-hypertension than in normotensive patients presenting for initial evaluation of elevated blood pressure. Further investigation is warranted.

0273

RAPID EYE MOVEMENT DENSITY IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA

Gleason B,[1] Bock E,[2] Song Y,[2] Bagai K[2]
(1) Vanderbilt University Medical Center, Nashville, TN, USA, (2) Vanderbilt University Medical Center, TN, USA

Introduction: The prevalence of obstructive sleep apnea (OSA) in children ranges from 1-3%. Diagnosing OSA in children is challenging due to variable symptomatology, non-standardized diagnostic criteria, and inconsistency of associated oxygen desaturations and arousals with the respiratory events. We hypothesize that differences in rapid-eye-movement (REM) sleep density and total REM sleep are potential markers of underlying OSA in children.
Methods: Overnight polysomnography (PSG) on fifteen children with OSA (mean age 7.4 ± 5.5) and fifteen children without OSA (mean age 3.6 ± 3.16) completed at the Vanderbilt Sleep Disorders Center were reviewed. Children with OSA were defined as having an apnea-hypopnea index (AHI) of ≥ one using our center´s standard pediatric protocol for scoring respiratory events. Percentage of REM sleep and number of distinct REM sleep periods were recorded. REM density was recorded as the incidence of rapid eye movements per minute of each distinct REM period. Statistical analysis was performed using Wilcoxon rank-sum test.
Results: Children with OSA had a higher mean total REM sleep percentage as compared to the non-OSA group (17.1 ± 5.9 vs. 12.2 ± 5.9, p = 0.02). Children with OSA had a mean number of 3.6 (SD ± 1.3) REM periods compared to 2.8 (SD ± 1.4) in children without OSA (p = 0.09). There was no statistically significant difference in average REM density (2.29 ± 1.09 vs.2.10 ± 0.7; p = 0.8) in the OSA and non-OSA groups. REM density was highest in the fourth REM period in both groups.
Conclusion: Children with OSA have a significantly higher percentage of total REM sleep compared to children without OSA. A trend towards a higher number of REM periods in children with OSA was observed. This contrasts the previous reports of decreased REM sleep and increased sleep fragmentation in children with OSA. Increased total REM sleep time and REM periods in children with OSA may be potential markers of OSA in children.
Support (optional): None

0274

EFFECTS OF SLEEP DISORDERED BREATHING ON LEPTIN, GHRELIN AND ADIPONECTIN IN CHILDREN

Tsaoussoglou M,[1] Bixler E,[1] Lin H,[2] Vlasic V,[1] Chrousos G,[3] Vgontzas A[1]
(1) Pennsylvania State University, Hershey, PA, USA, (2) Pennsylvania State University, PA, USA, (3) University of Athens, Athens, Greece

Introduction: In adults, sleep apnea is associated with several metabolic aberrations, including visceral adiposity, insulin resistance and hyperleptinemia. In children, sleep disordered breathing (SDB) has been traditionally viewed as a result of anatomic abnormalities whilst potential concurrent metabolic aberrations have not previously been examined. In this study, we examined the association of SDB in children with leptin, ghrelin and adiponectin, three hormones that have been associated with appetite, energy homeostasis and glucose metabolism.
Methods: 148 children of a wide age range (5-17 years) and body mass index were consecutively recruited from our sleep disorders clinic and from a subset of a community sample assessing the prevalence of SDB in children. Every child had a thorough clinical history and physical examination, subjective questionnaires, 9-hour complete polysomnographic study and a morning blood draw for the assessment of leptin, ghrelin and adiponectin using commercially available radioimmunoassay kits.
Results: In univariate analysis leptin and ghrelin, in an inverse manner, were significantly ($p<0.01$) associated with age, BMI percentile, indices of SDB and sleep disturbance. Adiponectin was negatively associated with age, BMI percentile, and indices of sleep disturbance ($p<0.01$). In stepwise multivariate regression analysis leptin levels were predicted by BMI percentile, age, and indices of SDB. Ghrelin levels were predicted by age, BMI percentile and indices of SDB. Finally, adiponectin levels were predicted by age and BMI percentile.
Conclusion: SDB in children is associated with an increase of leptin levels and a decrease of ghrelin levels independent of age or obesity. Obesity in children is associated with increased leptin, and decreased ghrelin and adiponectin, changes that have been associated with the metabolic syndrome in adults. Sleep apnea in children shares some metabolic abnormalities similar to those observed in adult sleep apnea that warrant further investigation.
Support (optional): NIH RO1 HL-64415
NIH RO1 HL-63772

0275

PERIODIC LIMB MOVEMENTS IN SLEEP STAGES OF CHILDREN

Calabro K,[1] Carole M,[1] Traylor J,[2] Schultz B,[2] Karamessinis L,[1] Bradford R,[2] Bintliff-Janisak B,[2] Mason T[1]
(1) Children's Hospital of Philadelphia, Philadelphia, PA, USA, (2) Children's Hospital of Philadelphia, PA, USA

Introduction: Periodic limb movements in sleep (PLMS) are stereotyped, repetitive leg movements that may disrupt sleep and have been associated with daytime behavioral issues in children, such as attention deficit-hyperactivity disorder. Prior analyses in adults have demonstrated that the periodic limb movement index (PLMI) was relatively decreased in slow wave sleep and REM sleep compared to lighter sleep stages (stages 1 and 2). Given their higher arousal thresholds, we hypothesized that children would have movement indices that are more consistent across sleep stages.
Methods: Overnight polysomnography data for 415 children ages 2-18 years meeting study inclusion criteria were retrospectively evaluated. Sleep stages and PLMS were scored according to standardized criteria. For all subjects having an overall PLMI greater than or equal to 2 (n=52), the number of limb movements in each sleep stage was divided by the sleep time spent in that stage to generate stage-specific movement indices. Statistical analyses were performed for comparisons of the PLMI in stages 1-2, stages 3-4, and REM sleep.
Results: The overall mean PLMI for all sleep stages was 4.43 (SD 3.07). The mean (SD) stages-specific limb movement indices were: stages 1-2 5.10 (4.6); stages 3-4 4.15 (13.6); and REM 3.51 (6.23). No significant differences were noted between these indices.
Conclusion: In contrast to adult subjects, the children in this study had periodic limb movements that did not differ significantly between lighter NREM, slow wave sleep, and REM sleep. These findings suggest that developmental factors may influence periodic limb movement frequency across sleep stages.
Support (optional): K23-RR16566 (TM); MO1-RR-000240

0276

LOW HEART RATE VARIABILITY DURING SLEEP IN CHILDREN WITH CHRONIC ARTHRITIS

Lopes M,[1] Roizenblatt S,[2] Guilleminault C,[3] Rosa A,[4] Passarelli C,[5] Poyares D,[6] Tufik S[7]
(1) Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil, (3) Stanford University, Stanford, CA, USA, (4) Lisboa, Portugal, (5) Sao Paulo, Brazil, (6) Federal University of Sao Paulo, Sao Paulo, Brazil, (7) Univ Fed Sao Paulo, SP

Introduction: Reduction in 24-h Heart rate variability (HRV) has been shown to be associated with disease outcome and aging. We sought to evaluate autonomic changes in children with chronic pain condition (Juvenile Idiopathic Arthritis- JIA)
Methods: 10 children and teen-agers with JIA [mean age=12±3.1] and 10 control group [mean age=13±2.1] matched for gender and Tanner stage were monitored by PSG following one night of habituation in the sleep laboratory. The HRV standard time and frequency domain were calculated for 5-minute periods in all sleep stages. Mann Whitney U-test was used to analyze the data.
Results: The means of the standard deviation of NN intervals (SDNN) during slow wave sleep (SWS) and of the total power in all sleep stages were significantly lower in JIA group compared to controls. The SDNN in SWS was 47±38.5 versus 94.6±75.2 (p=0.02), and the total power in stage 2: 7322±3206.5 vs 11703.7 ± 5068.6 (p=0.03); in slow wake sleep 5433.3±2802.2 vs 9108.5 ±5251.9 (p=0.04); and in REM sleep 10338±2856.6 vs 12995.2±2920.9 (p=0.03), respectively.
Conclusion: Chronic arthritis affects negatively the autonomic regulation in children. This is the first study showing low heart rate variability during sleep in children with chronic pain.
Support (optional): Supported by AFIP.

0277

TOTAL SLEEP TIME, SUBJECTIVE SLEEP QUALITY, AND BODY MASS INDEX IN ADOLESCENTS

Landis A, Parker K
Emory University, Atlanta, GA, USA

Introduction: Decreased total sleep time (TST) and poor sleep quality have been linked to an increased prevalence of obesity. Because obesity and both poor and insufficient sleep are common problems in adolescents, the purpose of this study was to explore associations among these variables and body mass index (BMI) in this population.
Methods: As part of an ongoing study on sleep and obesity, 25 adolescents were recruited through the community and school system. Each adolescent had anthropometric measurements (height, weight, BMI) and completed the Pittsburgh Sleep Quality Index (PSQI). Because the data met the appropriate assumptions, parametric procedures were used for analysis ($\alpha = .05$).
Results: The sample included 15 females and 10 males; 17 were Black and 8 were White. Age ranged from 14 to 18 (15.3 ± 1.2) years and BMI from 18.1 to 33.4 (23.5 ± 4.3) kg/m2. Mean bed and wake-up times were 11:48 p.m. and 6:33 a.m., respectively, representing a mean TST of 7.75 ± 1.3 hours, an amount well below the recommended 8.5 – 9.25 for this age group. Average PSQI global scores were 4.72 ± 1.9; 52% of the adolescents endorsed poor subjective sleep quality (PSQI global score > 5). Controlling for age and gender, PSQI global scores were negatively associated with TST ($r = -.591$, $p = .001$) indicating that sleep length was an important component of subjective sleep quality in this sample. BMI was not associated with either TST or PSQI global scores.
Conclusion: This exploratory study was limited by the small sample size. However, the findings suggest that obesity, decreased TST, and poor sleep quality are common problems in this age group. Although no relationships were observed between TST and PSQI global scores, because obesity and poor sleep are common problems in adolescents, further study with a larger sample size and additional outcome measures is warranted.
Support (optional): NIH Grant, NR009897-01

0278

FACTORS ASSOCIATED WITH SLEEP DURATION IN INFANTS – DATA FROM THE AVON LONGITUDINAL STUDY OF PARENTS AND CHILDREN (ALSPAC)

Taheri S,[1] Fleming P,[1] Blair P,[1] Henderson J,[2] Sam L,[2] Ness A,[2] Golding J[2]
(1) University of Bristol, Bristol, United Kingdom, (2) University of Bristol, AE (Europe)

Introduction: The aim of this study was to provide data from a large population study regarding factors associated with sleep duration in infancy.
Methods: In 1991-92, 14,541 pregnant women were recruited into ALSPAC, and their children have been followed with regular questionnaires and clinic assessments to the present. We present analyses of factors associated with sleep duration at age 6-8 months.
Results: On average, girls (n=5294) slept longer than boys (n=5615) at night (Mean 10h 52min Vs. 10h 43min; p<0.0001) , but there was no difference in daytime sleep duration. Preterm infants (n=589) slept less than term infants (n=10320) during nighttime (10hr 39min Vs 10hr 48min; p=0.007) but longer during daytime (2h 48min Vs 2h 28min; p<0.0001); overall total sleep duration was longer in preterm infants (13h 34min Vs 13h 20min; p=0.04). There was no association between multiple birth or high birthweight and sleep duration, but low birthweight infants slept less at night but longer during the day. First-born infants tended to sleep less both during the day and at night, sleeping on average 30 minutes less than their siblings. Infants from lower socioeconomic groups tended to sleep slightly shorter (4min; p<0.02) at night but slightly longer (8min; p=0.001) during the day compared to infants from more affluent families. Interestingly, infants belonging to obese mothers tended to sleep less at night. Maternal smoking in pregnancy was associated with longer daytime and total sleep duration. Infants belonging to married mothers slept longer at night, but less during daytime with no difference in total sleep time. Other important significant associations with sleep duration included maternal ethnicity, parental sleep duration (longer parental sleep associated with longer infant sleep), co-sleeping (shorter sleep), place for sleep (own/share room; longer sleep if not sleeping with carer), breastfeeding (shorter sleep), pacifier use (shorter nighttime but longer daytime sleep), and comforters (such as teddy bears; longer sleep).
Conclusion: We report on factors influencing sleep duration in infants from a large population-based cohort of children. This study provides one of the largest datasets regarding infant sleep allowing further research regarding factors influencing sleep in childhood and provides an evidence base for parental advice.
Support (optional): MRC (UK), Wellcome Trust

0279

HAPLOTYPE TREND REGRESSION ANALYSES TO DETERMINE APOE GENETIC VARIANTS ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA IN CAUCASIAN CHILDREN

Kalra M,[1] Pal P,[2] Kaushal R,[2] Amin R,[3] Dolan L,[1] Fitz K,[3] Sheng X,[2] Deka R,[2] Chakraborty R[4]
(1) Children's Hospital Medical Center of Cincinnati, Cincinnati, OH, USA, (2) University of Cincinnati, OH, USA, (3) Children's Hospital Medical Center of Cincinnati, OH, USA, (4) Unversity of Cincinnati, OH, USA

Introduction: Although the role of genetic predisposition in the pathogenesis of obstructive sleep apnea (OSA) is well accepted, the precise underpinning of genetic factors has not been achieved yet. Apolipoprotein E (ApoE) has been proposed as a candidate gene for OSA based on results from linkage and association studies. The objective of our study was to infer haplotypes using several single nucleotide polymorphisms (SNPs) in the region of ApoE and test their association with OSA status in children.
Methods: Caucasian children, age 2 to 21 years, with OSA (AHI>1) were recruited in the case group. Our race and gender matched control group was recruited from a population based cohort of children enrolled in the Princeton School District Study. Tag SNPs were selected based on an r2 of ≥ 0.8 and minor allele frequency of 5%. Haplotype construction was performed by HelixTree® version 3.1 using SNPs with genotyping call rate > 80% (5' to 3': rs157580, rs207560, rs8106922, rs405509) and the significance of comparisons between cases and controls was judged by permutation tests. The association of haplotypes with OSA was inferred by the haplotype trend regression method proposed by Zaykin *et al.* We tested 2-, 3-, 4- marker haplotypes from adjacent SNPs in a sliding-window fashion adjusting for age and body mass index (BMI).
Results: The case group (n=92) differed from the control group (n=92) in their age (13.3±4.6 vs14.5±2.3, P=0.02) and their BMI 30.2±11.427.3±2.6, P=0.02). All the genotyped SNPs met Hardy-Weinberg expectation. Haplotype `GAAA´ was observed more frequently in cases as compared to controls (p=0.0001). We observed strong linkage disequilibrium between the two associated markers rs405509 and rs769455. The sliding window haplotype trend regression test revealed that SNP rs405509 was included in all haplotypes that were significantly associated with OSA status.
Conclusion: Polymorphisms in ApoE gene and its regulatory region are associated with OSA in children.
Support (optional): Cincinnati Children's Research Foundation, Trustee Grant

0280

ACCRUED SLEEP DEBT IN HEALTHY AFRICAN AMERICAN CHILDREN AND ADOLESCENTS

Alfano C,[1] Huntley E,[1] Haak J,[1] Lewin D[2]
(1) Children's Hospital, Washington, Washington, DC, USA, (2) Washington, DC, USA

Introduction: Observational studies demonstrate that most people carry some amount of sleep debt. Considering increases in social and academic demands throughout early development, data are needed evaluating the presence and patterns of sleep debt and its impact on children´s neurobehavioral function.
Methods: (N=42) African-American children and adolescents from an urban environment, aged 6 to18, were recruited. Mean age was 10.5 (±3.2) years and 57% were female. Participants wore wrist actigraphs and completed daily sleep logs for 7 days.
Results: Significant differences in average total sleep time (TST) were detected between age groups (p<.001). Children ages 6-9 (M=493 min+10.9) averaged significantly more sleep than both 10-13 (M=426 min+12.1) and 14-18 year olds (M=443 min+18.7), who did not differ. Results of a regression analysis did not reveal weekday sleep debt (Mon-Thurs) to be a significant predictor of weekend (Fri-Sat) recovery sleep (p>.05), although there was a trend suggesting increased weekend "catch up" sleep among adolescents (n=11). In contrast to published norms (Iglowstein *et al.*, 2003), however, all three groups evidenced significantly less sleep overall compared to their same-aged peers (p<.001).
Conclusion: Accrued sleep debt during weekdays did not predict weekend recovery sleep based on a one-week prospective assessment, although some interesting sleep patterns across the week did emerge based on both gender and age. Overall, data suggest that African American youth living in an urban environment may be chronically sleep deprived. Because available normative data is based primarily on parental estimation of sleep, data suggest that use of objective methods of assessment may reveal significantly divergent findings for actual sleep among different populations of youth.
Support (optional): None.

0281

PREVENTING INFANT SLEEP PROBLEMS WITH AN INTERNET INTERVENTION: HOW GREAT IS THE NEED?

Bailey E,[1] Thorndike F,[1] Gonder-Frederick L,[1] Pastore L,[1] Freeman J,[1] Mindell J,[2] Palermo T,[3] Morin C,[4] Ritterband L[1]
(1) University of Virginia, Charlottesville, VA, USA, (2) Saint Josephs' University; Children's Hospital of Philadelphia, Philadelphia, PA, USA, (3) Oregon Health & Science University, Portland, OR, USA, (4) Laval University, Ste-Foy, Quebec, Canada

Introduction: People are increasingly turning to the Internet for information regarding health-related issues. Given this trend, we suspect that many new parents seek help for managing infant sleep, one of early parenthood´s greatest challenges. However, it can be difficult for sleep-deprived parents to find reliable, easy-to-digest advice that is relevant for their particular infant. In order to begin to understand parental usage of the Internet for sleep-related issues, as well as the potential need for and interest in additional web-based support, we surveyed current and expectant parents.
Methods: Parents of children 5 years old and younger (n = 274; 91% female; mean age = 32.2 years) and first-time expectant parents (n = 64; 91% female; mean age = 27.8 years) completed a brief survey on infant sleep and Internet use while waiting for their appointments in obstetrician, primary care, or pediatricians´ clinics, or while attending expectant parents´ classes.
Results: Eighty-seven percent of the sample reported having regular Internet access; one third (33%) of those with access reported using the Internet to seek information about infant sleep. Of all parents, 65% reported being at least "somewhat worried" about infant sleep (11% were "extremely worried"). Likewise, 73% reported being at least "somewhat worried" about their own sleep in the first postpartum months, with 13% reporting that they were "extremely worried". Most parents (84%) reported that they would be at least "somewhat interested" in using an Internet program to help in the prevention of infant sleep problems; 26% reported that they would be "extremely interested" in such a program.
Conclusion: Data from our survey support the belief that parents are using the Internet for sleep-related issues. There is also a need for (as indicated by high levels of sleep-related worry), as well as an overwhelming interest in, an online resource to help parents prevent infant sleep problems.

0282

PARENTAL AND CHILD REPORTED QUALITY OF LIFE IS POOR IN OVERWEIGHT CHILDREN WITH SYMPTOMS OF OSAS

Connolly H,[1] Ellis E,[2] Black J,[3] Kraus R,[3] Short R,[4] Carno M[5]
(1) University of Rochester, Rochester, NY, USA, (2) MI, USA, (3) University of Rochester, NY, USA, (4) University of Rochester, OK, USA, (5) Rochester, NY, USA

Introduction: Quality of life (QOL) is poor in children with obstructive sleep apnea syndrome (OSAS) and obesity which are common co-morbid conditions. It remains unknown whether one or both of these conditions contribute to the poor reported QOL. We proposed to examine the relationship between OSAS and QOL in a group of overweight children with symptoms of OSAS.
Methods: Subjects included children aged 8-18 (n=155, 92 males; age 12.4 ± 2.9 years) referred to the Pediatric Sleep Medicine Services at the University of Rochester with a BMI ≥ 85%ile for age and gender. Subjects and their accompanying parent/guardian completed the Pediatric Sleep Questionnaire (PSQ) developed by Chervin et. al. and the PedQL 4.0 developed by Varni. All subjects then underwent overnight polysomnography. Sleep studies were scored and interpreted based on standard pediatric criteria.
Results: Overall parental (55.82 ± 20.5) and child (63.75 ± 17.29) reported QOL is low. Increased symptoms of OSAS based on parental PSQ response negatively correlated with both the parental report of QOL and the child´s report of QOL ($p<0.000$) but did not correlate with severity of OSAS as measured by the apnea-hypopnea index (AHI). As anticipated, PSQ symptomatology did correlate with the AHI ($p=0.016$). Severity of obesity as measured by BMI Z-score did not correlate with QOL or severity of parentally reported symptoms of OSAS. Furthermore, severity of obesity as measured by BMI Z-score did not correlate with polysomnographic severity of OSAS as measured by the AHI.
Conclusion: Self and parentally reported QOL is quite poor in overweight children with symptoms of OSAS and is similar to reported QOL for children receiving chemotherapy for malignancy and those diagnosed with Juvenile Rheumatoid Arthritis. Interestingly, decrements in QOL correlate with symptoms but not objective measures of OSAS suggesting that even primary snoring may contribute to poor QOL in this population.
Support (optional): None

0283

USE OF OVERNIGHT PULSE OXIMETRY TO SCREEN FOR OBSTRUCTIVE SLEEP APNEA IN OVERWEIGHT AND OBESE CHILDREN

Crisalli J,[1] Fitz K,[2] Kumar S,[3] Kalra M[4]
(1) Children's Hospital Research Foundation, Cincinnati, OH, USA, (2) Children's Hospital Medical Center of Cincinnati, OH, USA, (3) Children's Hospital Research Foundation, OH, USA, (4) Children's Hospital Medical Center of Cincinnati, Cincinnati, OH, USA

Introduction: With increased prevalence of childhood obesity, a high risk group for obstructive sleep apnea (OSA), the number of children seeking evaluation for this disorder is increasing. Overnight polysomnography, the gold standard for diagnosis of OSA, is available only at a limited number of dedicated pediatric facilities. The purpose of this study is to determine the utility of overnight pulse oximetry in prioritizing overweight and obese patients for polysomnography.
Methods: All overweight and obese children who were participating in a genetic epidemiology study at Cincinnati Children´s Sleep Disorders Center and underwent polysomnography were eligible for recruitment. Children with craniofacial abnormalities, past history of airway surgery, and genetic syndromes were excluded from the study. Oxygen desaturation index (ODI) was calculated as the number of oxygen desaturations ≥4% per hour of sleep during polysomnography. Multivariate logistic regression analysis with age and BMI as covariates was performed to determine the association of oxygen desaturation index with OSA status. Receiver operating characteristic (ROC) analysis was performed to determine the ideal cut-off value of ODI for the detection of OSA (obstructive AHI ≥5).
Results: There were 119 children meeting inclusion criteria (59% males, 52 % with OSA) with mean age 14.3 ± 4.1 years and mean BMI 38.8 ± 11.1. Every unit increase in ODI increased the odds of having OSA 2 fold (OR 2.1, 1.5-3.0). ROC analysis demonstrated that an ODI threshold of 1.4 had a sensitivity of 82.3% and a specificity of 78.9% for the detection of OSA with area under the curve 0.88. An ODI threshold of 1.1 had a sensitivity of 87.1% (specificity 71.9%) for the detection of OSA.
Conclusion: Our data suggests that overnight oximetry can be used to prioritize overweight and obese children referred to a sleep center for polysomnography.
Support (optional): Children's Hospital Research Foundation, Trustee's Grant

0284

SLEEP CHARACTERISTICS OF TODDLERS WITH INFANTILE ANOREXIA

Monaghan M,[1] Lewin D,[1] Hahn A,[1] Ganiban J,[2] Morar V,[1] Brinkmeier L,[1] Chatoor I[1]
(1) Children's National Medical Center, Washington, DC, USA, (2) George Washington University, Washington, DC, USA

Introduction: Infantile Anorexia (IA) is a disorder characterized by poor appetite, food refusal, feeding related conflict, and growth failure. It is hypothesized that IA is associated with poor self-regulation, also manifesting as anxiety, and sleep problems. This study examines the prevalence of sleep difficulties in a sample of toddlers diagnosed with IA.
Methods: A sleep questionnaire was given to parents of children participating in a treatment study of IA (N=35, 47% female, 68% Caucasian, mean age = 27 months, range 13-40 months).
Results: Mean bedtime was 19:44 (SD 1.13) and toddlers slept for an average of 12.36 hours per night. 37% reported co-sleeping five or more nights/week; an additional 8% of children moved to the parent's bed during the night. Co-sleeping was more prevalent in minority families ($p<.05$) and more prevalent than in a normative sample ($p<.05$; Gaylor, et al, 2005). 14% reported bedtime resistance; however, 23% of co-sleepers reported daily bedtime resistance. 26% reported restless sleep five or more nights/week. Children >24 months had significantly more sleep difficulties than children ≤24mo ($p<.05$) and exhibited increased sleep related anxiety ($p=.05$). Total score on the sleep questionnaire was correlated with the CBCL Sleep Problems Scale score ($r = .66$, $p<.01$) and CBCL Total Problems score ($r = .43$, $p<.05$). On the CBCL, 33% of subjects were rated borderline clinical or clinical on the Sleep Problems Scale; 38% of this subgroup were co-sleepers.
Conclusion: This study provides preliminary evidence that IA is associated with increased rates of co-sleeping, bedtime resistance, and other sleep problems. Additionally, as rates of co-sleeping are higher than expected, parents may be compensating for self-regulation difficulties by encouraging co-sleeping. Comprehensive assessment and treatment of sleep problems in IA should be considered.

0285

SLEEP AND DAYTIME FUNCTIONING IN CHILDREN WITH AUTISM SPECTRUM DISORDERS AND THEIR PARENTS

Meltzer L,[1] Leas C,[1] Reamy A[2]
(1) Children's Hospital of Philadelphia, Philadelphia, PA, USA, (2) Saint Joseph's University, Philadelphia, PA, USA

Introduction: While a significant number of children with autism spectrum disorders (ASD) have sleep problems, the relationship between sleep and daytime behavior in this population has been understudied. In addition, although parents of children with ASDs report their child´s sleep problems, few studies have examined the impact of sleep problems in children with ASDs on caregivers´ sleep and daytime functioning.
Methods: To date, 23 mothers and 19 fathers (16 ASD children, 7 healthy children) have completed measures of parent and child sleep (PSQI, CSHQ, sleep diary, actigraphy), child daytime behavior (CBCL, DBC), and parent daytime functioning (CES-D, Iowa Fatigue Scale, SF-36). Participants were 79% Caucasian, ages 23.5-50.3 years (mean=38.8), and 76% were married. Children were 4-11 years (mean=6.6) and 70% male.
Results: Significant differences between children with ASDs and healthy children were found on subjective measures of sleep: bedtime resistance, $F(1,37)=7.78$, $p=0.008$, night wakings, $F(1,37)=5.90$, $p=0.02$, and total sleep time, $F(1,37)=5.10$, $p=0.03$, with more negative sleep patterns in children with ASDs. No differences were found for actigraphy variables. Child sleep variables were not significantly related to any child daytime behavior measure, however, child actigraphic total sleep time was significantly related to parents´ sleep quality, $r=0.38$, $p=0.02$, night waking frequency, $r=-0.43$, $p=0.01$, night waking duration, $r=-0.37$, $p=0.03$, depression, $r=-0.37$, $p=0.03$, and social functioning, $r=-0.38$, $p=0.03$, with all correlations indicating that shorter total sleep time was related to negative functioning.
Conclusion: These results support previous studies showing increased parental reports of sleep problems in children with ASDs, even though objective measures of sleep may not support parental complaints. However, the significant relationship between child sleep and parental functioning highlights the need for additional interventions to improve the sleep quality and quantity of children, as children´s sleep disruptions can have a significant negative impact on the entire family.
Support (optional): This study was supported by a J. Christian Gillin, M.D. Research Grant from the Sleep Research Society.

0286

RELATIONSHIPS BETWEEN SLEEP AND SMOKING AND DRINKING IN ADOLESCENTS

Liu X,[1] Buysse D[2]
(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) University of Pittsburgh, PA, USA

Introduction: Although sleep problems, sleep loss, and substance use are very prevalent in adolescence, few studies have examined the association between sleep and substance use. This study examined whether sleep loss or disturbed sleep was associated with elevated risk for adolescent smoking and drinking.
Methods: A questionnaire survey was conducted among 1,362 adolescents in 5 high schools in mainland China. Participants had a mean age of 14.6 years and 60% were males. A self-administered questionnaire was used to collect data on sleep patterns, sleep problems, smoking and drinking behavior, behavioral and emotional problems, life stress, and demographic characteristics of the adolescent and family.
Results: Overall, 20.1% of the sample had ever smoked, 4.3% were current smokers, 21.8% had experimented with drinking, and 16.4% currently drank alcohol. Both smoking and drinking tended to increase as aging and were more prevalent in boys than in girls. Logistic regression analyses showed that sleeping less than 8 hours at night (OR = 1.6, 95%CI = 1.1 – 2.3), frequent nightmares (OR = 1.6, 95%CI = 1.1 – 2.2), and difficulty initiating sleep (OR = 1.5, 95%CI = 1.1 – 2.1) were significantly associated with drinking after adjustment for various personal and family demographic variables. Smoking was related to sleeping less than 8 hours, bedtime later than midnight, nightmares, difficulty initiating sleep, difficulty maintaining sleep, and hypnotic medication use. Only nightmares were significantly (negatively) related to smoking after adjusting for personal and family demographic variables (OR = 0.6, 95%CI = 0.4 – 0.8).
Conclusion: These findings demonstrate significant associations between sleep quantity and sleep disturbances and smoking and drinking in Chinese adolescents. Although prospective, longitudinal studies are warranted, these findings suggest a potential role of sleep intervention (e.g., sleep hygiene education and treatment of sleep disturbances) in the prevention of adolescent substance use.

0287

SLEEP STAGES IN FIRST NREM CYCLE IN CHILDREN WITH AND WITHOUT ASTHMA

Kieckhefer G, Lentz M
University of Washington, Seattle, WA, USA

Introduction: Asthma is a chronic health condition marked by respiratory symptoms that parent´s of young children often report as disrupting the child´s sleep, but less is known about objective sleep patterns in older school age children. The purpose of this study was to compare minutes spent in sleep stages 2, 3, 4, in the first NREM cycle by 9 to 11 year old children with (n=28), and without (n=27) asthma.
Methods: Children were recruited using flyers posted in the community and by word of mouth. All were free of other chronic illnesses except allergy. Children did not have upper respiratory symptoms and had not taken systemic steroids in the two weeks preceding the study. Children with asthma maintained their regular prescribed management plan. Sleep was recorded with a standard montage and digitized using a computerized data acquisition system (EMBLA, Iceland). Data from the first night in the sleep laboratory was scored for wake and sleep stages in 30 sec epochs and NREM cycles were calculated (a sequence of NREM stages 2, 3 or 4 of at least 15 minute duration, terminated by 5 minutes or more of REM or wake) and used in this analysis.
Results: Children without asthma had mean duration in the first NREM cycle of 107.1+38.5 min with 15.7+8.4 min of stage2, 16.0+8.0 min stage3 and 70.6+30.4 min stage4. Children with asthma had mean duration in the first NREM cycle of 99.9+43.1 with 16.0+11.1 min stage2, 13.0+8.9 min stage3 and 64.2+31.1 min stage4.
Conclusion: There were no significant between group differences in sleep stages during the first NREM cycle for children with and without asthma.
Support (optional): NINR R01 NR08238 and P30 NR04001

0288

SLEEP DISORDERED BREATHING IN CHILDREN WITH JRA: A PRELIMINARY REPORT

Archbold K, Lentz M, Ward T, Wallace C, Landis C
University of Washington, Seattle, WA, USA

Introduction: Juvenile rheumatoid arthritis (JRA) is a chronic inflammatory disease associated with disturbed sleep. Little is known about symptoms of sleep disordered breathing (SDB) in children with

JRA. The purpose of this study was to describe subjective and objective indicators of SDB in children with JRA.
Methods: Data were collected from 60 children diagnosed with JRA. Children underwent 2 consecutive nights of polysomnography in a sleep research laboratory. Apnea/Hypopnea index (AHI, events/hr;≥ 10 seconds irrespective of oxygen saturation levels), total number of minutes snoring, and percent of total sleep time (TST) spent snoring (night 2)were used as objective indicators of SDB . Parents completed the Children's Sleep Habits Questionnaire and responses to two items were used as subjective indices of SDB.
Results: Data are reported as percent frequency or mean .± SD. Eight-three percent (n=50) of the children were female. Mean age of the children was 8.8 .±1.9 years and average BMI was 18.7 .± 3.5. The prevalence of parental report of snoring was twenty-two percent (n=13). Children spent an average of 205.5 .± 115.9 total minutes snoring, which was 37.4% .± 21.4% of TST (547 .± 40.3 minutes). The mean AHI was 0.7 .± 1.1 events/hr, and 23% of children (n=14) had an AHI of ≥1.±
Conclusion: We found a high prevalence of snoring and sleep disordered breathing patterns in children with JRA both by subjective and objective measures. Given that 300,000 children in the United States are estimated to have JRA, additional research is warranted to gain a better understanding of the severity of SDB and potential impact on neuropsychological performance and daytime functioning.

0289

EFFECTS OF PEDIATRIC SLEEP STUDY LENGTH ON SLEEP ARCHITECTURE

Ruse T,[1] Huntley E,[1] Winnie G,[2] Lewin D[1]
(1) Children's Hospital, Washington, Washington, DC, USA, (2) Children's National Medical Center, Washington, DC, USA

Introduction: Children and adolescents have greater sleep requirements than adults, and there are at least subtle differences in sleep architecture across the night. Results of pediatric studies may vary depending on sleep study length. Sleep related respiratory events such as obstructive apneas and hypopneas are more likely to occur in REM sleep and study length may have an impact on these parameters.
Methods: 15 subjects (avg. age 10.8 years) with no significant sleep pathology were monitored for one week prior to PSG with wrist actigraphy. PSG duration was based on prior average total sleep time which had an average duration of 9.75 hours. Lights on time was adjusted and sleep architecture is reported at the full study length, at 8 hours, and 6 hours. A repeated measure ANOVA was used to compare differences in the number of REM periods, REM percentages, and Delta percentages.
Results: Compared to the baseline study (9.75 hours), on the 8 hour study REM sleep was decreased by 4.49%, and on the 6 hours study, REM sleep decreased by 8.05%. These findings were statistically significant with a p value <.001. Among the 6-hour study reports, stage 2 sleep decreased by 6.55%, and stage 4 sleep increased by 4.7%. In the full length PSGs, the mean number of REM periods was 4.07, whereas in the 8-hour studies, the mean number of REM periods had decreased to 2.93. In the six-hour studies, the mean number of REM periods had decreased to 1.7.
Conclusion: There were significant changes in sleep architecture that could affect the outcomes of clinical studies that evaluate sleep disordered breathing. Further studies are needed to evaluate the impact of study length on arousal and RDI and guidelines for pediatric study length may be important.

0290

SCREENING STUDENTS FOR SLEEP DISORDERS AT SCHOOL: FREQUENCY OF SLEEP PROBLEMS IN GENERAL AND SPECIAL EDUCATION STUDENTS, SCHOOL BEHAVIOR AND ACADEMIC ACHIEVEMENT

Luginbuehl M, Ax E, Witte R, Bradley-Klug K
University of South Florida, Tampa, FL, USA

Introduction: The purpose of these studies was to examine the school behavior and academic achievement of students with and without sleep problems.
Methods: All studies utilized the Sleep Disorders Inventory for Students (SDIS), a school-based, parent-report sleep disorder screening tool. Participants in Study 1 included 86 “at-risk” preschoolers referred to a Child Find agency and screened for sleep problems, behavior problems, and academic assessment. Study 2 included 216 second and third grade students from New York State who had a sleep screening, teacher report of classroom behavior, and academic assessment. Study 3 included 595 students from Tampa Bay, FL and 5 sleep clinics who were screened for sleep problems, behavior problems, GPA, educational placement, and DSM-IV diagnoses. Twenty-four students with sleep disorders were compared on pre-post treatment GPAs and behaviors.
Results: In Study 1, preschoolers rated as high risk for having a sleep disorder displayed more externalizing (p=.0001) and internalizing (p=.001) problems, and poorer social (p=.003) and pre-academic skills (p=.0015) than peers without sleep problems. Thirty-three percent were at high risk for having a sleep disorder. In Study 2, 17% of the students were at-risk for having a sleep disorder. There was a significant difference between reading (p=.008), internalizing (p=.009) and externalizing (p=.012) scores. In Study 3, significant relationships were found between sleep problems, GPA (p<.0001) and problem behaviors (p<.0001). Furthermore, 49% of students with a diagnosed sleep disorder received special education services compared with 12 to 14 % nationally. Students´ GPAs (p<.01) as well as 11-out-of-12 behaviors improved significantly post-treatment (p<.0001 to p<.05).
Conclusion: Students who are experiencing academic or behavioral concerns may benefit from a sleep disorder screening. School psychologists and nurses should be trained to administer and interpret sleep disorders screening tools to improve the referral process.

0291

THE RELATIONSHIP BETWEEN THE PREVALANCE OF SLEEP DISORDERS SYMPTOMS AND ACADEMIC PERFORMANCE IN LOWER ELEMENTARY SCHOOL STUDENTS

Bachmann A,[1] Ax E[2]
(1) Chappaqua Public Schools, new york, NY, USA, (2) University of South Florida, New York, NY, USA

Introduction: Few studies of sleep disorders in children have been conducted in schools. The purpose of this school-based study was to identify the relationship between the prevalence of symptoms of sleep disorders and academic performance in second and third graders. The sleep disorders of concern included Periodic Limb Movement Disorder, Obstructive Sleep Apnea Syndrome, Delayed Sleep Phase Syndrome, and Excessive Daytime Sleepiness.
Methods: All students in second and third grades in one school district in a suburb of a large city in the Northeast were eligible to participate. Parents of 218 second and third graders completed Sleep Disorders Inventory for Students, Child Form (SDIS-C). The SDIS-C is a brief screening tool validated for use in the schools. Students whose parents endorsed symptoms of sleep disorders in the “cautionary” or “at-risk”

ranges were collapsed into the "Sleep Disorder" group. Math, Reading, and Writing report card grades were obtained for each student participant. Parents of 17.1% of the students in the sample reported symptoms of one or more sleep disorder.
Results: T-tests were conducted to examine the difference in math, reading, and writing grades of students with and without symptoms of sleep disorders. Students with reported symptoms of sleep disorders received significantly worse grades than students without symptoms of sleep disorders. Specifically, there were significant differences in math grades ($t(212)=2.82$, $p=.005$), reading grades ($t(211)=2.80$, $p=.006$), and writing grades ($t(212)=2.38$, $p=.018$). The magnitude of the difference in the means was small-moderate (eta squared=.06).
Conclusion: Almost one-fifth of a school-based sample of second and third grade sample exhibited symptoms of one or more sleep disorder. Students with symptoms of sleep disorders received significantly worse grades in math, reading, and writing than peers without symptoms of sleep disorders. Screening students at school with a validated school-based instrument may identify students to be referred for appropriate medical and/or behavioral treatment.

0292

NAPPING IN CHILDREN IS RELATED TO LATER SLEEP PHASE

Cairns A,[1] Harsh J,[1] Lebourgeois M[2]
(1) University of Southern Mississippi, Hattiesburg, MS, USA, (2) Brown University, Providence, RI, USA

Introduction: Few investigations of the relationship between childhood napping and nocturnal sleep have been conducted. Investigations of adult napping on sleep phase have indicated that daytime sleep delays nocturnal sleep phase and is associated with higher mortality in comparison to those that do not nap. The current study explores the relationship between childhood naps, bedtime, rise time, and mid-period time (MPT; midpoint between bedtime and rise time).
Methods: Data were collected from a representative community sample of 738 children (49% White, 50.4% Male) aged 2-12 years from South Mississippi. Caretakers reported on children´s typical weekend (WE) and weekday (WD) bedtime, rise time, and napping (frequency and duration). Naps were categorized as none, short (<60min), or long (>61min).
Results: Age by Nap ANOVAs revealed that napping was associated with later bedtimes, rise times, and MPTs on weekends. Long nappers had the latest WE bedtimes, rise times, and MPTs. Napping was also associated with later WD bedtimes and estimated sleep onset latencies. Compared to non-napping children, napping children had shorter WD but not WE nocturnal time in bed (TIB). These effects did not vary with age.
Conclusion: Children who nap have later weekend nocturnal sleep periods and restricted weekday nocturnal TIB. One explanation is that napping children have a later sleep phase because of a reduced evening sleep propensity. A later sleep phase would explain the later bedtimes, rise times, and MPTs on weekends when social constraints on sleep are reduced. A later sleep phase may not be evident during the week because of social demands, especially on rise times. These findings are important because children with later sleep phases may be disadvantaged in social and academic circumstances.

0293

AGGRESSIVE BEHAVIOR, BULLYING, AND SLEEP-DISORDERED BREATHING IN SCHOOLCHILDREN

O'Brien L, Hendrix N, Felt B, Hoban T, Ruzicka D, Chervin R
University of Michigan, Ann Arbor, MI, USA

Introduction: Aggressive behavior and bullying are common among schoolchildren and are likely to have multiple causes. Undiagnosed sleep-disordered breathing (SDB) is also a common condition, can affect prefrontal behavioral regulation, and may promote aggressive behavior. We investigated whether aggressive schoolchildren may be at higher risk for SDB than other children.
Methods: Children in grades 2-5 of an urban public school district were studied. Parents completed two well-validated instruments: the Conner´s Parent Rating Scale (CPRS) and the Pediatric Sleep Questionnaire SDB Scale, minus 6 of the 22 items that directly ask about daytime behavior. Teachers completed the Conner´s Teacher Rating Scale (CTRS). The numbers of discipline referrals in the previous 12 months were obtained from the six elementary schools.
Results: After attempts to recruit 1221 families, 345 CPRS´s and 245 corresponding CTRS´s were completed. Children with a CPRS-identified conduct problem (n=51), in comparison to the remainder, had higher mean SDB symptom scores (0.28±0.18 [s.d.] vs. 0.14±0.16; t-test $p<0.001$). Children reported by parents to bully others, either often or very often (n=27), had higher SDB scores on average than other children (0.24±0.17 vs. 0.16±0.16;$p=0.016$). In contrast, children with CTRS-identified conduct problems (n=36) did not have significantly increased SDB scores ($p=0.12$). However, children (n=30) with ≥2 discipline referrals by teachers, for bullying or other disruptive behaviors, showed higher SDB scores than the remaining children (0.21±0.14 vs. 0.15±0.16;$p=0.03$)
Conclusion: Urban schoolchildren with aggressive behavior, bullying, and discipline problems often had symptoms suggestive of SDB. A causative effect of SDB on such behavior remains to be proven, and some discrepancies between parent and teacher reports suggest caution in the interpretation of the present results. However, the findings overall raise the possibility that screening and treatment for SDB in schoolchildren may offer a novel approach to reduction of problematic behavior in school settings.
Support (optional): University of Michigan Medical School Clinical Research Initiatives Program; grant U014227

0294

POSITIONAL SLEEP APNEA IN CHILDREN

Gibson R, Palmisano J, Chervin R, O'Brien L
University of Michigan, Ann Arbor, MI, USA

Introduction: The supine sleep position often worsens the severity of sleep-disordered breathing (SDB) in adults. Few studies have explored the influence of sleep position on the apnea/hypopnea index (AHI) in children, or whether any such effect may depend on age or gender.
Methods: Retrospective, database analysis of pediatric polysomnograms performed at the University of Michigan Sleep Disorders Center for suspected SDB in children aged 3–13 years. Positional sleep apnea was defined as an AHI 2 or more times greater in the supine than the non-supine (prone or lateral) position.
Results: Data from 570 diagnostic polysomnograms were reviewed. Subjects were divided into three groups based on age: early childhood (3-6 years; n=209; 60% male), middle childhood (7-10 years; n=236; 58% male), and late childhood (11-13 years; n=125; 53% male). Overall, mean time asleep in the supine position was 2.7±1.9hrs and 4.3±2.1hrs in the non-supine position. Compared with the AHI while

sleeping non-supine, the AHI while supine was significantly higher for the middle and late childhood age groups (5.8/hr vs, 4.7/hr; p=0.01 and 7.4/hr vs. 5.3/hr; p=0.03 respectively) but not for the early childhood age group (6.3/hr vs. 6.6/hr;p=0.5). Analysis of gender differences revealed no differences in the proportion of children with positional sleep apnea in the middle or late childhood groups. However, boys in the early childhood group were more likely to have positional sleep apnea than girls (28% vs. 16%;p=0.045).
Conclusion: Young children at ages of maximal adenotonsillar hypertrophy show no difference between supine and non-supine severity of SDB. In contrast, older age groups gradually show greater severity of SDB in supine sleep, increasingly resembling adults. Gender seems to play a less prominent role than age in positional SDB, except perhaps in the youngest children.

0295

SLEEP PROBLEMS IN CHILDREN AND ADOLESCENTS WITH AND WITH OUT HUMAN IMMUNODEFICIENCY VIRUS INFECTION

Huntley E,[1] Haak J,[2] Daniel L,[3] Lewin D[4]
(1) Children's National Medical Center, North Bethesda, MD, USA, (2) Children's Hospital, Washington, Washington, DC, USA, (3) Drexel University, Philadelphia, PA, USA, (4) Washington, DC, USA

Introduction: There is growing evidence that children and adolescents with human immunodeficiency virus (HIV) infection have an increased risk of disrupted sleep and daytime fatigue. This study investigated the hypothesized association between HIV infection and sleep problems in children and adolescents.
Methods: The study sample consisted of 51 children (ages 6 – 18, mean age of 11(3.7) years); approximately 98% African American and 62.7% female. Parents and children completed standard measures assessing sleep habits, behavior and psychiatric symptoms and sleep parameters were estimated over one week utilizing wrist actigraphy and a daily sleep log.
Results: Both groups were comparable on measures of behavior (CBCL), depression (CDI), anxiety (STAIC), and quality of life (PedQL). Although actigraphy estimates of total sleep time indicated that HIV-positive participants slept less than the comparison group, differences were not significant. Parental report indicated that the HIV-positive children had trends for higher rates of excessive daytime sleepiness, insufficient sleep, nightmares, enuresis and symptoms of insomnia. Only the insomnia symptoms were significantly different between groups χ^2 (1, N=51) =7.6, p <.01. Logistic regression analysis indicated that HIV-positive status was significantly associated with an increased risk of insomnia symptoms (OR, 5.5; 95 % CI, 1.6 – 19.1; p< .01) independent of age and gender. Overall, 88.2% of parents of the HIV-positive group endorsed one or more clinically significant sleep problems compared to 29.4% of the comparison group χ^2 (1, N=51) =15.7, p<.001.
Conclusion: This study found a higher incidence of sleep problems in HIV-positive children, specifically clinically significant symptoms of insomnia. These problems could contribute to daytime fatigue, a particularly debilitating symptom of HIV infection. Evaluating and treating sleep problems in this population is warranted. It is recommended that clinicians routinely ask about the presence of sleep problems when conducting medical evaluations. Further research is required to identify additional factors associated with sleep problems.

0296

SLEEP DISORDERED BREATHING IN PEDIATRIC PATIENTS

Pu Y,[1] Cramer Bornemann M,[2] Patterson R[1]
(1) University of Minnesota, Minneapolis, MN, USA, (2) Hennepin County Medical Center, Minneapolis, MN, USA

Introduction: Sleep disordered breathing (SDB), especially OSA, affects not only cardiovascular system but also recognative function and developmental process in children. This study retrospectively analyzed the characteristics and complexity of pediatric SDB.
Methods: We selected records of those: aged from 2 to 20; suspected of SDB or sleep disorders and went through lab polysomnography (PSG) to rule out OSA at MRSDC-HCMC from 2000 to 2003. Each record included: standard PSG study, apnea diagnosis, and physician´s overall assessment on apnea severity and comments. Two-tailed t-tests (α=0.05) were used to assess the statistical significance between apnea group (overall AHI≥5) and non-apnea group (overall AHI<5).
Results: Eighty records (Age: 8.9±4.6, BMI: 23.1±9.0) were analyzed. Thirteen (16%) had more than one central apnea episode (central AHI: 0.3±1.4); one (1%) had mixed apnea; six (7.5%) had hypopneas (Hypopnea Index: 1.1±4.7). Thirty-three (41%) had Obstructive AHI≥5.0 vs. 47 (59%) with OAHI<5.0. OAHI was correlated with RDI (r=0.95), but had no correlation with BMI or lowest SpO2%. Apnea group (36 patients) had significant (α<0.05) difference from non-apnea group (44 patients) in REM%, average OSA duration, longest OSA duration, but no difference in BMI, age, hypoxic conditions, or arousals. Snorers accounted for 86% of the apnea group vs. 32% of the non-apnea group. Among all the patients, physicians considered 37 (46%) as normal or insignificant apnea, 4 (5%) as mild, 39 (49%) as abnormal or severe.
Conclusion: Only half of the pediatric PSG receivers were found abnormal in terms of AHI, although all patients were referred to rule out OSA. Hypopnea, central or mixed apnea was uncommon in this group. BMI or hypoxic conditions did not predict pediatric apnea or its severity.
Support (optional): Thanks to MRSDC – HCMC and Jeff Kuznia from Compumedics Inc.

0297

SHORT SLEEP DURATION AND RISK OF OBESITY IN EARLY CHILDHOOD – A LONGITUDINAL STUDY

Montplaisir J,[1] Touchette E,[2] Petit D,[3] Boivin M,[4] Tremblay R[1]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) University of Montreal, AE (Canada), (3) Sacre-Coeur Hospital, Montreal, Quebec, Canada, (4) Universite Laval, Quebec, Canada

Introduction: Childhood obesity is a public health problem in many industrial countries. The aim of the study was to verify to what extent short sleep duration during early childhood is an independent risk factor for obesity at school entry.
Methods: Body mass index was measured at 6 years of age in a sample of children born in a Canadian province (N=1138). Nocturnal sleep duration was reported yearly from 2.5 to 6 years of age by their mothers. Prenatal, postnatal (5 months), and lifestyle (6 years) potential confounding factors for excess weight were assessed by interviews, questionnaires, and hospital records. The association between BMI at 6 years and sleep duration pattern was assessed by a Kruskal-Wallis test. Logistic regressions evaluated whether sleep duration patterns is an independent risk of excess weight while controlling for a variety of obesogenic factors.
Results: The prevalence of excess weight was 13.8% for the 6-year-old children. We identified 4 sleep patterns: a short persistent pattern

(6.0%,n=109) where children slept less than 10 hours per night until age 6; a 10-hour persistent pattern (50.3%,n=920); a 11-hour persistent pattern (38.9%,n=712); and a short increasing pattern (4.8%,n=88) where children slept fewer hours in early childhood but increased their sleep duration at around 2.5 and maintained it until 6 years of age. A significant difference in the distribution of BMI as a function of sleep duration pattern (P<.001). The effect of sleep duration pattern on excess weight remained significant after adjusting for confounding variables. The odds ratio of being overweight was almost threefold higher for both short persistent sleepers and short increasing sleepers compared to 11-hour persistent sleepers (P=.01).
Conclusion: Short sleep duration (less than 10 hours) during early childhood significantly increases the risk of excess weight or obesity in childhood, and appears to be independent of other obesogenic factors.
Support (optional): Research supported by "Institut de la statistique du Québec, direction Santé Québec", "Canadian Institutes of Health Research " (CIHR) (grant to J. Montplaisir) and "Fonds de la recherché en santé du Québec" (doctoral studentship to E. Touchette)

0298

THE NEUROBEHAVIORAL CHANGE IN SUSPECTED SLEEP DISORDERED BREATHING PATIENTS AFTER TONSILLECTOMY & ADENOIDECTOMY

Kwon D,[1] Cho S,[2] Han J,[3] Hong I[3]
(1) korea University, Seoul, South Korea, (2) Korea University, South Korea, (3) Seoul Sleep Center, Seoul, South Korea

Introduction: Children with sleep disordered breathing(SDB) may develop various morbidities and there are association between behavioral and attention problems, such as attention deficit and hyperactivity disorder (ADHD) in children with SDB. This study was performed to evaluate the behavioral change after tonsillectomy and adenoidectomy(T&A) on suspected SDB. And we also assessed potential relationships between behavioral problems and suspected SDB, such as snoring or mouth breathing.
Methods: With a prospective interventional comparative trial, total of 51 children (30 men and 21 women), who visited for tonsillectomy and adenoidectomy were enrolled. 2 follow up losses. The parents of the children were asked to complete the ADHD Rating Scale-IV(ADHDRS-IV), Conners Rating Scale(CRS) and a sleep self questionnaire before and after the operation. The ADHDRS-IV score of each child was compared before and after surgery using a matched paired t-test.
Results: The mean preoperative ADHDRS-IV & CRS score were 15.4 ± 7.78 and 8.93±4.46. The mean postoperative score were 8.1±7.39 and 5.1±4.27 with 105 days of mean interval between scoring. A paired t-test showed that this difference is statistically significant (P<0.01). Of the 49 subjects, 17 (34.7%) had high preoperative ADHDRS-IV score (mean score, 24.18 ± 3.85) compatible to ADHD. The mean score significantly decreased as 13.06 ± 8.54 after the operation ($p < 0.01$). Of the 17 subjects, 13 (76.5%) had normal range of ADHDRS-IV after the operation. The preoperative frequent snoring patients are 45 children (91.8%) and mouth breathing patients are 42 children (85.7%). After the operation, the frequencies of snoring and mouth breathing also significantly decreased in 40 children (88.9%) and 37 children (88.1%), respectively.
Conclusion: T&A showed significant improved SDB and behavioral problems, such as ADHD symptoms. These findings may be important in understanding the impact of SDB and therapeutic interventions on pediatric behavioral problem patients.

0299

PARENTAL ATTITUDES AND AGREEMENT ABOUT INFANT SLEEP BEHAVIOR AND LEVELS OF PARENTAL DISTRESS

Mayer G, Teti D, Countermine M
Pennsylvania State University, University Park, PA, USA

Introduction: Infants´ sleep habits can be a cause for concern for many parents, and support from one´s partner may benefit mothers´ and fathers´ quality of adjustment to infant sleep difficulties (Boyle & Cropley, 2004). The present study will examine both mothers´ and fathers´ level of agreement, and attitudes and perceptions about their infant´s sleep behavior in relation to their own levels of distress.
Methods: As part of a larger project, the present study is collecting data from 40 families with infants ranging in age from 1 month to 24 months of age. Both mothers and fathers complete questionnaires concerning their infant´s sleep and daytime behavior. Additionally, video recordings of infants and parents are being made to assess infant sleep regulation in relation to the quality of parents´ behavior.
Results: Preliminary analyses have been conducted including 9 families. Results from these analyses indicate that mothers and fathers always agree about their preferences for their infant´s sleep location ($r = 1.00$, $p < .01$). Maternal distress is associated with having a problem with where the infant sleeps ($r = .69$, $p = .04$), but paternal distress is not ($r = .44$, $p = .24$). When mothers have difficulty putting their baby to sleep, both themselves ($r = .80$, $p < .02$) and their spouses ($r = .67$, $p < .07$) are more likely to experience anxiety.
Conclusion: The preliminary analyses indicate that parents´ perceptions about their infant´s sleep behavior may have important implications for their adjustment. At the completion of this research study, we anticipate a sample size of 40. With a larger sample size we expect to find stronger associations among the variables analyzed here. In addition, video recordings of parent-infant interactions will provide information about the parents´ emotional availability during bedtime and night wakings.

0300

EFFECTS OF SLEEP INERTIA ON SUBJECTIVE SLEEPINESS AND PERFORMANCE IN OLDER SUBJECTS

Silva E,[1] Czeisler C,[2] Duffy J[2]
(1) Division of Sleep Medicine, Brigham and Women's Hospital, Boston, MA, USA, (2) Division of Sleep Medicine, Brigham and Women's Hospital / Harvard Medical School, Boston, MA, USA

Introduction: The effects of sleep inertia are well established for younger, but not older subjects. The present study aims to explore whether sleep inertia is observed in healthy older subjects.
Methods: Ten healthy older volunteers (55-72 years, mean=64.90±5.47, 5f) participated in a study consisting of two conditions: 3, 24h baseline days (16h wake) followed by 18, 20h "days" (13.33h wake) during which scheduled waketimes occurred at all circadian phases. Karolinska Sleepiness Scales (KSS) and Digit Symbol Substitution Tests (DSST) were administered 1, 10, 20, and 30 minutes after each scheduled waketime. For each condition, observations from each subject were binned into four 10-minute bins according to time awake. Mean KSS ratings and DSST trials attempted were analyzed via mixed model analysis for factors TIME AWAKE (time after awakening of each observation) and CONDITION (baseline day or 20h "day") with post-hoc Bonferroni adjustment.
Results: During the first 40 minutes after awakening, subjective sleepiness declined while performance increased. Subjects were less sleepy and had better performance in the baseline condition than in the 20h day condition (when scheduled waketimes occurred at all circadian phases). There were significant main effects of TIME AWAKE ($p<0.01$) and CONDITION ($p<0.01$) for both subjective sleepiness and performance, but no significant interactions, suggesting that the dissipation of sleep inertia during the first 40 minutes after awakening across all circadian phases in the 20h day paralleled the dissipation of sleep inertia during baseline condition.
Conclusion: In this group of healthy older subjects, we observed a significant effect of sleep inertia which did not appear to plateau during the first 40 minutes after awakening. Because older people report frequent nocturnal awakenings, they may be more prone to adverse consequences of sleep inertia. Further investigation will be required to understand the effects of sleep inertia on alertness, performance, and motor ability in older subjects.
Support (optional): NIH-AG06072; NIH-AG09975; NIH-RR02635

0301

EFFECTS OF AN AT-HOME NAP REGIMEN ON NIGHTTIME SLEEP IN OLDER SUBJECTS

Perillo A, Meyers E, Murphy P, Campbell S
Weill Medical College of Cornell University, White Plains, NY, USA

Introduction: An age-related decline in average nighttime sleep duration has been documented in numerous studies. The capacity to nap, on the other hand, may be differentially conserved with aging 1,2. In an ongoing study to examine whether daily naps can supplement 24-hour sleep amounts in older individuals, and the effects of such a nap regimen on nighttime sleep and waking function, actigraphy was recorded continuously throughout a month-long protocol.
Methods: Actigraphy records from 6 healthy older subjects (4M,2F; 61-87y; 70±10y old) yielded 153 nighttime sleep episodes. Of these, 83 were preceded by a nap between 10h-18h; 70 were preceded by no nap. All sleep episodes were analyzed using the validated ActiWare algorithm. Sleep period duration (DUR) and sleep efficiency (SE) on `Post-nap´ nights vs. `Post-no-nap´ nights were compared, and correlations between the timing, DUR, and SE of Naps and Post-nap night sleep were calculated.
Results: SE in night sleep post-nap was 75.7±9.8 vs. 78.4±8.0 when no nap was taken (n.s.). Night sleep DUR post-nap was 7.71±1.65h vs. 7.82±1.54h when no nap was taken (n.s.). As well, the timing of night sleep did not differ (post-nap 2429-0821h vs. 2425-0826h post-no-nap, n.s.). Finally, there were no significant correlations between timing, DUR, or SE of naps and timing, DUR or SE of the subsequent nocturnal sleep period (all $r < \pm.18$, n.s.).
Conclusion: The duration quality, and timing of nighttime sleep, measured by actigraphy, was not affected by a daytime nap, compared to nights not preceded by a nap. In addition, characteristics of the nap were unrelated to the subsequent night sleep period. These data add to the expanding literature indicating that taking a nap is not deleterious to subsequent nighttime sleep quality, and may be a useful, non-pharmacological strategy to supplement age-associated decreases in sleep duration.
1Campbell SS, Murphy PJ (2006). The nature of spontaneous sleep across adulthood. J Sleep Res, in press, 2007
2Monk *et al.* (2001). Effects of afternoon "siesta" naps on sleep, alertness, performance, and circadian rhythms in the elderly. Sleep 24:680-7.
Support (optional): Research support provided by NIH grants R01 AG12112 and R56 AG15370.

0302

SLEEP AS ANALGESIC: IMPROVING SLEEP AND PAIN IN OLDER ADULTS

Vitiello M,[1] Rybarczyk B,[2] Stephanski E[3]
(1) University of Washington, Seattle, WA, USA, (2) Virginia Commonwealth University, VA, USA, (3) Accelerated Community Oncology Research Network, Inc., Memphis, TN, USA

Introduction: Osteoarthritis (OA) pain affects over half of all older adults; the vast majority of whom experience significant co-morbid sleep disturbance. While pain initiates and exacerbates sleep disturbance, disturbed sleep in turn maintains and exacerbates pain. Such interaction implies that improving the sleep of OA patients may also reduce their pain. We examined this possibility by reanalyzing a sub-set of data from a recently published RCT of CBT-I to improve sleep in a sample of older adults complaining of insomnia co-morbid with OA, CAD or COPD (Rybarczyk et al, 2005).
Methods: 20 OA patients (mean age 68.9, 17 women and 3 men) were randomly assigned to CBT-I and 26 OA patients (mean age 66.7, 25 women and 1 man) to an attention-control. Neither treatment protocol specifically addressed pain management. Sleep and pain were assessed by patient self-report at baseline, post-treatment and at one-year follow-up.
Results: At post-treatment, CBT-I subjects reported significantly decreased Sleep Latency (39.4 (21.2) vs. 24.6 (23.1), mean (SD), p=.042) and WASO (61 (47) vs. 25 (23), p=.000) and increased Sleep Efficiency (71.9 (10.7) vs. 83.9 (8.5), p=.000); they also reported significantly reduced pain on the SF-36 Pain (56.0 (19.7) vs. 64.4 (24.3), p=.020) and a non-significant trend for reduced pain on the McGill Pain Questionnaire (10.6 (9.9) vs. 7.9 (6.7), p=.109). One-year follow-up demonstrated maintenance of both improved sleep and reduced pain. Control subjects reported no significant improvements in self-assessed sleep or pain from baseline to post-treatment and were not assessed at follow-up.
Conclusion: CBT-I successfully improved both immediate and long-term self-reported sleep and pain in a group of older OA patients. These results demonstrate that improving sleep can be "analgesic" in OA patients and that techniques to improve sleep should be considered for

addition to treatment programs for pain management in OA and possibly other pain-states.
Support (optional): This research was supported by AG017491 to BDR and AG025515 to MVV.

0303

DOES MEASURED SLEEP PREDICT CHANGES IN BODY MASS INDEX AND GLUCOSE METABOLISM? THE CARDIA SLEEP STUDY

Lauderdale D,[1] Knutson K,[2] Rathouz P,[2] Van Cauter E,[1] Yan L,[3] Liu K[4]
(1) University of Chicago, Chicago, IL, USA, (2) University of Chicago, IL, USA, (3) Peking University, China, (4) Northwestern University, IL, USA

Introduction: Epidemiologic studies report that short sleep is associated with increased risk of obesity and diabetes, however, those studies rely on self-reported sleep. The aim of this investigation was to determine if actigraphically-measured sleep similarly predicted changes in body mass index (BMI), glucose, insulin, or insulin sensitivity over 5 years.
Methods: This is an ancillary study to an ongoing cohort study, the Coronary Artery Risk Development in Young Adults (CARDIA). Participants wore wrist actigraphy monitors for two three-day periods approximately one year apart between the Year 15 and Year 20 clinical exams of CARDIA participants, yielding a 6-day average sleep duration. Outcome measures are the 5-year change in BMI, fasting glucose levels, fasting insulin levels, and insulin sensitivity derived from homeostatic model assessment (HOMA). Regression models were used to estimate mean outcome measures as a function of sleep duration, adjusting for age, race, sex, education, income, current smoking and, in the glucose/insulin models, BMI and 5-year change in BMI. The quadratic term for sleep duration was added to test for U-shaped associations.
Results: Participants were aged 38-50 years in 2003 (n=669). Mean sleep duration was 6.1 hours. Sleep duration was significantly associated with change in insulin (p=.02 for quadratic term) and change in HOMA (p=.01 for quadratic term) in a U-shaped fashion such that the shortest and longest sleep durations were associated with reduced insulin sensitivity. The nadir for smallest change was estimated to be at 5.75 hours of sleep for insulin and 5.5 hours for insulin sensitivity. Sleep duration did not predict change in BMI or glucose.
Conclusion: These findings are consistent with experimental research suggesting that sleep affects risk of diabetes. However, an association between sleep duration and change in BMI was not observed.
Support (optional): Research for this study was supported by grant AG 11412 from the National Institute on Aging. CARDIA is supported by US Public Health Service contracts NO1-HC-48047, NO1-HC-48048, NO1-HC-48049, NO1-HC-48050, and NO1-HC-95095 from the National Heart, Lung, and Blood Institute.

0304

AGE DIFFERENCES IN THE TEMPORAL ORGANIZATION OF STAGE 2 SLEEP SPINDLES

Peters K,[1] Vlaskalin M,[2] Ray L,[1] Smith V,[2] Smith C[1]
(1) Trent University, Peterborough, Ontario, Canada, (2) Trent University, Ontario, Canada

Introduction: Previous studies have shown that the number and density of sleep spindles decreases with age. The objective of this investigation was to determine whether there were age differences in the temporal organization as well as the number of Stage 2 sleep spindles.
Methods: In-home sleep recordings were performed on 14 younger (17-24 yrs) and 14 older adults (62-79 yrs) for two consecutive nights. The first night was discarded and the second night served as the baseline night. There were four key spindle-related variables: (a) the total number of spindles in Stage 2 sleep, (b) the percentage of spindles within a cluster (i.e., three or more spindles with an inter-spindle-interval less than 5 seconds), (c) the percentage of spindles within a double (i.e., two spindles with an inter-spindle-interval of less than 5 seconds), and (d) the percentage of individual spindles (i.e., isolated spindles with an inter-spindle-interval greater than 5 seconds).
Results: Consistent with previous studies, the number of Stage 2 spindles was significantly greater in younger subjects (M=1337.07; SD=383.98) than older subjects (M=613.21; SD=414.88), $t(26)=4.79$, $p<.001$. The percentage of spindles within clusters was also significantly greater in younger subjects (49.73%) than in older subjects (18.28%), $t(26)=5.67$, $p<.001$. Younger and older subjects did not differ significantly in the percentage of spindles within doubles (20.72% and 22.70% respectively), $t(26)=1.33$, $p=.194$. The percentage of individual spindles was significantly greater in older subjects (59.02%) than in the younger subjects (29.14%), $t(26)= 5.55$, $p<.001$.
Conclusion: These results suggest that not only do younger and older adults differ in their overall number of Stage 2 sleep spindles, they also appear to differ in how their spindles are organized temporally within Stage 2 sleep.
Support (optional): Canadian Institutes of Health Research and the Alzheimer Society of Canada

0305

SLEEP DISTURBANCE PREDICTS FUNCTIONAL IMPAIRMENT AMONG OLDER PEOPLE IN ASSISTED LIVING FACILITIES

Alessi C, Martin J, Josephson K, Khan-Hudson A, Vandenberg T, Birath J, Martinez S
VA Greater Los Angeles Healthcare System and University of California, Los Angeles, Sepulveda, CA, USA

Introduction: Sleep disturbance predicts impaired functioning among nursing home (NH) residents. Older people increasingly reside in assisted living facilities (ALFs) when they cannot live independently but don´t yet need NH care. The purpose of this study was to determine whether sleep disturbance was common and associated with functional impairment among older people in ALFs.
Methods: Descriptive cohort study of ALF residents (aged > or = 65 years, able to self-consent) in Los Angeles. Measures included demographics, body mass index (BMI), Mini Mental State Exam (MMSE), 5-item Geriatric Depression Scale (GDS-5), self-reported general health and functional status (Instrumental Activities of Daily Living, IADL). Sleep assessments included Pittsburgh Sleep Quality Index (PSQI), 72-hour wrist actigraphy (day=0800-2000h, night=2000-0600h) and symptoms of restless legs syndrome (RLS) and sleep apnea (Berlin Questionnaire).
Results: 72 residents from 12 community ALFs participated (mean age 85.5 years, 74% female, 92% non-Hispanic white, mean BMI 25.6, mean MMSE 26.1, mean GDS-5 1.2). Mean PSQI was 8.3 (SD 4.3); 69% had PSQI > 5 (suggesting sleep disturbance). 11% endorsed RLS symptoms. 32% had high sleep apnea risk. By actigraphy, participants slept 1.3 (SD 1.0) daytime hours, and at night slept 68.2% (SD 19.3), with 2.5 hours (SD 1.5) awake and 10.5 (SD 4.2) awakenings per night. Higher (better) IADL scores were associated with higher MMSE (r=.35), better general health (r=-.23), female gender (r=.21), and actigraphically better nighttime sleep (fewer minutes awake, r=.25; higher percent sleep, r=.25; and fewer awakenings, r=-.34, all $p<.03$), but not PSQI. In regression analysis adjusting for MMSE, gender and general health; fewer nighttime awakenings significantly predicted

higher IADL scores (F = 8.02, p<.0001). Results were similar with other nighttime actigraphy variables.
Conclusion: Nighttime sleep disturbance is common among older ALF residents, and associated with worse functional status. Further research should address whether sleep disturbance predicts functional decline and NH placement, and whether interventions on sleep can delay these outcomes in ALF residents.
Support (optional): UCLA Academic Senate Council on Research; VA Greater Los Angeles Geriatric Research, Education and Clinical Center; VA Health Services Research and Development

0306

THE RELATIONSHIP OF SLEEP DISORDERED BREATHING AND COGNITION: THE MROS SLEEP STUDY

Stone K,[1] Blackwell T,[2] Yaffe K,[3] Ancoli-Israel S,[4] Ensrud K,[5] Stefanick M,[6] Redline S[7]
(1) California Pacific Medical Center (CPMC), San Francisco, CA, USA, (2) California Pacific Medical Center (CPMC), CA, USA, (3) University of California, San Francisco, CA, USA, (4) University of California, San Diego, CA, USA, (5) Veterans Affairs Medical Center and University of Minnesota, Minneapolis, MN, USA, (6) Stanford University, CA, USA, (7) Case Western Reserve University, OH, USA

Introduction: The association between sleep disordered breathing (SDB) and cognitive function among community dwelling older adults is uncertain.
Methods: To test the hypothesis that SDB is associated with poorer cognitive function in older men, we measured cognitive function and recorded in-home polysomnography (PSG) in a cohort of 2,909 men (mean age 76.3 years) in the MrOS Sleep Study. Global cognitive function was measured with the Modified Mini-Mental State Examination (3MS), executive function with Trails B, and sustained attention and psychomotor speed with a Digit Vigilance test (DVT). PSG measures included apnea-hypopnea index (AHI) and oxygen saturation levels (SaO2). Linear regression models were used to examine the association between SDB and cognition, adjusting for age and race, then further adjusting for education, depression, comorbidities, caffeine and alcohol use, functional status, and use of antidepressants and sleep medications.
Results: The average of the cognitive measures were: 3MS score 92.8 (100 possible points); Trails B 119.8 seconds; DVT 551.7 seconds. The mean AHI was 17.1, with about 7% who experienced any desaturation below 80% (SaO2 < 80%). After adjusting for age and race, each standard deviation increase in AHI was associated with a 1.9 second increase in time to complete the Trails B (p=0.02). SaO2<80% was associated with a 33.4 second increase in time to complete the DVT (p=0.003). After multivariate adjustment associations were somewhat attenuated with a reduction in statistical significance (AHI and Trails B association 1.2 seconds, p=0.09; SaO2<80 and DVT association 16.8 seconds, p=0.11). There were no significant associations found between SDB and 3MS scores.
Conclusion: SDB may be associated with impairments in cognitive function in older men, although the associations are weak and limited particularly to domains of vigilance and executive function. Global tests of cognition such as the 3MS may not be sensitive to the effects of SDB.
Support (optional): The National Heart, Lung, and Blood Institute (NHLBI) provides funding for the MrOS Sleep ancillary study "Outcomes of Sleep Disorders in Older Men" under the following grant numbers: R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, R01 HL070837, R01 HL070838, and R01 HL070839.

0307

CPAP IMPROVES SLEEP IN PATIENTS WITH ALZHEIMER´S DISEASE AND SLEEP DISORDERED BREATHING

Cooke J,[1] Liu L,[1] Fiorentino L,[1] Lawton S,[1] Corey-Bloom J,[1] Loredo J,[1] Palmer B,[1] Natarajan L,[2] Ancoli-Israel S[3]
(1) University of California, San Diego, San Diego, CA, USA, (2) University of California, San Diego, CA, USA, (3) Dept. of Psychiatry, University of California, San Diego, San Diego, CA, USA

Introduction: Patients with both Alzheimer´s disease (AD) and sleep disordered breathing (SDB) experience disrupted sleep, resulting in increased nocturnal awakenings and decreased percent REM sleep. This study examined the effect of CPAP on sleep in AD patients with SDB, hypothesizing that sleep would improve with treatment.
Methods: 48 subjects (mean age=77.8 years, SD=7.3; 12f) with AD (mean MMSE=25.3, SD=2.9) and SDB (mean AHI=28.5, SD=16.2) were randomized to 6 weeks of therapeutic CPAP or 3 weeks placebo CPAP followed by 3 weeks therapeutic CPAP. Sleep from screening, baseline, 3 and 6 weeks, recorded with the Embla (Flaga Medical Devices/Medcare, Reykjavik, Iceland), were analyzed. Records were scored for % of each stage of sleep, TST, WASO, and oximetry. A randomized design comparing one night of placebo to one night of therapeutic CPAP and a paired design analysis combining 3 weeks of therapeutic CPAP in both groups were performed.
Results: After one night, there were significant improvements in the CPAP group, but not in the placebo group, in %-time < SaO2 90% (p<0.001), % Stage 1 (p<0.03) and % Stage 2 sleep (p<0.01). Three weeks of therapeutic CPAP resulted in decreases in mean WASO (124.8 min, SD=78.9 vs. 92.1 min, SD=44.1; p=0.005), mean % Stage 1 sleep (23.5%, SD=14.3 vs. 16.3%, SD=9.9; p=0.001), % time < SaO2 90% (6.7%, SD=11.1 vs. 3.1%, SD=10.7; p=0.001), and increases in mean SaO2 (93.4%, SD=2.3 vs. 94.8%, SD=1.9; p<0.001), mean % Stage 2 (59.7%, SD=13.7 vs. 64.2%, SD=11.3; p=0.05) and mean % Stage 3 sleep (1.8%, SD=3.1 vs. 3.9%, SD=6.1; p=0.005).
Conclusion: In patients with AD and SDB, three weeks of therapeutic CPAP resulted in less time spent awake during the night and more time spent in deeper levels of sleep as well as in improved oxygenation. Placebo had no effect. Clinicians should consider treating SDB in this patient population.
Support (optional): NIA AG08415, GCRC M01 RR00827, P50 AG05131, and the Research Service of the Veterans Affairs San Diego Healthcare System

0308

PREDICTORS OF PLANNED AND UNPLANNED NAPPING IN OLDER ADULTS

Vitiello M,[1] Foley D[2]
(1) University of Washington, Seattle, WA, USA, (2) Substance Abuse and Mental Health Services Administration, Rockville, MD, USA

Introduction: Epidemiological studies report that napping increases with age, but few examine napping behaviors and its predictors. We assessed the predictors of scheduled versus unscheduled frequent napping amongst older adults using the NSF´s 2003 Sleep in America Poll.
Methods: Older adults (55-84 years) were polled from geographically-representative random samples of telephone listings for US households. Twenty-six percent of solicited individuals (n=1,506) participated in the 20-minute telephone interview. Thirty-six percent of these (n=515) reported napping 1-7 times/week with half (50.7%) reporting planned versus unplanned napping. Predictors of planned versus unplanned

frequent naps were assessed using Chi-square tests and multiple logistic regression.
Results: Unplanned nappers tended to be older, female and reported more nocturia, pain, health burden, poor memory, lack of interest (anhedonia), feeling depressed/hopeless, excessive daytime sleepiness (EDS) and sleeping <6 hours/night. Stepwise multiple regression analysis, forcing in age and gender, yielded the following independent predictors of unplanned napping: age 75-84 (OR=2.2, 1.4-3.7); EDS (OR=2.2, 1.3-3.8); anhedonia (OR=1.9, 1.1-3.2). Being married (OR=0.7, 0.4-0.98) and drinking >4 coffees/day (OR=0.5, 0.3-0.85) decreased the likelihood of unplanned napping.
Conclusion: About one-third of this sample reported napping at least weekly and about half of these planned their naps. Being older and unmarried, EDS, anhedonia and drinking <4 coffees/day were all predictors of unplanned napping. While anhedonia increased the odds for unplanned napping, feeling depressed/hopeless, a history of, or current treatment for diagnosed depression, were not associated with unplanned napping. In addition, no measures of nighttime sleep complaint nor of health burden predicted unplanned napping, suggesting, albeit counter-intuitively, that these factors have little influence on one´s plans for napping compared with one´s behavior, such as high coffee consumption and sleeping >6 hours per night. Napping behavior in older adults needs further study and clarification as a component of total sleep time in late life.
Support (optional): The National Sleep Foundation 2003 Sleep in America Poll. Washington, DC: National Sleep Foundation; 2003, and PHS Grant NIA025515 to MVV.

0309

MULTI-COSINOR ANALYSIS ON LOCOMOTOR ACTIVTIVITY RHYTHM OF ALZHEIMER´S DISEASE

Asayama K,[1] Volicer L,[2] Harper D[3]
(1) Mclean Hospital, Belont, MA, USA, (2) University of South Florida, Land O'Lakes, FL, USA, (3) Harvard University, Belmont, MA, USA

Introduction: The human daily activity rhythm has strong circadian (24hour) and hemicircadian (12hour) components. Cosinor analysis is a useful technique to estimate the phase of the components if the cycle length is known a priori. However, cosinor analysis has not been used for activity analysis due to the discreteness of the underlying data. We hypothesized that we can find parametric and sinusoidal components in activity data and extract oscillations representing important information from the internal time keeping system and its relationship to sleep disturbance.
Methods: We compared activity data of 21 men with Alzheimer´s disease in Geriatric Care Unit with and without observed sleep disturbance and 7 elderly, healthy male volunteers recruited from the community. We began with preliminary examination of the harmonic components of the activity data using spectral analysis. The data were then modeled by COSIFIT (Teicher M, 1990) program using multioscillator (two oscillators in our study) cosinor models. For this analysis, the frequency of the 2 harmonics of this model is set to 1 cycle/day and the second to 2 cycle/day. Nadir of each time series component was obtained to compare between AD and Control group.
Results: There were no significant differences in the spectral variances and the nadir time of the 24 hour frequency component in AD; mean Nadir (clock time), AD;3:36, Control; 1:53(F=2.694, p=0.113; Watson-Williams F-test). However phase difference between the 24 hour and 12 hour components in a subjects are significantly larger in AD group; mean Nadir time(min±SE); AD(227min±56.5), Control(32min±93.1), (F=7.968, p=0.0023; ANOVA). In addition, among AD subjects, larger Nadir time difference between subjects with and without objective sleep disturbance was found.
Conclusion: We conclude that the cyclic components of the activity rhythm in AD subject have reduced coherence. We assume that these differences represent the deterioration of neural network of human time keeping system due to AD.

0310

REDUCTIONS IN SLOW WAVE SLEEP ACROSS THE LIFE SPAN ARE RELATED TO AGE-RELATED ATROPHY IN THE CEREBRAL CORTEX

Nofzinger E,[1] Aizenstein H,[1] Miewald J,[1] Lu X,[2] Thompson W,[1] Reynolds C,[1] Bell B,[2] Price J,[2] Monk T[1]
(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) PA, USA

Introduction: Aging is associated with reductions in slow wave sleep (SWS), though the neurobiological causes of this are not known. Aging is also associated with reductions in brain volume, most notable in the lateral prefrontal cortex. The current study aimed to determine whether the age-related changes in SWS were related to age-related atrophy of the brain.
Methods: 15 healthy young (mean + s.d. age = 31.5 + 8.1 yrs) and 15 healthy late-life (mean + s.d. age = 78.6 + 4.6 yrs) adults received EEG sleep studies for 2 full nights. Power spectral analysis was used to quantify EEG spectral power in the 0.5 - 4.0 Hz frequency range. Subjects also received a magnetic resonance imaging (MR) scan of the brain using a GE Signa 1.5 Tesla scanner. To determine regional gray matter volumes, we used the Automated Labeling Pathway (ALP) which automatically labels specific anatomic regions of interest using public software packages (AFNI, BET, FLIRT, and ITK) as well as locally developed programs to implement atlas-based segmentation of MRIs. We focused on whole brain and lateral prefrontal cortex volumes, given age-related reductions in these areas.
Results: In relation to young adults, late-life adults showed reductions in SWS (t= -3.36, p = .002, df = 28), whole brain volume (t= -8.14, p < .001, df = 28), lateral prefrontal cortex volume (t= -9.08, p < .001, df = 28), and relative lateral prefrontal cortex volume after correcting for changes in whole brain volume (t= -4.55, p < .001, df = 28). Across the lifespan, SWS positively correlated with whole brain volume (r2 = .49, p=.006) and lateral prefrontal cortex volume (r2 = .46, p=.011).
Conclusion: Age-related reductions in slow wave sleep are related to age-related reductions in the volume of the cerebral cortex, likely due to a decreased number of synapses.
Support (optional): MH66227; MH061566; AG020677; MH52247; MH01414; MH24652; RR00056; PR054093

0311

OBJECTIVE MEASURES OF SLEEP DURATION AND OBESITY IN OLDER MEN AND WOMEN

Stone K,[1] Blackwell T,[2] Ancoli-Israel S,[3] Ensrud K,[4] Stefanick M,[5] Orwoll E,[6] Cauley J,[7] Lewis C,[8] Redline S[9]
(1) California Pacific Medical Center (CPMC), San Francisco, CA, USA, (2) California Pacific Medical Center (CPMC), CA, USA, (3) University of California, San Diego, CA, USA, (4) University of Minnesota, Minneapolis, MN, USA, (5) Stanford University, Stanford, CA, USA, (6) Oregon Health & Science University, Portland, OR, USA, (7) University of Pittsburgh, Pittsburgh, PA, USA, (8) University of Alabama at Birmingham, AL, USA, (9) Case Western Reserve University, Cleveland, OH, USA

Introduction: Experimental and epidemiologic studies have suggested a link between short sleep duration and obesity. We studied the relationship between actigraphic measures of sleep duration and obesity

in older adults.
Methods: We measured mean nightly total sleep time (TST) using wrist actigraphy (Ambulatory Monitoring, Inc.) worn for a minimum of 72 hours in 3,052 women (mean age 84) and 3,058 men (mean age 76) participating in the Study of Osteoporotic Fractures and the MrOS Sleep Study, respectively. In addition, in men overnight polysomnography was performed, yielding measures of sleep disordered breathing (apnea-hypopnea index[AHI]). Body mass index (BMI, kg/m2) was measured in both cohorts. Obesity was defined as BMI ≥ 30. We used logistic regression to test the association between sleep duration and obesity, adjusting for age, clinic, race, comorbidities, depression, physical activity, and use of sleep medications. All models were stratified by gender.
Results: Mean BMI was 27 in both men and women. 9% of women and 12% of men had TST < 5 hours, respectively. Compared to older men with TST ≥ 7 to < 8 hours, those with TST < 5 hours had a 3.7-fold increased odds of obesity (odds ratio[OR]=3.7; 95% CI 2.7 – 5.0) whereas those with TST ≥ 5 to < 7 hours had intermediate odds of obesity (OR=1.5; 1.2– 1.9). Results were consistent, but less striking in older women (OR=2.3; 1.6-3.1 and OR=1.3; 1.1-1.6 for TST < 5 and TST ≥ 5 to < 7 hours, respectively). Among men, the relationship of TST and obesity was independent of AHI.
Conclusion: Objectively determined estimates of short sleep were strongly related to obesity in older men and women. These associations were not explained by potential confounders, and at least in men, not explained by sleep disordered breathing. Longitudinal studies are needed to explore directionality of this association.
Support (optional): The National Heart, Lung, and Blood Institute (NHLBI) provides funding for the MrOS Sleep ancillary study "Outcomes of Sleep Disorders in Older Men" under the following grant numbers: R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, R01 HL070837, R01 HL070838, and R01 HL070839.
The National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS) and National Institute on Aging (NIA) provide funding for the "Study of Osteoporotic Fractures" under the following grant numbers: R01 AG05407, R01 AR35582, R01 AG05394, R01 AR35584, R01 AR35583.

0312

SLEEP AND FRONTAL LOBE FUNCTION IN MILD COGNITIVE IMPAIRMENT (MCI) PATIENTS

Lee J, Kim S, Hwang H, Jhoo J, Kim T
Kangwon National University College of Medicine, Chuncheon, Kangwon-do, South Korea

Introduction: In MCI patients, impaired executive function reflecting frontal lobe dysfunction was suggested as a risk factor for converting to dementia. Nocturnal intermittent hypoxia in SDB was known to result in decreased executive function. Particularly, frontal lobe dysfunction by SDB affected the occurrence of dementia in vulnerable elderly subjects. We aimed to illustrate the relationship of nocturnal sleep with frontal lobe function in the normal control (NC) and MCI groups, and examine the difference in nocturnal sleep according to ApoE genotype.
Methods: Among the elderly subjects above 60 yr. who visited to the Public Heath Center in Chuncheon City, 29 MCI patients (Age: 67.7±3.9) and age- and sex-matched 29 NC subjects (Age: 67.1±3.6) were selected. Frontal lobe function tests including Stroop Color Word Test (SCWT), Similarity Test, Digit Span Test (DST), and Benton Visual Retention Test (BVRT) were administered. Nocturnal polysomnography was done for each subject, and ApoE genotypes were obtained for 20 MCI patients.
Results: In NC subjects, sleep efficiency (SE) was correlated with DS score (r=0.53, p<0.05). And REM sleep amount (REMS) was correlated with Stroop Interference (SI) score and Similarity score (r=0.39, 0.41). In MCI patients, slow wave sleep (SWS) was negatively correlated with false score (r=-0.59) of BVRT, and REMS was correlated with Stroop Color-Word score (R=0.40), Time spent below 90% of oxygen saturation tends to be negatively correlated with DS score (r=-0.34, p=0.08). ApoE4 positive MCI group showed higher mean hypopnea index compared to ApoE4 negative MCI group.
Conclusion: In both NC and MCI groups, decreased REMS was associated with impaired executive function, and poor sleep quality was with impaired working memory. Greater severity of SDB in MCI patients was possibly associated with working memory decline. Genetic risk factor of AD increased the severity of SDB in MCI patients.
Support (optional): This research was supported by the grant (R04-2004-000-10131-0) from the Korea Science & Engineering Foundation (Seoul, Korea)

0313

MORE DAYTIME SLEEPING IS ASSOCIATED WITH HIGHER PROINFLAMMATORY CYTOKINE LEVELS IN OLDER POST-ACUTE REHABILITATION PATIENTS

Martin J,[1] Irwin M,[2] Martinez S,[3] Birath J,[3] Josephson K,[4] Alessi C[3]
(1) VA Greater Los Angeles Healthcare System and University of California, Los Angeles, North Hills, CA, USA, (2) University of California, Los Angeles, Los Angeles, CA, USA, (3) VA Greater Los Angeles Healthcare System and University of California, Los Angeles, Sepulveda, CA, USA, (4) VA Greater Los Angeles Healthcare System, Sepulveda, CA, USA

Introduction: Sleep disruption has been associated with elevations in proinflammatory cytokines and negative health outcomes among older people. We have found an association between more daytime sleeping and less functional recovery among older post-acute rehabilitation (PAR) patients. Here we examined sleep and levels of two markers of proinflammatory cytokine activity: interleukin-6 (IL-6) and soluble intercellular adhesion molecule-1 (sICAM-1]) among older (age>65) PAR patients.
Methods: 32 patients were enrolled on admission to PAR at one Veterans Administration Medical Center. Measures included the Mini-mental State Examination (MMSE), 5-item Geriatric Depression Scale (GDS-5), Pittsburgh Sleep Quality Index (PSQI) and 72 hours of wrist actigraphy (Octagonal actiwatch-L, Ambulatory Monitoring, Inc). Actigraphy measures included daytime (8:00-20:00h) hours and percent time asleep, nighttime (2200-0600h) hours and percent time asleep, and number and length of nighttime awakenings (Action4; TAT; default algorithms). Cytokines were measured by duplicate enzyme-linked immunosorbent assays (ELISA) from one morning (8:00-9:00h) blood sample.
Results: 32 patients (97% men, 41% non-Hispanic white; mean age 77.5 years, mean MMSE 25.0; mean GDS-5 1.3) participated. Mean PSQI total score was 8.9 (SD 3.4). 74% of participants had PSQI>5 (indicating sleep disturbance). Mean IL-6 was 9.6 (SD 3.3) and mean sICAM-1 was 294.7 (SD 110.2) pg/ml. By actigraphy, participants slept 2.0 (SD 1.4) hours (17%) during the day, and 3.6 (SD 1.7) hours (45%) at night. More hours and higher percent time asleep during the day were associated with higher IL-6 (r=.39, p=.08; r=.40, p=.07, respectively) and sICAM-1 (r=.50, p=.02; r=.50, p=.02, respectively) levels. PSQI and nighttime sleep were unrelated to cytokine levels (p's>.12).
Conclusion: Findings suggest less daytime sleeping is associated with higher circulating levels of proinflammatory cytokines among older PAR patients. Larger studies are needed to determine whether the

relationship between daytime sleep and cytokines partially mediates the negative impact of daytime sleeping on rehabilitation outcomes.
Support (optional): UCLA Claude Pepper OAIC (AG-10415, Career Development Award and Pilot Award, Martin), UCLA Cousins Center for Psychoneuroimmunology, VA Health Services Research & Development (IIR 04-321-3, Alessi) VA Greater Los Angeles Healthcare System GRECC and Research Service.

0314

BEHAVIORAL INDICATORS TEST-RESTLESS LEGS

Richards K,[1] Lambert C,[2] Beck C[3]
(1) Central Arkansas Veterans Healthcare System, North Little Rock, AR, USA, (2) University of Arkansas for Medical Sciences, North Little Rock, AR, USA, (3) University of Arkansas for Medical Sciences, Little Rock, AR, USA

Introduction: The purpose of this research was to develop an objective method to diagnose a prevalent sleep disorder, restless legs syndrome (RLS), in elders with dementia. RLS is characterized by uncomfortable leg sensations that disturb sleep and are associated with significantly decreased health and cognitive functioning. Cognitive and language deficits prevent elders with dementia from reporting sensory symptoms, and there are no objective methods to diagnose RLS. Elders with dementia are likely to have RLS because they often have RLS risk factors like iron deficiency and taking dopamine antagonists. Motor activity like leg movement and signs of leg discomfort like rubbing legs may indicate RLS. A National Institutes of Health (NIH) conference recommended testing the validity of these RLS objective indicators in elders with dementia.
Methods: Our research team used the NIH recommendations and prior instrument development experience to develop an observational RLS measure, the 10-item Behavioral Indicators Test-Restless Legs (BIT-RL). After a 3-member expert panel reviewed the instrument, trained raters observed 39 elders with dementia in their homes from 7 pm -12 am Night 1 and 10 pm-6 am Nights 2 & 3 with the BIT-RL. The raters made 19 hours of observation with 228 discrete data points for each elder. Interrater reliability was 92% at training and 100% at 6-month intervals during data collection.
Results: The 13 women and 26 men had a mean age of 79.9 years (s.d. 6.5); mean Mini- Mental State Examination score of 21.2 (s.d. 6.2); and mean behavioral indicators index (frequency of behaviors per hour) of 4.06 (s.d., 5.2, range 0-21.2). Sixteen (41%) exhibited 4 or more RLS indicators. The most frequent behaviors were periodic leg movements and flexing legs.
Conclusion: Behaviors consistent with RLS were common in elders with dementia. Future research should determine the sensitivity, specificity, and optimal cut-off value for the BIT-RL.
Support (optional): Richards *et al.* Sleep and Behavioral Disturbance in Dementia, Department of Veterans Affairs, NRI 01-077-1 & Richards. Advanced Career Development Award, Department of Veterans Affairs.

0315

REGULAR AEROBIC EXERCISE IMPROVES SLEEP AND QUALITY OF LIFE IN OLDER ADULTS WITH CHRONIC INSOMNIA

Naylor E,[1] Ortiz R,[2] Ortiz N,[2] Lu B,[2] Wolfe L,[1] Keng J,[2] Huber G,[2] Zee P[1]
(1) Northwestern University, Chicago, IL, USA, (2) Northwestern University, IL, USA

Introduction: Previous studies have shown that regular physical activity can improve sleep quality in older adults. Although regular exercise is recommended as part of sleep hygiene education, little is known regarding its effectiveness as treatment for chronic insomnia. The aim of this study is to determine the effects of an aerobic exercise intervention on sleep, performance and quality of life in older adults with chronic insomnia.
Methods: Sedentary older adults (age 55+) with chronic insomnia were randomized to either an aerobic exercise intervention (3-5x/wk, 30-40 min) and sleep hygiene education (exercise group) or a non-physical activity program of similar frequency and duration and sleep hygiene (standard care). Patients with other sleep disorders, unstable medical conditions and major psychiatric disorders were excluded. Baseline and post-tx evaluation included cardiopulmonary testing, sleep and quality of life questionnaires, one week of actigraphy and admission to the hospital for three nights of polysomnography. During the entire intervention all participants continuously wore an Actiwatch and maintained sleep/activity diaries.
Results: To date, 25 number of subjects have been enrolled, of which six exercise and four standard care subjects have completed all study phases. Preliminary results indicate that those in the exercise group showed significant improvement ($p<0.05$) from baseline measures as compared to the standard care group in the following measures: (exercise v standard care) subjective sleep quality (PSQI: 48% v -22%), latency to stage 2 sleep (-6.00 min v 9.75 min) and quality of life (SF-36 vitality: 7.2 v 0.3 pts). Additionally, exercise decreased ($p=0.06$) wake after sleep onset (-21 min v 42 min).
Conclusion: Our early results indicate that regular aerobic exercise combined with sleep hygiene education improves subjective sleep quality and quality of life to a greater extent than sleep hygiene alone when administered to older patients with chronic insomnia.
Support (optional): Research was supported by National Institutes of Health grant #: P01 AG 114 12, T32 AG020506-02 and, in part, by M01 RR-00048 from the National Center for Research Resources

0316

PROCEDURAL AND DECLARATIVE LEARNING TASKS INFLUENCE THE DENSITY OF SLEEP SPINDLES IN ELDERLY SUBJECTS

Glamann C,[1] Hornung O,[2] Hansen M,[2] Heuser I,[2] Danker-Hopfe H[2]
(1) Charite Berlin, Berlin, Germany, (2) Charite Berlin, AE (Europe)

Introduction: There is more and more evidence that sleep is related to the consolidation of memories. One of the most interesting findings is that sleep spindles might be linked to learning processes. It has been demonstrated that spindle activity increases following successful learning in young subjects and studies have given evidence for a correlation between overnight memory improvement and sleep spindle activity. Results indicate that spindle activity during non-REM sleep is related to declarative and procedural memory in young subjects.
Methods: The present study examines the question whether a declarative and a procedural learning task increase the amount and density of sleep spindles during non-REM sleep in elderly subjects. 20 healthy participants (eight males) aged between 60 and 85 years were examined. Subjects stayed three consecutive nights in the sleep laboratory. The first night served only as adaption night and was also used to control sleep disturbances. The second night was used as baseline night. On the third night, test night, the subjects performed two cognitive tasks, a word-pair association list (declarative learning) and a mirror tracing test (procedural learning). The next morning, a test of the two memory tasks was given again to measure performance. Spindle detection was based on an automatic algorithm.
Results: The density of fast sleep spindles was significantly higher ($p<0.05$) after the learning task as compared with the baseline night. Furthermore, the time used to perform the mirror tracing test improved

significantly (p<0.05) in the morning as well as the results of the word-pair association list.
Conclusion: These findings suggest that sleep spindles might be linked to declarative and procedural learning performance in elderly subjects.
Support (optional): This study was supported by the German Research Foundation (GK 429).
We would like to thank Peter Anderer, Georg Gruber and the Siesta group for the automatically detection of sleep spindles.

0317

PHYSICALLY ACTIVE ELDERLY WOMEN SLEEP MORE AND BETTER THAN SEDENTARY WOMEN

GuimarãEs L,[1] Carvalho L,[2] Prado G[2]
(1) Federal University of Sao Paulo, Lavras, Minas gerais, Brazil, (2) Federal University of sao Paulo, Sao Paulo, Brazil

Introduction: Population studies carried out in many countries have shown that sleep is a growing reason for complaints with increasing age. Experimental evidence indicates that a program of regular physical exercise can improve sleep quality in elderly individuals. The objective of the present study was to compare the sleep of physically active and sedentary elderly women.
Methods: We evaluated 101 elderly women, with 53 women practicing physical activity and 48 being sedentary. All women kept a sleep log and were asked to rate their sleep quality on a Visual Analog Scale (VAS) daily for 30 days. Total sleep time (TST), total nap time (TNT) during the 30 days of the study, number of naps, number of awakenings after sleep onset, and VAS scores were analyzed.
Results: Mean daily sleep time was 7 h 12 min for physically active elderly women and for sedentary women (p<0.01). Mean TNT over the 30 days as a whole was 4 h 22 min in the physically active group and 7 h 6 min in the sedentary group (p<0.05). The number of naps was 6 and 12 in the physically active and sedentary groups, respectively (p<0.05). The number of awakenings during the night was one in the physically active group and two in the sedentary group (p<0.05). The mean perception of sleep quality was 8.3 for physically active elderly women and 5.8 for sedentary women (p < 0.0001).
Conclusion: Physically active women sleep more and better than sedentary women.

0318

OXIDATIVE STRESS AND CARDIOVASCULAR RISK PARAMETERS IN POSTMENOPAUSE COMPARISON BETWEEN PATIENTS WITH ISOLATED INSOMNIA AND APNEA PLUS INSOMNIA

Hachul De Campos H,[1] Brandao L,[2] D'Almeida V,[3] Grego B,[2] Bittencourt L,[2] Baracat E,[2] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil, (3) Universidade Federal de São Paulo, São Paulo, Sao Paulo, Brazil

Introduction: Sleep complaints increase after menopause. It has been reported that 63% of postmenopausal women had insomnia. Sometimes they complain of insomnia and have another sleep disturbance such as apnea or periodic leg syndrome. Apnea increases after menopause and may contribute to oxidative stress. Postmenopausal women are also at risk for health problems related to estrogen deficiency, such as cardiovascular disease. Homocysteine (Hcy) has been shown to be an independent factor for cardiovascular disease. It is also reported to be related to estrogen status. Recent studies have documented that estrogens are potent antioxidants.
The aim of this work was to compare cardiovascular risk factors and oxidative stress parameters in 38 Brazilian postmenopausal women (age varying from 50 to 65 years old) with either isolated insomnia or sleep apnea plus insomnia.
Methods: For sleep analysis polysomnographys had been conducted. The sample was distributed in two groups: 18 women with insomnia and 20 with apnea (and insomnia). The oxidative stress parameters were analyzed by measuring blood concentrations of catalase, superoxide dismutase (SOD), thiobarbituric acid (TBARS) and glutathione using spectrophotometric methods. As cardiovascular risk factors we measured Hcy, folate and B6-vitamin concentrations by HPLC.
Results: The polysomnography reaveled that sleep efficiency in both groups were similar. IAH in the apnea plus insomnia group was 9.2 (5.7) whereas in the isolated insomnia group was 2.7(1.2). The concentrations of SOD, TBARS, Hcy, and folate were not statistically different between groups. A decrease in catalase 90.99(24.5) /mgHb vs 74.8 (25.4) U/mgHb ; p= 0.05) and glutatione 6.6 (1.0) µmol/gHb vs 5.7(1.0) µmol/gHb ; p= 0.01) were observed in the apnea plus insomnia group.
Conclusion: The results showed that there were alterations in some oxidative parameters in the apnea plus insomnia group which could indicate an oxidative stress status. The menopausal women with apnea plus insomnia presented alterations in oxidative stress rather than isolated insomniac patients. Probably hipoxia is the responsible for the increase in the oxidative stress and not the sleep fragmentation.
Support (optional): CNPq, Fapesp and AFIP.

0319

URINARY SYMPTOMS ARE RELATED WITH SLEEP COMPLAINTS AND DAYTIME SLEEPINESS IN HEALTHY OLDER PEOPLE

Scheuermaier K, Guzik A, Row J, MüNch M, Loughlin K, Duffy J
Brigham and Women's Hospital, Boston, MA, USA

Introduction: Urinary dysfunction and sleep disruption are frequent complaints in older people. However, few studies have examined the relationship between urinary symptoms, sleep disruption, and daytime sleepiness. This study was conducted to explore these relationships.
Methods: We recruited healthy older people who complained of disrupted sleep for a laboratory study. Screening included 3 questionnaires: the American Urological Association symptom index questionnaire (AUA); the Pittsburgh Sleep Quality Index (PSQI); and the Epworth Sleepiness Scale (ESS). Correlation analysis was used to examine the relationship between urinary symptoms and sleep disruption or daytime sleepiness.
Results: The group included 28 volunteers (16 F; 12 M; mean age 64, range 55-79). Average AUA score was 8.57±6.88; average PSQI score was 7.55±4.56; and average ESS score was 8.07± 4.99. AUA and PSQI scores were significantly correlated (r=0.46, p=0.0135), as were AUA and ESS scores (r=0.601, p=0.0007). There appeared to be a gender difference, whereby in the men AUA and ESS were strongly correlated (r=0.72, p=0.0071) and in women they were not. In contrast, in women the correlation between AUA and PSQI was significant (r=0.46, p=0.05) while in men it was not.
Conclusion: We found a significant positive correlation between urinary discomfort and complaints of sleep disruption and daytime sleepiness in healthy older people. Men reported more daytime sleepiness associated with urinary discomfort, while women reported more sleep disruption associated with urinary discomfort, a possible gender difference which needs further investigation. Recently, we reported that older people have a greater nocturnal urinary output compared to young adults. While the cause(s) of this altered circadian rhythm of urine output need further study, when combined with less consolidated sleep experienced

by most older people, it likely exacerbates sleep disruption, leading to daytime sleepiness.
Support (optional): R01 AG06072, BWH GCRC RR02635.

0320

STAYING UP LATE OR WAKING UP DURING THE NIGHT AFTER TAKING A HYPNOTIC IMPAIRS WALKING STABILITY IN HEALTHY COMMUNITY-DWELLING OLDER ADULTS

Frey D, Ortega J, Wiseman C, Farley C, Wright K
University of Colorado at Boulder, Boulder, CO, USA

Introduction: Approximately 33-52% of falls in older adults occur during the nighttime/early morning. It is unknown if sleep inertia alone or in combination with hypnotics increases the risk of falling. Therefore, we tested the hypothesis that sleep inertia with and without a hypnotic would impair walking stability.
Methods: Twenty-three healthy, community-dwelling adults, twelve older (8 females, 4 males), aged 67.42±4.23 (mean±SD) and eleven younger (5 females, 6 males), aged 21.82±2.36 participated in a randomized, double-blind, placebo-controlled, counterbalanced protocol. Participants completed three laboratory conditions: (a) sleep inertia-placebo, (b) sleep inertia-hypnotic (5mg Zolpidem), and (c) wakefulness-placebo. Hypnotic/placebo was administered 10 min prior to lights out/wakefulness (scheduled at habitual bedtime). Walking stability was assessed ~120 min after drug administration with two tasks using force platforms (AMTI Inc., Newton, MA): (a) walking across level force platforms (2.44mx0.61m, lengthxwidth), (b) walking across a beam on the force platforms (2.44mx0.10mx0.04m, lengthxwidthxheight). Condition differences in the number of participants who stepped off the beam was analyzed with Fisher´s Exact Test, and biomechanical assessments of average lateral force and forward velocity were analyzed with repeated measures ANOVA.
Results: No subject stepped off the beam during baseline practice sessions. The number of older participants who stepped off the beam was significantly greater in the sleep inertia-hypnotic condition (58%) versus sleep inertia-placebo and wakefulness-placebo conditions (0% and 33% respectively)($p<0.05$). Significant condition differences were not observed in younger participants. Significantly increased lateral force and decreased forward velocity during level and beam walking were observed in older adults during the sleep inertia-hypnotic condition ($p<0.05$).
Conclusion: Sleep inertia combined with a hypnotic or staying awake ~2h later than usual significantly impaired walking stability in older adults suggesting that the risk of falling may be increased when older adults staying up late or taking hypnotics get out of bed during the night (e.g., to use the restroom).
Support (optional): Research supported by NIH AG024621, NIH M01RR00051, Beverly Sears Graduate Student Grant and a grant from the Undergraduate Research Opportunities Program in collaboration with the Biological Sciences Initiative at the University of Colorado at Boulder.

0321

FALLS IN THE ELDERLY: THE ROLE OF SLEEP PROBLEMS AND PSYCHO-ACTIVE MEDICATIONS

Reid K,[1] Martinovich Z,[2] Finkel S,[3] Zee P[1]
(1) Northwestern University, Chicago, IL, USA, (2) Northwestern University, IL, USA, (3) Chicago, IL, USA

Introduction: Sleep problems and falls are common in the elderly. Hypnotics, particularly benzodiazepines and other medications have been implicated as a risk factor for falls in this group. Recent reports indicate that sleep problems rather than hypnotic use are associated with a risk of falls. This study examines the relationship between falls, sleep and psycho-active medications including comparisons of benzodiazepine and non-benzodiazepine hypnotics.
Methods: 1863 participants (mean age 75.8 ± 6.8 years) from primary care sites serving predominantly elderly patients were interviewed. Subjects completed a brief questionnaire about sleep and falls in the past six months. A systematic medical chart review to determine the use of 34 psycho-active medications including benzodiazepine (temazepam, flurazepam, triazolam) and non-benzodiazepine (zolpidem, zaleplon) hypnotics was conducted.
Results: Sleep problems were reported by 66% of subjects and falls by 19%. Sleep problems were significantly associated with falls compared to patients without sleep problems. There was an increased odds of a fall (OR 1.60) in patients reporting a sleep problem but not using psycho-active medications. A significant but weaker odds of a fall (OR 1.49) was found when both psycho-active medications and sleep problems were present. Taking non-benzodiazepine hypnotics or trazadone was not associated with an increased risk of falls, but taking benzodiazepine hypnotics was ($p=0.01$). However, there was no significant difference in the report of falls between patients taking benzodiazepines and those taking non-benzodiazepine hypnotics.
Conclusion: While both sleep problems and psycho-active medication use increased the odds of a fall, having a sleep problem alone presented a higher risk of falls. This finding suggests that untreated sleep complaints may pose a risk for falls. Interestingly, our data suggest that there is no significant difference in the report of falls between those taking a benzodiazepine compared to non-benzodiazepine hypnotic. Further studies with larger numbers are needed to confirm these finding.
Support (optional): Council for Jewish Elderly, 1P01 AG 11412

0322

DECREASED HEART RATE VARIABILITY FROM POLYSOMNOGRAPHY PREDICTS MORTALITY IN THE ELDERLY

Stein P,[1] Domitrovich P,[2] Lundequam E,[2] Redline S[3]
(1) Washington University in St. Louis, Saint Louis, MO, USA, (2) Washington University School of Medicine, St. Louis, MO, USA, (3) Case Western Reserve University, Cleveland, OH, USA

Introduction: Decreased heart rate variability (HRV) has been shown to be associated with increased risk of mortality. HRV is usually measured over 24 hours or sometimes from much shorter daytime recordings. Whether HRV measured during polysomnograpy (PSG) predicts mortality is unknown.
Methods: Heart rate data were extracted from a bipolar ECG recording from overnight PSGs performed in 272 participants 118 M, 154 F, age 76±4 in the first examination of the Sleep Heart Health Study (SHHS). This subsample of SHHS participants also had Holter recordings in the Cardiovascular Health Study, although Holter data were not considered here. After 5 years, 44 had died. PSG ECGs signals were analyzed to research standards on a commercial Holter scanner (MARS 8000, GE

Medical Systems, Milwaukee, WI). HRV was calculated for the entire PSG, using standard techniques, and adjusted for age and gender in the Cox regression model.
Results: There were significant associations between increased mortality and decreased HRV on the PSG. Representative values for HRV for survivors and non-survivors and the odds ratio and 95% CI for survival include: SDNNDIX 43±1 ms for survivors vs. 37±2 for non-survivors (RR= 0.96 [0.93-0.99], p<0.001); rMSSD 27±1 ms for survivors vs.22±1 ms for non-survivors (RR=0.96 [0.93-0.99], p=0.02); pNN625 4.0±0.3% for survivors vs. 2.7±0.6% for non-survivors (RR=0.92 [0.84-1.00], p=0.05); ln total power for 5 min 7.2±0.1 for survivors vs. 6.9±0.1 for non-survivors (RR=0.51 [0.33-0.80], p<0.001), ln very low frequency power 7.0±0.1 for non-survivors vs.6.7±0.1 for survivors (RR=0.54 [0.35-0.85], p= 0.01); ln low frequency power 5.8±0.1 for survivors vs. 5.4±0.1 for non-survivors (RR=0.59 [0.41-0.85], p<0.001), ln high frequency power 4.9±0.1 for survivors vs. 4.5±0.1 for non-survivors (RR=0.65 [0.46-0.92] p=0.01).
Conclusion: Decreased HRV, consistent with decreased parasympathetic control of heart rate, was associated with 5-year mortality in the elderly. HRV extracted from PSGs may potentially be useful for risk stratification.

0323

THE RELATIONSHIP OF ACTIGRAPHIC SLEEP CHARACTERISTICS AND MEASURES OF COGNITION: THE MROS SLEEP STUDY

Blackwell T,[1] Yaffe K,[2] Redline S,[3] Ancoli-Israel S,[4] Ensrud K,[5] Stefanick M,[6] Stone K[1]
(1) California Pacific Medical Center (CPMC), San Francisco, CA, USA, (2) University of California, San Francisco, CA, USA, (3) Case Western Reserve University, OH, USA, (4) University of California, San Diego, San Diego, CA, USA, (5) University of Minnesota, Minneapolis, MN, USA, (6) Stanford University, CA, USA

Introduction: The association between objectively measured sleep and cognition among older adults remains understudied. We hypothesized that poorer sleep quality would be associated with lower cognitive function in older community-dwelling men.
Methods: We measured cognitive function and recorded objective sleep measures with wrist actigraphy in a cohort of 3,053 men (mean age 76.3 years) in the MrOS Sleep Study. 53 men taking Alzheimer´s disease medication were excluded. Global cognitive function was measured with the Modified Mini-Mental State Examination (3MS), executive function with Trails B, and sustained attention and psychomotor speed with the Digit Vigilance test (DVT). Sleep parameters included total sleep time (TST), sleep efficiency (SE), sleep latency, wake after sleep onset (WASO), and number of long wake episodes (>5 minutes). We used linear regression models to examine the association between sleep and cognition, adjusting for age, race, education, depression, stroke, diabetes, caffeine and alcohol use, functional status, and use of antidepressants, benzodiazepines, and sleep medications.
Results: Average cognitive measures were: 3MS score 92.8; Trails B 120.5 seconds; DVT 553.2 seconds. Trails B scores were worse among those with poorer sleep quality on WASO (2.3 seconds per 30 minute increase), long wake episodes (0.55 seconds per episode), and SE (1.35 per 10% decrease). 3MS scores were worse among those with more WASO (0.2 points per 30 minute increase) and more long wake episodes (0.1 point per episode). DVT scores were lower for those with more WASO (3.6 seconds per 30 minute increase) (p<0.05 for all). TST and sleep latency were not significantly related to cognition.
Conclusion: More sleep measures were related to Trails B, a measure of executive function, than to global cognitive function or vigilance. Sleep fragmentation (WASO) was consistently related to poorer cognition, while total sleep time and sleep latency were not. These results may suggest disturbance of sleep quality rather than quantity affects cognition.
Support (optional): The National Heart, Lung, and Blood Institute (NHLBI) provides funding for the MrOS Sleep ancillary study "Outcomes of Sleep Disorders in Older Men" under the following grant numbers: R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, R01 HL070837, R01 HL070838, and R01 HL070839.

0324

EVENING AMBIENT LIGHT, NOCTURNAL SLEEP, AND PSYCHOLOGICAL ADJUSTMENT IN COMMUNITY DWELLING OLDER ADULTS

Stripling A,[1] Gamble J,[2] McCrae C,[1] Rowe M[1]
(1) University of Florida, Gainesville, FL, USA, (2) University of Florida, FL

Withdrawn

0325

SLEEP-DISORDERED BREATHING AND NOCTURNAL BLADDER SYMPTOMS IN OLDER AMERICANS

Williams L,[1] Pryor E,[2] Umlauf M[2]
(1) University of Alabama at Birmingham Doctoral Student, Russellville, AL, USA, (2) University of Alabama at Birmingham, Birmingham, AL, USA

Introduction: The relationship between sleep-disordered breathing(SDB) and nocturia among elders is poorly understood.
Methods: SDB and bladder symptoms(BSx) were examined in a random telephone survey of 585 (35%men, n=202) community dwelling elders(age>60 years) in the Southeast US. SDB symptoms included subjective report of loud snoring, snorting/gasping, or stopped breathing/struggles for breath during sleep. BSx included subjective report of frequency of nocturia, bladder emptying problems, urinary frequency(less than q 2hrs), difficulty postponing urination and weak urinary stream. Difficulty returning to sleep after nocturia events and use of diuretics were also surveyed. The SDB and BSx variables were independently combined into index scores(SDBI and BSxI, respectively). A SDBI of >21 was deemed highly suggestive of SDB and a BSxI score of >20 represents significant bladder dysfunction. The significance level for statistical analyses was set at p<.05.
Results: Analysis of variance of subjects by gender and older/younger age using median age(72 years)showed no differences in BSxI or nocturia frequency between the 4 groups. However, older men and older women had more hours of sleep per night(Mean=7.4 and 7.1, respectively, F=4.9, p<.002)and more SDB symptoms(F=4.05, p<.007) than younger men/women. Overall, 18.8% of the sample reported no nocturia, 31.5% 1-2 per night and 49.7% reported 3 or more episodes of nocturia nightly. Most diuretic users (53% n=161, males-55%, females-53%)experienced three or more nocturia episodes per night and a greater proportion of diuretic users were women(32%). Over one-third of subjects experienced difficulty in returning to sleep after nocturia episodes(35%, n=106, male-14%, females-21%).
Conclusion: Nocturia is a major contributor to sleep disruption in elders but is no more severe in the oldest old or among men or women. Further, diuretics do not seem to offer any advantage in reducing nocturia in men or women over age 60 years.

0326

DAILY VARIABILITY IN OBJECTIVE AND SUBJECTIVE SLEEP AND COGNITION IN OLDER ADULTS WITH INSOMNIA

Dzierzewski J,[1] McCrae C,[1] Marsiske M,[1] McCoy K,[2] McNamara J,[1] Dautovich N,[1] Ross A,[1] Stripling A[3]
(1) University of Florida, Gainesville, FL, USA, (2) Vateran's Administration, San Antonio, TX, USA, (3) University of Florida, FL, USA

Introduction: Older adults suffer from insomnia at a higher rate than younger adults and also experience a general cognitive decline. Additionally, older insomniacs frequently complain of impaired daytime functioning as a result of their insomnia. We examined the relationship between sleep and cognitive performance in older adults with insomnia at both the between-person and within-person (day-to-day variability) levels.
Methods: Baseline sleep and cognitive data were obtained from 48 community-dwelling older adults with insomnia (M=69.91, SD=7.24) participating in cognitive-behavioral treatment study in North-Central Florida. Sleep was assessed via 14 consecutive days of sleep diaries and actigraphy. Sleep variables analyzed include: sleep onset latency (SOL), wake after sleep onset (WASO), and morning snooze time (Snooze). Reasoning was measured with daily Letters Series and processing speed with daily Symbol Digit for the 14 days.
Results: Descriptive analysis revealed that participants displayed a considerable amount of within-person variability. Letter series and subjective WASO exhibited nearly 50% of the amount of between-person variability as within-persons while all other variables displayed either equivalent or much larger amounts of variability within-persons as between-persons. Multilevel modeling revealed significant associations between average snooze time, β=.21, t(35.31)=3.6, p<.001, and daily sleep onset latency, β=-.002, t(460.05)=-2.17, p<.05, with symbol digit. A significant association between daily snooze time and letter series was also found, β=-.007, t(461.81)=-2.11, p<.05.
Conclusion: Sleep and cognition are related in older insomniacs. At the between-persons level, better average sleep was associated with better cognitive performance. Interestingly, at the within-person level, on days when an individual experienced above-average sleep they also experienced above-average cognitive performance. Results support the idea that the greater examination of within-person variability in sleep and its correlates is warranted and yields fruitful information. An important question that remains to be addressed is whether cognitive-behavioral treatment for insomnia will result in more consistent sleep and cognition.
Support (optional): Research supported by NIH/NIA AG024459-01(McCrae, PI).

0327

THE EFFECTS OF PHYSICAL ACTIVITY AND LIGHT EXPOSURE ON SLEEP QUALITY IN AFRICAN-AMERICAN ELDERS

Williams J,[1] Umlauf M,[1] Buckner E[2]
(1) University of Alabama at Birmingham, Birmingham, AL, USA, (2) University of Alabama at Birmingham, AL, USA

Introduction: As people age, sleep quality may also deteriorate as a function of light exposure and work/health status. This pilot study was developed as an undergraduate honors project to examined physical activity, light exposure and sleep quality in a small sample of community-dwelling African-American elders (age>65 years).
Methods: Three cognitively intact subjects were recruited: one employed, one retired and one was home-bound (wheelchair dependent). Actigraphy was used over 7 consecutive 24-hour days to quantitate sleep and wake patterns. The Epworth Sleepiness Scale, the Pittsburgh Sleep Quality Index and an investigator-devised Daylight Exposure Tool were used to assess daytime sleepiness, sleep quality and daylight exposure.
Results: There were distinct differences among the three participants that apparently reflected work/health status. The working elder had the most consistent pattern sleep and a sleep efficiency of 88% by actigraphy, the highest self-report of light exposure, the highest quality of sleep, and a low sleepiness score. The retired and home-bound individuals had more irregular sleep and less bright light exposure. This retired individual showed the lowest activity counts, poor sleep efficiency (64%) and the highest daytime sleepiness score of the three subjects. As might be expected, the Epworth score and minutes of sleep were inversely associated (r= - .997, p<.05) in the sample. Also, sleep quality decreased as sleepiness increased and as sleep quantity decreased.
Conclusion: These preliminary findings suggest that poor sleep quality and excessive daytime sleepiness may be important health issues among retired African-American elders. Recreational and volunteer activities that increase exposure to bright sunlight and regularize activity patterns can be potent interventions to maintain health and improve sleep quality among elders. Further research is needed to examine activity and sleep patterns of retired minority elders and to determine barriers to bright light exposure that can reinforce consolidated circadian patterns of activity and sleep.

0328

SLEEP HABITS AND SLEEP THOUGHTS IN AGED INDIVIDUALS SHOWING PSYCHOLOGICAL DISTRESS

Lorrain D,[1] BéLisle D,[2] PréVille M[3]
(1) Universite de Sherbrooke, Sherbrooke, Quebec, Canada, (2) University of Sherbrooke, Sherbrooke, Quebec, Canada, (3) University of Sherbrooke, Canada

Introduction: Sleep disorders, anxiety or depression co-occur frequently in the elderly population (Morgan, 2000; Giron, 2002;). While the physical and affective symptoms tends to be thoroughly looked at by the physician or therapist, other aspects of the problems, such as the attitudes, beliefs and habits, surrounding the sleep problems of the elders are often neglected.
Methods: Participants were 1245 adults (M age=73.9, SD=6.0 years) selected from a probabilistic sample composed of individuals living at home in the province of Québec, Canada. The inclusion criteria´s were: being older than 65 years old and having no diagnostic of cognitive disorders. The DIS was used to evaluate the presence of depression or anxiety symptoms in the last 12 months, whereas the PSQI was used to measure sleep quality (Buysse, 1989). Sleep habits, thoughts and beliefs, were investigated with chosen items from different questionnaires (Morin, 2004).
Results: A subgroup of particular interest was identified from the 20.4 % of the participants that had at least 1 diagnostic of mental health problem and the 18.3% had a PSQI score greater than 5: 147 subjects, 11.8% of the total sample, presented those two conditions. Concerning sleep habits, this subgroup of subjects reported practicing relaxation, watching TV or reading in bed, doing lots of thinking during the night and awaking in a bad mood more often than the subjects without a diagnostic (p<.01). They also believed that they should stay in bed, trying harder to fall asleep, and that it is normal that their sleep is worst because of the aging process itself (p<.01).
Conclusion: Psychological distress is related to several bad habits and

dysfunctional beliefs that could contribute to exacerbate and perpetuate the sleep problems. Together with pharmacological and/or psychological treatments, these aspects should be looked at more closely while treating anxiety or depression symptoms in aged individuals.
Support (optional): This research was funded by the Canadian Institute of Health Research.

0329

ANEMIA OF AGING & OBSTRUCTIVE SLEEP APNEA

Khan A,[1] Ashizawa S,[2] Hlebowicz V,[3] Appel D[2]
(1) Albert Einstein College of Medicine, bronx, NY, USA, (2) Albert Einstein College of Medicine, NY, USA, (3) NY, USA

Introduction: WHO defined anemia of aging (AOA) (Hemoglobin (Hgb)<13 & 12 g/dl in men & women respectively) is likely a chronic inflammatory process involving interleukins (IL) 6 & 12, C-reactive protein & hepcidin. Among elderly with obstructive sleep apnea (OSA) hypoxic stimulation of erythropoesis may obscure AOA. Treatment of OSA may paradoxically restore AOA. We sought to identify OSA & AOA coexistence & OSA-treatment AOA interaction.
Methods: Retrospective records of 101 successive patients > 65 years old & with OSA were analysed. Differences among pre /post- treatment of OSA hemograms were assessed using paired two-tailed Student's t-test. For correlative significance, hemogram changes were compared to apnea-hypopnea index (AHI), respiratory related arousals (RERA) & duration patients slept with oxy-hemoglobin saturation < 89% (HT).
Results: 82/101 patients (27 men, 55 women, average age 71 years) had all the data variables cited above. Mean pre-treatment & mean 1-year post-treatment of OSA Hgb/hematocrit (Hct) for men & women respectively were 13g/dl/40.7% -- > 12.7g/dl/39.1% & 12.1g/dl/38.1% -- > 11.9g/dl/37.6%. Hct changed significantly ($p<0.05$). Respectively among 54% & 33% of the 82 patient study cohort, 1- year post-treatment of OSA Hct either declined (mean 3.7%) & increased (mean 4.8%); both changes were significant ($p<0.01$). These changes did not correlate significantly with AHI, RERA, or HT.
Conclusion: We did not see AOA before OSA treatment and we did see AOA 1-year after OSA treatment. More accurately post-treatment of OSA - Hct distributed bimodally among groups with significant increases & declines of Hct. While these Hct changes did not correlate significantly with selected sleep-breathing variables, we remain intrigued by a possible AOA-OSA interaction. AOA & OSA share common inflammatory processes. We believe OSA inflammatory processes interact with OSA hypoxia induced erythropoesis. The balance of these sets of processes determines the effect of OSA & OSA treatment on AOA.
Support (optional): NA

0330

DIFFERENCES BETWEEN MEN AND WOMEN ON TOPOGRAPHICAL SLEEP EEG DURING THE MIDDLE YEARS OF LIFE

Frenette S,[1] Paquet J,[2] Carrier J[3]
(1) Hopital du Sacre-Coeur de Montreal, Montreal, Quebec, Canada, (2) Hôpital du Sacré-Coeur de Montréal, Quebec, Canada, (3) Universite de Montreal, Quebec, Canada

Introduction: We reported that women between 20 and 60 years old show higher N-REM sleep spectral power for C3 in delta, theta, low alpha, and high sigma frequencies than men. Studies have shown that age-related effects on sleep EEG vary across topographical derivations. We aimed to evaluate how gender effects interact with aging and EEG sleep topography in the middle years of life.
Methods: The sleep of eighty-seven healthy volunteers with no sleep disorders was analyzed. Subjects were separated in two groups: A) Young (22F, 26H; 23,3y ±2,4) and B) Middle-aged (21F, 18H; 51,9y ±4,6). Spectral analyses were performed on N-REM sleep for Fp1, F3, C3, P3, and O1 (linked-ears). Three-way ANOVAs (Age, Gender, Derivations) were performed on 1-Hz bins (1-25 Hz).
Results: Polysomnographic sleep was similar in men and women. Compared to young subjects, middle-aged subjects showed lower sleep efficiency, sleep duration, SWS%, and higher Stage 2%. Women showed higher power than men between 2-4 Hz, 13-14 Hz and 23-25 Hz. Significant interactions between gender and derivations were found between 4-6Hz, 7-11Hz, and 14-19Hz. Women showed higher power than men; this effect was more prominent in C3, P3 and O1 than in Fp1 and F3. Middle-aged subjects showed lower power between 23-25Hz. Significant interactions were found between age and derivations between 2-6 Hz and 7-21 Hz, with middle-aged subjects showing lower power. Between 2-6 Hz, this effect was more prominent in Fp1 and F3, while it was more prominent in FP1, F3 and O1 between 7-21 Hz.
Conclusion: In the middle years of life, gender and age effects on N-REM sleep EEG show different topographical distributions. Gender effects are more prominent in posterior derivations, while age effects are more prominent in anterior and occipital areas. We found no interactions between age and gender, suggesting that aging does not influence men and women differently.
Support (optional): The Fonds de recherche en Santé du Quebec, Natural Sciences and Engineering Research Council of Canada

0331

POLYSOMNOGRAPHIC DESCRIPTION OF FIRST NIGHT EFFECTS IN OLDER ADULTS, AGE 70 AND OLDER

Carlson B, Carlson J, Neelon V, Saksatit B, Hartman M, Dogra S
University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Introduction: Common sleep laboratory practice is to keep bed and wake times (time in bed=TIB) constant across subjects—a practice which reduces subjects´ TIB by 1 or more hours than usual. Anecdotal reports suggest that this reduced bedtime may lead to improved sleep quality on the next night. In young adults, this response to the laboratory environment is called the "first night effect." This study describes the first night effect in older adults, age 70 and older.
Methods: One hundred and fifteen adults (mean age=78.3yrs, F=64%, minorities=13%) underwent two nights of standard polysomnography (mean TIB=7.2 hours). Based on their self-report of usual sleep, 101 subjects were classified as long (TIB ≥ 7 hours) sleepers and 14 were classified as short (TIB < 7 hours) sleepers. Repeated measures analysis of variance was used to test trends and group differences in total sleep time (TST), sleep latency, SWS latency and REM latency, and the time spent in Stage1&2 NREM (S1&2), Stage 3&4 NREM (S3&4), and REM sleep.
Results: Sleep latencies were lower in short sleepers ($F_{(1, 113)}=3.8$, $p=.05$) but did not differ across nights. The remaining sleep parameters did not differ between long and short sleepers but both groups showed similar trends in sleep parameters. For all subjects, TST ($F_{(1, 113)}F_{(1, 113)}=13.4$, $p<.001$), and the amount of time spent in S1&2 ($F_{(1, 113)}=3.9$, $p=.05$) and REM sleep ($F_{(1, 113)}=13.8$, $p<.001$) increased, but the time spent in S3&4 did not change ($F_{(1, 113)}=.52$, NS) between nights. REM sleep latency decreased ($F_{(1, 113)}=10.05$, $p=.002$) but there was no significant change in SWS latency across nights ($F_{(1, 113)}=.20$, NS)
Conclusion: Regardless of their usual TIB, older adults exhibited similar responses to the sleep laboratory environment. The changes in sleep across nights are consistent with the first night effect found in

younger samples.
Support (optional): The study was supported by grants from the National Institute for Nursing Research (NR08032) and the General Clinical Research Center, UNC Hospitals (RR00046).

0332

HEALTHY OLDER ADULTS HAVE FEWER ATTENTIONAL FAILURES THAN YOUNG ADULTS DURING EXTENDED WAKEFULNESS

Willson H,[1] Ellis J,[2] Guzik A,[3] Czeisler C,[4] Duffy J[4]
(1) Brigham and Women's Hospital / University of Surrey, Boston, MA, USA, (2) University of Surrey, Guildford, England, United Kingdom, (3) Brigham and Women's Hospital, Boston, MA, USA, (4) Brigham and Women's Hospital / Harvard Medical School, Boston, MA, USA

Introduction: It is widely believed that older people are sleepier during the day than young adults due to their reduced ability to sleep at night. However, data from some studies suggest that this may not be the case for healthy older people. The present study aimed to examine whether there is an age-related difference in objective sleepiness across 26 hours of wakefulness.
Methods: Ten healthy older [68.2±3.8 years; 2 women] and eighteen younger [21.3±3.2 years; 6 women] adults were studied. After 3 baseline nights (8h in bed at their habitual times) in the laboratory, at their usual wake time, they began a constant routine (CR) that lasted for at least 27h. The CR consisted of wakeful bed rest (monitored by a technician in the room) in low light, with EEG and EOG recorded continuously. After the study, each 30-s epoch was scored for slow eye movements (SEMs) and sleep intrusions.
Results: None of the older subjects fell asleep during the CR, although 10 young subjects (56%) did [7 had <5 min Stage 1; 2 had up to 26 min of Stage 1+Stage 2]. After controlling for those sleep intrusions, the older subjects had fewer overall SEMs than the younger subjects [109.9±42.5 vs. 359.3±244.3; p=0.001] and fewer SEMs each hour [$F(1,24)=12.135$, p=0.002]; there was also a significant interaction between age and time awake [$F(25,576)=1.993$, p=0.004].
Conclusion: Under conditions of acute sleep deprivation, healthy older adults appear to be less drowsy than younger adults, both during the usual waking day and throughout the night. Further research is needed to determine whether these results are due to: 1) an age-related reduction in sleep need; 2) a compensatory process related to a history of insufficient sleep; or 3) an age-related change in the ability to sleep that does not reflect a reduction in sleep need.
Support (optional): NIH Grants AG06072; MH45130; AG09975; RR02635.

0333

AGE-RELATED EFFECTS OF 200 MG OF CAFFEINE ON DAYTIME RECOVERY SLEEP

Fernandez-Bolanos M, Girouard L, Roy J, Paquet J, Filipini D, Carrier J
Centre du sommeil et des rythmes biologique, Universite de Montreal, Montreal, Quebec, Canada

Introduction: We reported that caffeine produces almost similar effects on nocturnal sleep in young and middle-aged subjects. Recently, we have shown that the effects of caffeine on sleep are more prominent when caffeine is taken during the night before daytime recovery sleep than in the evening before nocturnal sleep. We aimed to evaluate the effects of caffeine on daytime recovery sleep after a 25-hour sleep deprivation in young (Y) and middle-aged (MA) subjects.
Methods: Twenty-four subjects participated in both caffeine (200 mg) and placebo (lactose) conditions in a double-blind crossover design (12 Y, 20-40 y.; 12 MA, 40-60 y.; one month between conditions). For each condition, subjects came for a baseline night after which they were sleep-deprived for one night. Recovery sleep started the next morning after 25 hours of wakefulness. Subjects received a 100 mg capsule of caffeine (or placebo) 3 hours before daytime recovery sleep (around 5AM), and the remaining dose 1 hour before (around 7AM). Three-way ANOVAs (Age, Night, and Condition) were performed.
Results: Sleep latency was shorter during daytime recovery sleep than during baseline sleep, but this effect was reduced in the caffeine condition. SWS was higher in young compared to middle-aged subjects, and its total amount increased in daytime recovery sleep compared to baseline. Caffeine reduced SWS rebound during daytime recovery sleep. Sleep efficiency, sleep duration, stage 2 and REM sleep were lower in daytime recovery sleep compared to baseline, and these effects were enhanced by caffeine. Importantly, the reduction of sleep duration and sleep efficiency by caffeine was more prominent in the MA than in the Y.
Conclusion: These results support the notion that caffeine highly disrupts daytime sleep recovery, especially in the MA. With increasing numbers of the MA population now facing challenges such as shift work and jet lag, these questions are more than simply of academic interest.
Support (optional): Fonds de recherche en santé du Canada, Natural Sciences and Engineering Research Council of Canada, Canadian Institutes of Health Research

0334

SUBJECTIVE SLEEP, ADVERSE EVENTS AND ACTIGRAPHY IN NONDEMENTED OLDER ADULTS TAKING DONEPEZIL

Friedman L,[1] Haagenson L,[1] Hernandez B,[1] Noda A,[1] Mumenthaler M,[2] Yesavage J[3]
(1) Stanford University, Palo Alto, CA, USA, (2) Cephalon Inc., Redwood City, CA, USA, (3) Veteran Affairs Palo Alto Health Care System, Palo Alto, CA, USA

Introduction: Donepezil is an acetylcholinesterase inhibitor commonly used to treat Alzheimer´s disease (AD). Insomnia is reported to occur in at least 5% of AD patients receiving 10 mg/day of donepezil, likely due to the cholinomimetic properties of the drug. We determined the subjective and objective sleep-related impact of 5 or 10 mg/day of donepezil in non-demented adults.
Methods: Community-dwelling, non-demented adults (n=116, 64.7±7.5 years) with memory complaints (MMSE=28.5±1.3) completed the Pittsburgh Sleep Quality Index (PSQI) prior to and at the end of 12 weeks of a randomized, double-blind treatment with drug (n=55) or placebo (n=61). A subset (n=39, 16 on drug, 23 on placebo) completed up to 7 days of actigraphy at these two time points. Sleep-related adverse events were recorded throughout.
Results: After 12 weeks of treatment, the change in global PSQI scores was greater (i.e., worse sleep) in donepezil as compared to placebo ($p<0.05$). There were more sleep-related adverse events (insomnia, abnormal dreams) in drug (27%) than placebo (11%) ($p<0.05$). There were no significant between-group differences in the change in actigraphy total sleep time (p=0.13), wake after sleep onset(p=0.95), or sleep efficiency (p=0.77).
Conclusion: In non-demented, older adults with memory complaints, subjective sleep (measured by the PSQI) was worse in those administered donepezil, as compared to placebo. There were also more sleep-related adverse events in those taking donepezil, both compared to those given placebo and to those previously reported for AD patients. Objective sleep, however, did not differ by treatment, similar to published data. Given the likely effects of donepezil on REM sleep, the

divergence between the subjective and objective sleep data may be due to a worsening sleep quality rather than quantity in the donepezil group.
Support (optional): Research supported by the Medical Research Service of the Palo Alto Veterans Affairs Health Care System, by the Department of Veterans Affairs Sierra-Pacific MIRECC, and by AG 12914.

0335

THE RELATIONSHIP BETWEEN SWS AND COGNITIVE FUNCTIONING IN ELDERLY INDIVIDUALS WITH SLEEP DISORDERS

Maczaj M,[1] Wortman A[2]
(1) State University of New York at Stony Brook, Stony Brook, NY, USA, (2) State University of New York at Stony Brook, E. Setauket, NY, USA

Introduction: There is a recognized age-related trend for decrease in slow-wave sleep (SWS) (Bliwise, 1993). SWS refers to NREM sleep stages 3 and 4 characterized by the appearance of high amplitude (>75 mV), low frequency (<4.75 cps) brain waves .(Kryger, 2000). The diminution of SWS from infancy to old age is well-documented (e.g. Landolt, Dijk, Achermann, & Borbely, 1996; Van Couter, Leproult, & Plat, 2000; Gaudreau, Carrier, & Montplaisir, 2001).While sustained deficits in SWS tend to be greater in men than in women (Ehlers & Kupfer, 1997; Wauquier & Van Sweden, 1992); the overall decline is significant for both sexes. Cognitive abilities and language follow a similar attenuation with increasing age (Albert & Killiany, 2001). Several studies have found that SWS amount is positively correlated with daytime functioning in normal young adults (e.g. Jurado, Luna Villegas, & Buela-Casal, 1989; Ferrara, De Gennaro, & Bertini, 1999). In addition, there is mounting evidence indicating the importance of SWS for cognitive processes (Gais, Plihal, Wagner, & Born, 2000). Evidence exists suggesting a significant relationship between SWS amount and subsequent cognitive functioning among older individuals with insomnia complaints (Crenshaw & Edinger, 1998). Most research on SWS and cognition has neglected to include individuals from either of these populations. This study evaluates the data for a sample of elderly sleep disorders patients to further investigate the relationship between SWS and cognitive performance in this population. We hypothesized that among these individuals, a positive correlation would exist between SWS amount and variables of cognitive performance.
Methods: This study was a retrospective analysis of patients (age > 55) of the SBUH Sleep Disorders Center in a two year period. We examined the SWS% in these patients and compared it to normative data in normal age and gender equivalent individuals to assess for significant differences. We also compared these patients' SWS% to the patients' reports of memory and concentration deficits. Statistical analysis included one-way ANOVA and correlations, and t-test for dependent samples to determine if the results were significant. SWS was scored according to R&K criteria. Memory and concentration deficits were assessed by Yes/No choice.
Results: There was a total of 127 subjects; 86 male and 41 female. The age range was 55-85; mean age was 63.6 and median age was 61.0. SWS% analyzed by t-tests for dependent samples revealed the following statistically significant findings: negative correlation between SWS% and age ($p<.01$); positive correlation between SWS% and memory ($p<.01$) and positive correlation between SWS% and concentration ($p<.01$).
Conclusion: Despite the small sample size, in this elderly group of subjects with OSA and PLMDS, our data supports a correlation between memory and concentraion problems and decreased SWS% in these patients.
Support (optional): N/A

0336

LONG SLEEP DURATION AND ALL CAUSE MORTALITY IN LATER LIFE: A POSSIBLE CONSEQUENCE OF SEDENTARY DEATH SYNDROME

Morgan K
Loughborough University, Loughborough, United Kingdom

Introduction: Increased all-cause mortality has been associated with longer (8-10 hours+) and (though less consistently) shorter (<5 hours) self-reported sleep durations. While the physiological consequences of sleep loss may help to explain excess mortality associated with shorter sleep durations, it has been pointed out that " no hypothetical mechanisms for long sleep causing disease or death " have yet been investigated (Knutson & Turek, 2006). The present analyses explore the possibility that longer sleep durations act as a proxy for physical inactivity and influence survival through sedentary lifestyles.
Methods: Detailed profiles of sleeping patterns, health, and physical activity were obtained from a random community sample of 1042 older people (aged 65+) interviewed in 1985 for the Nottingham Longitudinal Study of Ageing. In the 21-year period 1985-2006 the project received notification of 919 deaths. To assess sleep-mortality relationships, baseline sleep durations were categorized <5, 6, 7 (reference), 8, 9 or >9 hrs, and 3 separate Cox survival models were fitted adjusted for: age and sex (model 1); age, sex, socioeconomic status and physical and mental health variables (model 2); and as model 2 plus customary physical exercise levels and time in bed (model 3).
Results: The modal self-reported sleep duration was 7 hrs. In models 1 and 2 longer sleep durations (>9 hrs) were significantly associated with mortality (HR 1.6, CI 1.17-2.18 & HR 1.6, CI 1.13-2.21 respectively). However, in model 3, lower levels of customary exercise (HR 1.5, CI 1.2 – 1.8), but not longer sleep durations, were significantly associated with mortality. Shorter sleep durations were not significantly associated with mortality in any of these models.
Conclusion: Time in bed and consequent physical inactivity are under-researched confounders in long sleep duration-mortality relationships. The evidence suggests that survival outcomes associated with longer sleep durations may be influenced by Sedentary Death Syndrome.

0337

OBJECTIVE AND SUBJECTIVE SLEEP DIFFERENCES IN CAREGIVING AND NONCAREGIVING OLDER ADULTS

Dubyak P,[1] McCrae C,[2] Rowe M[1]
(1) University of Florida, Gainesville, FL, USA, (2) Gainesville, FL, USA

Introduction: Both caregiving and noncaregiving older adults often complain of sleep problems. However, whether poor sleeping caregivers have worse sleep than poor sleeping noncaregivers is unclear. This study examined sleep differences in poor sleeping caregiving and noncaregiving older adults.
Methods: Caregivers (n=24, mean age=70.17years, SD=7.06) were recruited for an ongoing study of dementia caregivers. Noncaregivers (n=43; mean age=72.28years, SD=7.29) were recruited for a community-based study of older adults´ sleep patterns. One week of objective (actigraphy-ActiWatch-L) and subjective (sleep diaries) sleep data were collected. All participants were `poor sleepers´ based on sleep diary reports of 3+ nights of 31+ minutes of sleep onset latency (SOL) or wake time after sleep onset (WASO). Sleep variables analyzed included: SOL, WASO, total sleep time(TST), and sleep efficiency(SE).

Results: Caregivers had lower objective and subjective SEs compared to noncaregivers [t(58)=3.433, p<0.001; t(54)=2.025, p<0.05, respectively]. Specifically, caregivers had 5% lower objective (80.98% vs. 85.81%) and subjective (74.17% vs. 79.78%) SEs. Caregivers also had lower objective and subjective TSTs [t(41.82)=1.688, p<0.05; t(54)=1.949, p<0.05, respectively] and longer objective SOLs [t(57)=-1.986, p<0.05] than noncaregivers. There were no significant differences for objective and subjective WASO or subjective SOL.
Conclusion: Poor sleeping caregivers have `even poorer´ sleep than poor sleeping noncaregivers. Interestingly, both caregivers and noncaregivers reported sleeping less efficiently than actigraphy indicated. Absolute differences between the groups were consistent across the 2 modes of measurement with caregivers sleeping 5% less efficiently than noncaregivers. This 5% SE difference is large enough to suggest `clinical significance.´ Additionally, poor sleeping caregivers spent less time sleeping and took longer to fall asleep than poor sleeping noncaregivers. Poor sleeping caregivers may benefit from treatment that decreases unwanted nightly awake time (specifically, sleep latency) and increases total sleep time. Future research examining the factors (stress, fatigue, depression) that contribute to caregivers´ `poorer´ sleep is warranted.

0338

A MULTICOMPONENT APPROACH TO THE STUDY OF NAPPING BEHAVIOR IN OLDER ADULTS

Dautovich N,[1] McCrae C,[2] Rowe M[1]
(1) University of Florida, Gainesville, FL, USA, (2) Gainesville, FL, USA

Introduction: Nocturnal sleep disturbances in older adults are associated with a number of factors including napping. Previous research has examined the association between napping and sleep but the results have been mixed. These studies have typically focused on only a single component of napping behavior, such as duration or frequency. The current study is unique, because it examines multiple components of napping behavior – duration, frequency, and time of day. The main goal of this study is to extend previous napping research by examining the relationship between multiple components of napping behavior and sleep in older adults.
Methods: 103 community-dwelling older adults (M age=72.81, SD=7.12) wore an Actiwatch-L® (24hs/day) for 14 days and concurrently completed daily sleep diaries.
Results: Four canonical correlation analyses were conducted. Subjective nap variables (frequency and duration) were significantly correlated with objective (Wilk´s Λ =.78, $p < .01$) and subjective sleep (Wilk´s Λ =.80, $p < .01$). Subjective nap frequency and duration were most strongly negatively associated with objectively measured total sleep time and sleep efficiency and with subjectively measured total sleep time. The derived canonical variate accounted for 21% and 18% of the variance in the relationship between subjective napping and subjective sleep and objective sleep, respectively. Objective nap variables (frequency, duration, time of day) were not found to be significantly correlated with subjective or objective sleep.
Conclusion: Older adults who reported engaging in shorter and less frequent naps during the day also reported spending more time asleep at night. Interestingly, according to actigraphy, such older individuals also experienced more sleep time and slept more efficiently at night. Implications for the measurement of napping in future research and the methodology used to examine `actigraphically´ measured naps in the present study will be discussed. Implications for the use of napping as a treatment for late-life insomnia will also be presented.

0339

PREDICTORS OF SLEEP QUALITY IN WOMEN IN THE MENOPAUSAL TRANSITION

Pien G,[1] Sammel M,[2] Freeman E,[2] Lin H[2]
(1) University of Pennsylvania, Philadelphia, PA, USA, (2) University of Pennsylvania, PA, USA

Introduction: How reproductive hormone levels affect sleep quality and whether specific risk factors for poor sleep exist among menopausal women are not well understood. The present study examines subjective sleep quality over an 8-year period in the Penn Ovarian Aging Study.
Methods: Data were obtained from a randomly identified, population-based sample of African-American and Caucasian women, who were 35-47 years of age and had regular menstrual cycles at recruitment. The primary outcome measure was the Sleep Quality factor score, derived from the St. Mary´s Hospital Sleep Questionnaire, which was adapted for this population and collected regularly over the 8-year follow-up period. Associations between menopausal status, reproductive hormone levels, menopausal symptoms and sleep quality were examined in multivariable regression analyses.
Results: Overall menopausal status was not significantly associated with sleep quality (p=0.09). However, postmenopausal women reported better sleep quality than premenopausal women (p=0.02). In the adjusted model, independent predictors of sleep quality were hot flashes (p=0.0003), CES-D scores (p<0.0001) and levels of the reproductive hormone inhibin B (p=0.04).
Conclusion: Sleep quality did not worsen with advancing menopausal status alone, but was predicted by hormone changes and symptoms that occur in the menopausal transition. Declining inhibin B levels, hot flashes and symptoms of depression were all strong and independent predictors of difficulty sleeping. Race was not a significant contributor to sleep quality in our analyses. Together, the findings demonstrate women who experience other perimenopausal symptoms are also likely to experience sleep problems during the menopausal transition.
Support (optional): Supported by grants K23-HD-41465, RO1-AG-12745 and 2MO1RR-00040-37 from the National Institutes of Health.

0340

SLEEP AND THE METABOLIC SYNDROME IN MID-LIFE WOMEN

Hall M,[1] Sowers M,[2] Owens J,[3] Matthews K,[3] Kravitz H,[4] Gold E,[5] Feinberg I,[5] Bromberger J,[6] Buysse D,[3] Sanders M[3]
(1) Pittsburgh, PA, USA, (2) University of Michigan, Ann Arbor, MI, USA, (3) University of Pittsburgh, Pittsburgh, PA, USA, (4) Rush University Medical Center, Chicago, IL, USA, (5) University of California, Davis, Davis, CA, USA, (6) University of Pittsburgh, PA, USA

Introduction: Sleep disordered breathing (SDB) is a recognized risk factor for cardiovascular disease. Less understood is the extent to which other dimensions of sleep contribute to cardiovascular disease risk above and beyond the effects of SDB. We evaluated relationships among the metabolic syndrome, which represents a clustering of risk factors for cardiovascular disease, and subjective sleep quality and PSG-assessed indices of sleep continuity and architecture in a multi-ethnic sample of mid-life women.
Methods: Participants were 334 women (Mean age = 51; 37% African-American, 18% Chinese, 46% Caucasian) enrolled in the multi-site SWAN Sleep Study. Clinically-defined metabolic syndrome (NCEP criteria with adjustments for waist circumference in the Chinese) was present in 33% of the sample. Sleep studies (PSQI, 3 nights of PSG) were conducted in participants´ homes. SDB was evaluated once; other

PSG measures were averaged over Nights 2 and 3. Age, race, menopausal status and AHI were included as covariates in logistic regression analyses.
Results: Consistent with previous research, AHI was significantly higher among women with the metabolic syndrome (10.53 vs. 7.05, p < .01). Independent of age, race, menopausal status and AHI, participants with the metabolic syndrome had less favorable PSQI scores (7.34 vs 6.32) and lower percent SWS (1.78 vs. 2.72%) in comparison to participants without the metabolic syndrome (p values < .01). Sleep continuity was not associated with the metabolic syndrome.
Conclusion: These findings suggest that SDB is not the only dimension of sleep associated with the metabolic syndrome. Regardless of age, race, menopausal status or AHI severity, subjective sleep complaints and lower percent SWS were associated with increased likelihood of the metabolic syndrome. The extent to which the links between subjective sleep complaints, SWS and the metabolic syndrome may be mediated by immune, endocrine and oxidative stress pathways, similar to the pathways linking SDB to the metabolic syndrome, merits exploration.
Support (optional): The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health, DHHS, through the National Institute on Aging, the National Institute of Nursing Research and the NIH Office of Research on Women's Health (Grants NR04061, AG012505, AG012554, AG012546, AG019360, AG019361, AG019362, AG019363) and by the National Institutes of Health (RR00056 and RR023506).

0341

SLEEP DURATION AND THE METABOLIC SYNDROME

Hall M,[1] Muldoon M,[1] Flory J,[2] Buysse D,[1] Manuck S[1]
(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) Mount Sinai School of Medicine, New York, NY, USA

Introduction: Although a number of studies have implicated sleep in the development of cardiovascular disease, the biobehavioral pathways important to the sleep-CVD relationship are only now being explored. Emerging evidence suggests that abnormal sleep duration (<6 or >9 hours) is associated with obesity, hypertension and inflammation. We hypothesized that sleep duration would be similarly predictive of the metabolic syndrome, which represents a clustering of risk factors for cardiovascular disease.
Methods: Reported habitual sleep duration and components of the metabolic syndrome were evaluated in a population-based sample of 1,295 adults (52% female, 16.5% black, age range = 30 54 years). NCEP-defined metabolic syndrome was present in 21% of the sample. Logistic regression was used to model the hypothesized U-shaped relationship between sleep duration (quadratic term) and the metabolic syndrome, after adjusting for the effects of age, sex and race.
Results: The curvilinear relationship between sleep duration and the metabolic syndrome was significant (p< .05). Metabolic syndrome prevalence rates were highest (28%) among both short (<6 hrs) and long (>9 hrs) sleepers and lowest among individuals with habitual sleep durations of 7-8 hrs per night. With respect to sleep duration and individual components of the metabolic syndrome, significant U-shaped relationships were observed for abdominal adiposity, impaired glucose regulation (p < .05), and insulin resistance (p < .01). In all models, abdominal adiposity and impaired glucose metabolism was highest among short and long sleepers, as compared to the 7-8 hour reference group. Other components of the metabolic syndrome were not significantly associated with sleep duration.
Conclusion: Results suggest that risk for the metabolic syndrome is elevated in short and long sleepers among mid-life men and women without clinical history of atherosclerotic disease. Research is needed on the mediating pathways linking sleep duration to the metabolic syndrome and CVD risk, which may differ for short and long sleepers.

0342

SCALING AND NONLINEAR PROPERTIES ACROSS SLEEP STAGES

Schmitt D, Ivanov P
Boston University, Boston, MA, USA

Introduction: Previous studies have shown that cardiac dynamics exhibit non-random fluctuations characterized by complex temporal structure. This structure remains unchanged when data are analyzed at different timescales; suggesting a robust fractal-like organization. It has been shown that this fractal behavior changes with different pathologic conditions, sleep and wake state, and across circadian phases, and that scale-invariant markers of these fractal dynamics also have predictive power. We hypothesize that: (1) the fractal organization in heartbeat fluctuations in healthy subjects changes across sleep stages; (2) this organization at a given sleep stage may change with advances age and cognitive impairment.
Methods: We have analyzed 24 records of heartbeat intervals obtained from 12 young subjects, 19 healthy elderly subjects and 5 elderly subjects identified as demented from the Sleep Heart Health Study database during standard polysomnographic recordings. We use Detrended Fluctuation Analysis (DFA) to quantify the temporal structure of heartbeat fluctuations during each sleep stage.
Results: For the group of young subjects we find that cardiac dynamics change significantly with transitions from deep to light to REM sleep stage, with heartbeat fluctuations exhibiting stronger long-range correlations during REM sleep, weaker correlations during light sleep, and random-like behavior during deep sleep. A similar behavior characterized by similar values of the DFA fractal measure we observe for the group of healthy elderly subjects. However, for the dementia subjects we find do not find a significant change across sleep stages.
Conclusion: The neuroregulation of cardiac dynamics changes significantly not only during sleep and wake state but also across different sleep stages. We find no significant change in the temporal fractal organization with healthy aging for each sleep stage compared to the young subjects. However, a significantly different behavior we find for elderly subjects with dementia.
These observations indicate a strong link between the sleep regulation, the cognitive funstion, and the neuroautonomic cardiac regulation.

0343

MAPPING OF NEURONAL ACTIVITY BY IMMEDIATE EARLY GENE EXPRESSION DURING SLEEP DEPRIVATION AND RECOVERY SLEEP

Thompson C,[1] Wisor J,[2] Gerashchenko D,[2] Fischer S,[1] Pathak S,[3] Hawrylycz M,[3] Jones A,[4] Kilduff T,[2] Lein E[1]
(1) Neuroscience Department, Allen Institute for Brain Science, Seattle, WA, USA, (2) Biosciences Division, SRI International, Menlo Park, CA, USA, (3) Informatics Department, Allen Institute for Brain Science, Seattle, WA, USA, (4) Allen Institute for Brain Science, Seattle, WA, USA

Introduction: Identification of brain regions activated by sleeping, waking and sleep deprivation (SD) may help to understand sleep regulation and deficits associated with SD. Changes in gene expression can reflect altered neuronal activity, particularly rapidly regulated genes like immediate early genes (IEGs). In the current study, high throughput in situ hybridization (ISH) was used to map dynamic expression of 48 genes in association with sleeping, waking and sleep-deprived behavioral states.
Methods: Male C57BL/6 mice underwent 6 hr SD (ZT0-ZT6) by cage tapping and introduction of novel objects; a subset were subsequently allowed recovery sleep (RS) for 4 h (ZT6-ZT10). Time of day controls and a spontaneous waking timepoint (ZT18) were collected. ISH was performed on brains for 48 mRNAs including c-fos, arc, nr4a1, egr3, fosb, junb, egr1, homer1, and fosl2 using high throughput colorimetric ISH, and fluorescent co-labeling of c-fos with gad1 mRNA. Images collected on an automated microscopy platform were analyzed by manual and automated image processing.
Results: SD and RS mice were awake >95% during SD; during the hour subsequent to sleep onset after SD, RS mice had greater %NREMS, NREMS delta power and NREMS bout duration than controls. A quarter of the genes exhibited changes in expression correlated with sleep state in regions associated with functional deficits incurred by SD. Prominent patterns included SD-associated gene induction in caudate putamen, cerebellum, visual cortex, and basomedial amygdala, and SD- and wake-associated induction in cortical amygdala and orbital cortex. IEG expression in striasomes varied across conditions. The absence of c-fos and gad1 colabeling in most regions suggests SD preferentially affects excitatory neurons.
Conclusion: Sleep deprivation leads to altered gene expression in brain regions associated with cognitive, emotional, and memory deficits. Similar activation patterns are observed across immediate early genes in response to sleep deprivation and/or recovery sleep, with a few gene-specific differences.
Support (optional): Supported by the Department of Defense USAMRAA award W81XWH-06-1-0131 and NIH 5RO1HL59658.

0344

HEART RATE VARIABILITY AFTER PARTIAL SLEEP DEPRIVATION WITH OR WITHOUT CIRCADIAN MISALIGNMENT

Holmbäck U,[1] Leproult R,[2] Van Cauter E[1]
(1) University of Chicago, Chicago, IL, USA, (2) University of Chicago, IL, USA

Introduction: Partial sleep loss has been associated with decreased heart rate variability, a risk factor for cardiovascular disease. Epidemiological studies have shown that shift workers, who are chronically sleep deprived, have an increased risk of developing cardiovascular disease. It is not known whether circadian misalignment (sleeping during the daytime) impacts heart rate variability independently of sleep loss.
Methods: 19 healthy males (age 24±1 y, BMI 23.1±0.5 kg/m2) participated in one of two protocols: extended wakefulness (EW) or extended wakefulness with displaced sleep (EWD). Following 3 baseline nights with 10-h bedtimes, the subjects had 8 days with 5-h bedtimes, either from 0030 to 0530 every night (EW protocol), or with daytime sleep (0900-1400) on the 2nd, 3rd, 5th and 6th nights (EWD protocol). The recovery period (two 12h nights and one 10h night) were identical for both protocols. Heart rate variability was measured with a portable cardiac impedance device; from 2 PM to 9 PM and 8 AM to 2 PM before and after the 3rd baseline night as well as before and after the 8th sleep deprivation night. RR-interval, respiratory sinus arrhythmia (RSA) and interbeat interval (IBI) were calculated.
Results: Total sleep time over the 8 days of sleep restriction was similar in both protocols. There was no change in RR-interval and RSA in either of the protocols. EW subjects decreased their IBI 4.9± 4.3% and the EWD subjects decreased their IBI 7.7 ± 4.0% after sleep deprivation ($p<0.05$, p=NS for difference between protocols).
Conclusion: Recurrent partial sleep was associated with a slightly decreased heart rate variability, with no additional effect of circadian misalignment. Possibly the effect of sleep deprivation was big enough to obscure any smaller difference due to circadian misalignment.
Support (optional): NIH, National Sleep Foundation - Pickwick Fellowship, Johan and Henning Throne Holst Foundation

0345

WITHIN-NIGHT CORRELATION OF SWS WITH PERFORMANCE DURING RECOVERY FROM SLEEP LOSS

Bonnet M,[1] Arand D[2]
(1) Wright State University, Dayton, OH, USA, (2) Kettering Medical Center, OH, USA

Introduction: A recent study showed a significant relationship between SWS and improved performance following shortened sleep using a pharmacological manipulation. This suggests that the association of performance improvement with SWS might be due to within sleep factors associated with partial sleep periods. To determine if SWS amounts during discrete parts of the night were related to immediate or later performance, memory and reaction time tasks were examined after awakenings following 2, 4, 6, and 8 hours of sleep on baseline and recovery nights prior to, during, and following 64 hours of total sleep deprivation.
Methods: Fourteen male subjects, ages 55-70 and without sleep apnea or PLMS, slept in the laboratory for four baseline nights followed by two nights of total sleep deprivation and four recovery sleep nights. Each night, Subjects were awakened every two hours from stage 2 sleep and performed a 20-minute test battery including the Williams Word Memory task and a 10-minute simple reaction time test. Each night was extended by an hour to allow 8 hours for sleep.
Results: Expected rebounds in SWS (164% increase) were found during the first recovery night. In parametric analyses, greater SWS on baseline nights was related to slower reaction time after sleep deprivation. However, at all times with both memory and reaction time variables, significant correlations with SWS were fewer than expected by chance and about half were in the wrong direction. Performance was correlated at greater than chance levels with latency to persistent sleep, stage 1, arousals, and total sleep during the middle half of the recovery night.
Conclusion: These data do not suggest any positive relationship between SWS parameters and partial-sleep recovery of performance following sleep deprivation. Potential correlates of performance recovery during sleep seem to include middle of recovery night amounts of total sleep and arousal parameters.

Support (optional): Supported by the Dayton Department of Veterans Affairs Medical Center, Wright State University School of Medicine, and the Sleep-Wake Disorders Research Institute.

0346

RESPONSE TO SLEEP RESTRICTION DEPENDS UPON PRE-EXISTING SLEEP DEBT

Banks S,[1] Van Dongen H,[2] Dinges D[1]
(1) University of Pennsylvania School of Medicine, Philadelphia, PA, USA, (2) Washington State University, Spokane, WA, USA

Introduction: Cumulative effects of chronic sleep restriction on behavioral alertness have been carefully documented, but little is known about the role of pre-existing sleep debt on the subsequent response to sleep restriction. This issue was addressed by determining whether a single night of sleep restriction to 4h TIB following partial recovery from a sleep debt resulted in the same degree of neurobehavioral deficit as that found after a single night of sleep restriction to 4h TIB following a period without sleep debt.
Methods: N=13 subjects (M=29.4y; 5 females) participated in a laboratory-controlled protocol, undergoing 2 nights of baseline sleep (B1-B2; 10h TIB) followed by 5 nights of sleep restriction (SR1-SR5; 4h TIB), then a recovery night (R1; 8h-12h TIB) followed by another night of sleep restriction (SR6; 4h TIB). A 10min Psychomotor Vigilance Test (PVT) was completed every 2h (08:00h to 20:00h) as part of a neurobehavioral test battery. PVT lapses were averaged within days for each subject. Change scores were calculated between B2 and SR1 (acute sleep restriction after no sleep debt), and between R1 and SR6 (acute sleep restriction after sleep debt). Change scores between the two conditions were compared using a Wilcoxon signed ranks test.
Results: PVT lapses increased by an average of 2.96 per test bout after SR1 following baseline sleep. Lapses increased an average of 5.73 per test bout after SR6 following a single recovery sleep preceded by 5 nights of prior sleep restriction. The differences between the lapse increase was significant (p=0.033).
Conclusion: The change in PVT performance upon acute sleep restriction to 4h TIB after incomplete recovery from prior sleep debt was nearly twice the change in PVT performance upon acute sleep restriction after a period without sleep debt. Thus, when recovery from sleep debt is incomplete, neurobehavioral vulnerability to further sleep restriction appears to be disproportionately increased.
Support (optional): NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute.

0347

SLOW WAVE ACTIVITY DYNAMICS DURING CONSECUTIVE WEEKS OF SLEEP RESTRICTION TO 4 HOURS PER DAY

Avinash D,[1] Banks S,[1] Van Dongen H,[2] Dinges D[1]
(1) University of Pennsylvania School of Medicine, Philadelphia, PA, USA, (2) Washington State University, Spokane, WA, USA

Introduction: While sleep restriction (SR) to 4h per night results in cumulative waking neurobehavioral deficits, inconsistent results have been reported for the SR response of NREM EEG slow wave activity (SWA)—the putative marker of sleep homeostasis.
Methods: As part of a larger study on N=80 subjects, N=27 healthy adults (29±7y; 13 females) underwent 2 nights of baseline sleep (B;10h TIB), 5 nights of sleep restriction (SR1-5;4h TIB), one variable night of randomized TIB (C1;0,2,4,6,8,10,12h), 5 more nights of sleep restriction (SR6-10;4h TIB), and 2 recovery nights (R;10h TIB). EEG was recorded at baseline, restriction nights 1 and 5 (SR1a, SR5a), variable night (C1), restriction nights 6 and 10 (SR6, SR10), and recovery night (R1) and analyzed for NREM SWA (0.5-4.5Hz, sampled at 120Hz) for the C3-Ax derivation. After artifact removal, FFT analysis was performed in 5s bins, and the average delta power for every 30s epoch was computed.
Results: N=16 subjects from the 6h, 8h, 10h and 12h C1 TIB sleep doses were pooled and SWA was analyzed in the first 5 days of SR. Compared to baseline, SWA was reduced on SR1 and SR5 by 36% ($p<0.001$) and 31% ($p<0.001$) respectively; there was no significant difference between SR1 and SR5. For subjects who received 6h-12h TIB on C1, SWA increased by 36% (p=0.001) on C1 relative to SR5. SWA decreased from C1 to SR6 by 28% (p=0.01) and from SR6 to SR10 it decreased further by 16% (p=0.05). On R1 (10h TIB), SWA increased by 46% ($p<0.001$) over SR10 and by 12% (p=0.05) over baseline.
Conclusion: These results provide preliminary evidence that SWA undergoes homeostatic changes with SR. SWA is reduced when sleep is restricted to 4h TIB, and increased when TIB is subsequently increased to 6h-12h. These SWA effects were found on both the first and second week of sleep restriction.
Support (optional): NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute and NIH RR00040.

0348

EXECUTIVE FUNCTIONING FOLLOWING FIVE NIGHTS OF SLEEP RESTRICTION

Caruso H, Banks S, Minkel J, Dinges D
University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: Total sleep deprivation has been reported to produce decrements in neuropsychological performance mediated by the prefrontal cortex (PFC), but it is unknown whether partial sleep restriction (PSD) has such effects. The aim of this study was to investigate PFC-mediated tests of planning, verbal fluency and flexibility following chronic partial sleep restriction.
Methods: N=133 healthy subjects (29.9 ± 6.8y, 68 female) participated in a controlled laboratory protocol. N=120 underwent 2 nights of baseline sleep (10h TIB) followed by 5 nights of sleep restriction (4h TIB). At baseline, subjects completed the PFC-related tasks: North American Adult Reading Task (NAART) and 1 letter-set (C,F,L) of the Controlled Oral Word Association Task (COWAT). Following the fifth night of 4h TIB, subjects completed the remaining half of the COWAT (letters P,R,W), the Tower of London (TOL) and the Hayling and Brixton tests (HBT). N=13 served as 10h TIB per night control subjects.
Results: Mann-Whitney U tests were conducted to test for differences between the control and sleep-restricted groups. A significant difference was found between the control and the sleep-restricted groups in the Hayling scaled errors score of response inhibition (p=0.028). No other differences were significant between the control group and experimental group on any of the other tasks (4 other HBT outcomes; 3 NAART outcomes; 7 TOL outcomes; 2 COWAT outcomes).
Conclusion: Previous studies have elucidated a known anatomical basis for increased involvement of Broca´s Areas 9, 10 and 45 during Hayling response inhibition as compared to response initiation. These results suggest that 5 nights of restriction of sleep to 4h TIB has a specific effect on these areas. It remains unclear as to why this effect has not been shown in any of the other PFC tests examined.
Support (optional): Supported by NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute, NIH NR04281 and RR00040.

0349

SYNTHETIC WORK PERFORMANCE FOLLOWING FIVE NIGHTS OF SLEEP RESTRICTION

Lakhtman L, Banks S, Goel N, Dinges D
University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: Laboratory performance tests that simulate aspects of work processes have been referred to as synthetic work tasks. The aim of this study was to investigate the effect of sleep loss and learning on a classic synthetic work (SYNWORK) performance battery.
Methods: N=41 healthy subjects (28.9 +/- 6.8y, 21 female) participated in a controlled laboratory protocol involving 2 nights of baseline sleep (10h TIB), followed by 5 nights of sleep restriction (4h TIB), followed by recovery sleep. N=4 subjects had 10h TIB each night as a control. SYNWORK performance testing was conducted twice each day (10:30h-12:00h and 18:30h-20:00h) for 15 minutes each session, and consisted of 4 tasks performed simultaneously: an arithmetic task, a Sternberg (working memory) task, an auditory vigilance task, and a visual tracking task. A score for each task was recorded, as well as the total score for each session. Mixed model ANCOVA controlling for baseline day one was conducted to examine the effects of sleep restriction.
Results: There were significant improvements across sleep restriction days in the arithmetic ($p=0.001$) and Sternberg ($p<0.001$) tasks, and the total SYNWORK score ($p=0.045$), but the effects of sleep restriction were evident only on arithmetic performance ($p=0.010$) and total SYNWORK score ($p=0.01$).
Conclusion: The only SYNWORK task that was differentially affected by sleep restriction (relative to the control condition) was arithmetic performance, which was also the only subject-paced (as opposed to work-paced) task in SYNWORK. Thus it appears that sleep restriction resulted in subjects being slower on this task, and since this task can contribute more points to the SYNWORK total score than the other tasks, total score was also differentially affected by sleep restriction. These findings replicate a long-standing observation in sleep deprivation research—namely that cognitive and psychomotor slowing are the dominant effects of sleep loss on subject-paced tasks.
Support (optional): NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute and NIH RR00040.

0350

THE HUMAN EMOTIONAL BRAIN WITHOUT SLEEP

Gujar N, Walker M
Harvard University, Boston, MA, USA

Introduction: A commonly reported consequence of sleep-deprivation is altered mood and affect. Furthermore, a hallmark feature of many affective psychiatric conditions is abnormal sleep. Despite this implied interplay, few studies have examined the consequence of sleep-deprivation on human emotional brain processing. Here we investigate the neural impact of sleep-deprivation on the evaluation of negative emotional stimuli using functional MRI (fMRI).
Methods: Subjects (n=28) were either sleep-deprived for 38hr (deprivation group) or allowed to sleep normally (control group) before performing an emotional picture-slide assessment during fMRI scanning. Subjects viewed a series of standardized emotional pictures, ranging form neutral to highly negative, and made an emotional strength judgment to each.
Results: The control group demonstrated moderate limbic brain activation to increasingly negative stimuli, specifically in bilateral amygdala regions. The deprivation group also demonstrated bilateral amygdala activation, but to a far great magnitude, levels that were +60% more intense than the control group ($P=0.009$). Moreover, sleep-deprived subjects expressed a near three-fold greater extent of amygdala volume activation to negative stimuli ($P=0.03$). Most interesting, this amplified amygdala response in the deprivation group resulted in a different pattern of functional brain connectivity, most prevalent in cingulate and medial prefrontal regions; potentially indicating a top-down control dysregulation.
Conclusion: These findings demonstrate that a single night of sleep-deprivation profoundly alters the basic human brain response to affective emotional challenges, resulting in a hyper-limbic reaction to negative stimuli. As a consequence, a different network of functional connectivity was instantiated during the processing of aversive stimuli. These results suggest that a principal function of sleep may be to `reset´ the correct affective reactivity of the human brain to next-day emotional challenges. Furthermore, these data offer instructive insights into clinical depression, where the symptoms of fragmented sleep and negative emotional predisposition may not simply be correlative, but instead, causally related.
Support (optional): NIMH, AASM

0351

VISUAL SHORT-TERM MEMORY CAPACITY DECLINE FOLLOWING SLEEP DEPRIVATION AND ITS ANATOMICAL CORRELATES

Chee M,[1] Chuah L[2]
(1) Duke-NUS Graduate Medical School, Singapore, Singapore, (2) Duke-NUS Graduate Medical School, Singapore

Introduction: Sleep deprivation (SD) impairs short-term memory but it is unclear if this is due to reduced storage capacity or processes related to degraded information encoding. Prior work using a working memory task in the context of SD found response patterns that point to deficits in attention as underlying or contributing to this memory decline.
Methods: Thirty participants were tested in two sessions, following a night of normal sleep and after 24h of SD. Each volunteer underwent fMRI, performing two tasks in each state. In the Visual Short Term Memory (VSTM) task they were shown between 1 to 8 uniquely colored squares. About a second later, they were shown a colored square and indicated if they had seen that color. This sought to evaluate the neural substrate for VSTM, the intra parietal sulcus (IPS). In the visual array size control (VAC) task, identical arrays of colored squares appeared but participants were required only to indicate the presence or absence of a centrally-located square. This sought to evaluate the substrate (extrastriate cortex) for perceptual load.
Results: VSTM capacity, decreased to around 2 colors from 3 colors following sleep deprivation. IPS activation magnitude tracked VSTM performance. SD depressed IPS activation in both tasks and at all set sizes. Activity in the extrastriate cortex also decreased substantially following sleep deprivation for both tasks. Reduced activation was not a result of falling asleep as those with <5% lapses during SD showed similar activation responses.
Conclusion: The functional imaging and behavioral changes observed in this study suggest that deficits in visual processing with or without accompanying loss of sustained attention account for the degradation of VSTM capacity following sleep deprivation.
Support (optional): DSO National Laboratories, Singapore (No. DSOCL05141), SingHealth Foundation and the Shaw Foundation

0352

EFFECTS OF OVARIECTOMY AND ESTROGEN REPLACEMENT ON SPONTANEOUS SLEEP AND RECOVERY SLEEP AFTER SLEEP DEPRIVATION IN RATS

Deurveilher S, Wilkinson M, Rusak B, Semba K
Dalhousie University, Halifax, Nova Scotia, Canada

Introduction: The influence of ovarian hormones on sleep-wake states and sleep homeostasis is not well characterized, although there is evidence that hormone withdrawal (e.g., during menopause) alters sleep characteristics. We investigated the effects of ovariectomy and of estrogen (E) replacement on spontaneous sleep, and on recovery sleep after total sleep deprivation (SD) by "gentle handling" for 6 h in female rats. Intact male rats were also studied for comparison.
Methods: Adult female and male Wistar rats were housed under a 12:12 light:dark cycle. Female rats were ovariectomized (OVX) and implanted subcutaneously with silastic capsules containing oil vehicle (Oil), 10.5 µg of 17β-E to mimic diestrus levels of E (Low E), or 60 µg of 17β-E to mimic proestrus levels of E (High E). Male rats were intact but implanted with oil-filled silastic capsules. All animals were also implanted with EEG and EMG electrodes. Two weeks after surgery, EEG/EMG were recorded during a 24 h baseline period, followed by 6 h SD in the second half of the light phase, and an 18 h recovery period beginning at the onset of the next dark phase.
Results: During the 24 h baseline recording, Low E and High E OVX rats spent less time than those in the Oil group in both slow wave sleep (SWS; 39, 37 and 44%, respectively) and rapid eye movement (REM) sleep (9, 8 and 12%, respectively). During the 18 h recovery period after SD, the three groups showed similar amounts of SWS (46-50%) and REM sleep (11-12%). The rate at which lost SWS recovered was also similar across groups. OVX rats treated with Oil, however, recovered very little of their lost REM sleep, and the rate of recovery of REM sleep was markedly reduced in this period, compared to Low E and High E rats (4 vs. 89, 98%, respectively). Male rats resembled E-treated females in terms of baseline sleep parameters and in the amount and rate of recovery of SWS and REM sleep after SD.
Conclusion: Ovariectomy without hormone replacement increased levels of baseline SWS and REM sleep in female rats relative to those receiving E replacement and to intact males. It also decreased the rate of recovery of REM sleep, but not SWS, during the 18 h recovery period after 6 h SD. Collectively, the results indicate that the presence or absence of E can affect sleep regulation and REM sleep homeostasis in female rats. We are also examining the effects of progesterone with or without E on sleep and sleep homeostasis and the effects of both hormones on EEG power spectra during spontaneous and recovery sleep.
Support (optional): CIHR (MOP-67085)

0353

SLEEPINESS AND SLEEP QUALITY AMONG UNIVERSITY MAJORS

Karpinski A, Montgomery-Downs H
West Virginia University, Morgantown, WV, USA

Introduction: Sleepiness and poor sleep quality are prevalent among university students, affecting their academic performance and daytime functioning. However, variation of these measures based on students´ area of study or `major´ has not been examined. The current study compared sleepiness and sleep quality among undergraduate students whose majors were either medically or humanities-oriented.
Methods: Students enrolled in 3 sections of the psychology course Introduction to Human Development at West Virginia University were administered the self-report Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS). Students were categorized based on major: "STEM" (Statistics, Technology, Engineering, Math, and medical-related majors) or Humanities (i.e., Psychology, Education).
Results: Participants (N=129) were 19.9 years of age (84 female, 98.4% White). Participants were mainly 3rd (47%) and 4th (35%) year students. 55% of participants were STEM majors and 45% were Humanities. Mean ESS scores were 7.97 (SD±2.6) with no group difference. Mean global PSQI score was 6.21 (SD±2.9) with group effects: 6.8 (SD±2.8) for STEM and 5.5 (SD±2.8) for Humanities ($p=0.015$), as well as for the PSQI components of sleep duration: 0.70 (SD±0.8) for STEM and 0.36 (SD±0.7) for Humanities ($p=0.008$), and use of sleep medications: 0.90 (SD±1.0) for STEM and 0.28 (SD±0.6) for Humanities ($p<0.001$).
Conclusion: The results show that while there were no differences found between STEM and Humanities majors´ self-reported sleepiness, there were significant differences in their self-reported sleep quality with STEM majors reporting worse global PSQI scores. Further, global PSQI scores for the sample indicate poorer quality of sleep compared to the population norms. Sleep duration was longer and frequency of sleep medication use was higher in STEM compared to Humanities. Continued research in this area will investigate whether STEM (medical-related) majors may have more education about or access to sleep medications.

0354

GABOXADOL ENHANCES SLOW WAVE SLEEP AND REDUCES DAYTIME SLEEPINESS DURING SLEEP RESTRICTION

Walsh J,[1] Snyder E,[2] Randazzo A,[1] Griffin K,[1] Eisenstein R,[1] Schweitzer P,[3] Dickey P,[1] Feren S[1]
(1) Sleep Medicine and Research Center, Chesterfield, MO, USA, (2) Merck Research Laboratories, Upper Gwynedd, PA, PA, USA, (3) Chesterfield, MO, USA

Introduction: Slow wave sleep (SWS) has been hypothesized to be a time of heightened restoration. We explored the impact of pharmacologically enhanced SWS on sleepiness during sleep restriction (SR).
Methods: A double-blind, parallel group, placebo-controlled design compared gaboxadol 15mg (GBX) to placebo (PBO) during four SR nights (5 hours/night; Nights 1-4). Subjects received either GBX or PBO on all SR nights; and PBO on baseline (Nights -1, -2) and recovery (Nights 5, 6). Multiple Sleep Latency Test (MSLT) and Karolinska Sleepiness Scale (KSS) measures of sleepiness were compared between groups at baseline, during SR and following recovery sleep in forty-one healthy adults [PBO: 9m, 12f; mean age (SD) 32.0 (9.9) yr; GBX: 10m, 10f; mean age 31.8 (10.2) yr]. Treatment group daily/nightly means were compared using longitudinal-data-analysis (LDA) and supportive ANCOVA with age, gender, and baseline value as covariates. Least square means (+/- SE) are reported below. Association between SWS and MSLT was tested post-hoc with Pearson partial correlations adjusted for age and gender.
Results: SWS increased with GBX on all SR nights. Mean minutes of SWS were 91.7+/-3.6 for GBX and 71.2 +/- 3.5 for PBO ($p<.001$) on Nights 3 and 4. PBO displayed the predicted deficits due to SR on the MSLT and KSS. Compared to placebo, the GBX group showed significantly longer mean MSLT latency during SR in the ANCOVA analysis (7.8+/-0.7 vs 5.8+/-0.7 min; $p=.033$) and lower mean KSS scores during SR (5.9=/-0.3 vs 6.7=/-0.3; $p=.036$). The LDA analysis was similar (MSLT, $p=.047$; KSS, $p=.058$). The adjusted correlation between change from baseline (Day -1) in MSLT on Day 4 and change

from baseline in SWS on Night 4 was significant in the GBX group (r = .64, p=.006) and in all subjects (r =.53, p=.001).
Conclusion: These data indicate that GBX enhances SWS and reduces physiological and introspective sleepiness which result from sleep restriction.
Support (optional): Merck and Lundbeck

0355

RECOVERY PROCESS OF SLEEP PATTERNS AFTER FOUR CONSECUTIVE NIGHTSHIFTS

Kubo T,[1] Takeyama H,[2] Tachi N,[3] Ebara T,[4] Inoue T,[4] Takanishi T,[4] Arakomo Y,[5] Murasaki G,[5] Itani T[4]
(1) Nagoya City University Graduate School of Medical Sciences, Nagoya, Aichi, Japan, (2) Tokai Gakuen University, Aichi, Japan, (3) Chubu University, Aichi, Japan, (4) Nagoya City University Graduate School of Medical Sciences, Aichi, Japan, (5) Japan Post, Aichi, Japan

Introduction: Management of fatigue is an effective strategy for preventing human error and work-related diseases, as well as for improving quality of life. Work safety and workers´ health decline over consecutive nightshifts. Although some investigations have analyzed the effects of consecutive nightshifts on workers´ fatigue and sleep, little is known about the process of recovery from fatigue after consecutive nightshifts. Therefore, the recovery process of sleep patterns after four consecutive simulated nightshifts was investigated.
Methods: Male participants (n = 10; Mean±SD; 22.9 ± 3.2 yr) were required to attend a laboratory for nine consecutive nights for recording under the following conditions: Adaptation sleep, Simulated Dayshift-1, Baseline sleep, followed by four simulated nightshifts and subsequent daytime sleep, Recovery-Sleep-1, off duty (in the laboratory), Recovery-Sleep-2, Simulated-Dayshift-2, Recovery-Sleep-3, and Simulated-Dayshift-3. During each shift, participants completed performance tests at hourly intervals. Sleep pattern was evaluated by ActiWatch (AW64, Mini-Mitter Co. Inc., USA). A deterioration of over 10% sleep efficiency from the baseline during recovery sleep was regarded as "Poor recuperative sleep". Recovery Sleep-1 was, however, excluded from the analysis because the duration when participants were awake before sleeping again was only six hours.
Results: Six cases with poor recuperative sleep were observed. Three trends of individual sleep patterns were included in the cases: increased sleep latencies, frequent awakenings during the night, and early morning awakenings. Data of Participant 3 were representative of participants who did not recover from the effect of consecutive nightshifts. The sleep efficiency at Recovery-Sleep 2 and 3 were 61.0% and 61.4 %. Moreover, compared to Baseline sleep, a 35% deterioration of sleep was observed at each recovery sleep period.
Conclusion: The findings of this study suggest that consecutive nightshift work may contribute to sleep disturbances, especially at the time of re-adapting to dayshifts.
Support (optional): This study was supported by a Grant-in-Aid for Occupational Medicine Research from Japan Post (2005).

0356

CHANGE IN PSYCHOMOTOR VIGILANCE TEST LAPSES PREDICTS CHANGE IN DIGIT-SPAN MEMORY PERFORMANCE DURING SLEEP RESTRICTION

Avery N, Banks S, Dinges D
University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: It is controversial whether lapses of attention measured by the Psychomotor Vigilance Test (PVT) relate to other cognitive deficits due to sleep deprivation. To address this issue, we compared changes induced by sleep restriction in PVT lapse rates to changes in Digit Span (DS) working memory capacity performance from the Wechsler Adult Intelligence Scale, to determine if those people who had greater lapse rates also had greater memory capacity deficits across days of sleep restriction.
Methods: N=38 healthy adults (M=30yr; 19 males) underwent 2 baseline nights (10h TIB), followed by 5 sleep restriction nights (4h TIB/night) in a controlled laboratory setting. Subjects completed a 35-min. test battery that included a computerized visual DS task and a 10-min. PVT. The battery was completed every 2h from 08:00 to 21:00. Mean performance on each day for each subject, and change scores between baseline day 2 and sleep restriction day 5 were calculated for PVT lapses and DS total scores.
Results: Sleep restriction resulted in progressive increases in PVT lapses ($p<0.001$; linear trend $p<0.001$). DS total score decreased slightly but not reliably across sleep restriction days ($p=0.156$). While baseline performance on the PVT and DS tasks was uncorrelated, change in lapses and memory capacity from baseline to sleep-restriction day 5 was correlated (rho=-0.53, $p<0.01$), indicating that the more subjects lapsed on the PVT in response to sleep restriction, the more they declined in DS performance.
Conclusion: Subjects who were more severely affected by sleep restriction as manifested in their greater increases in lapses during vigilant attention performance, also had greater declines in working memory capacity over 5 nights. This suggests these neurobehavioral effects are not entirely orthogonal, but instead share some common biological basis via homeostatic sleep drive.
Support (optional): Supported by NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute and NIH NR004281 and RR00040

0357

INTRAINDIVIDUAL DECREMENTS IN SLEEPINESS AND PERFORMANCE FOLLOWING SLEEP RESTRICTION ARE UNRELATED

Schweitzer P,[1] Griffin K,[1] Roth T,[2] Walsh J[3]
(1) Sleep Medicine and Research Center, St. John's Mercy Medical Center and St. Luke's Hospital, Chesterfield, MO, USA, (2) Henry Ford Hospital, Detroit, MI, USA, (3) Sleep Medicine and Research Center, St. John's Mercy Medical Center and St. Luke's Hospital; St. Louis University, Chesterfield, MO, USA

Introduction: Previous research demonstrates that neurobehavioral response to sleep deprivation/restriction varies considerably among individuals and is reasonably stable within an individual. The degree to which the response to sleep restriction correlates among various measures is not well-studied.
Methods: Data from 40 individuals (22 F, 18 M, mean age 29.9, SD 10.41 years) from two studies in which sleep was restricted (SR) to five hours per night for four nights were examined. Two nights with time in bed of 9-10 hours preceded baseline (BSLN) measures of Multiple Sleep Latency Test (MSLT), Karolinska Sleepiness Scale (KSS, ratings range from 0 – 9), and Psychomotor Vigilance Test (PVT), which were repeated following 4 nights of SR.
Results: Compared to BSLN, SR produced a mean MSLT decrease of 6.8 minutes (range: -14.4 to 3.2), a mean KSS rating increase of 2.6 points (range: -1.6 to 7.0), and a mean increase in PVT reaction time of 28.6 msec (range: -32.5 to 140.5; $p< .001$ for all). At BSLN, only MSLT and KSS were moderately correlated (Pearson r = -.39, p = .01; $r_{MSLT-PVT}$ = -.08, $r_{PVT-KSS}$ = .05). Spearman correlations were similar. After SR, MSLT and KSS showed r = -.30 (p = .07), $r_{MSLT-PVT}$ was -.15, and $r_{PVT-KSS}$ was -.10. There were no significant correlations among

measures in the change from BSLN to SR ($r_{MSLT-KSS}$ = -.19, $r_{MSLT-PVT}$ = -.07, $r_{PVT-KSS}$ = - .01).
Conclusion: These data demonstrate that the response to SR varies widely among individuals and that individuals most impaired on one measure of alertness/performance are not necessarily most impaired on other metrics. This suggests that different aspects of neurobehavioral function are affected differentially by SR.
Support (optional): Cephalon, Inc. and Merck & Co., Inc.

0358

FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY OF RECALL AFTER SLEEP DEPRIVATION: SHORT SLEEPERS V. LONG SLEEPERS

Carr W,[1] Phillips B,[2] Wetherell L,[3] Salamat J,[3] Taylor M,[4] Sausen K,[5] Drummond S[6]
(1) Naval Medical Research Center, Silver Spring, MD, USA, (2) DePaul University, IL, USA, (3) Veterans Affairs San Diego Healthcare System, CA, USA, (4) Naval Health Research Center, San Diego, San Diego, CA, USA, (5) Naval Health Research Center, San Diego, CA, USA, (6) University of California, San Diego, San Diego, CA, USA

Introduction: Short Sleepers (SS) and Long Sleepers (LS) have different habitual sleep duration. We asked how this difference in sleep duration affects performance and response to sleep deprivation (SD). Verbal encoding is a cognitive ability sensitive to SD and has been used successfully in functional magnetic resonance imaging (FMRI) research. We report the difference between SS and LS on an FMRI word learning task after normal sleep and after SD.
Methods: Six SS and six LS were identified with 2 weeks at home actigraphy. Both groups attempted to learn 24 words during a 5-minute FMRI session. Their free recall of those words was tested immediately after FMRI. They performed this task 12 hours after sleep (rested condition) and 36 hours after sleep (SD condition). We compared brain activation during encoding periods and number of words correctly recalled.
Results: The number of words recalled did not differ between SS and LS groups or across rested and SD conditions (total mean words recalled = 6.5, SE = 0.5). FMRI during verbal encoding, however, showed relatively greater brain activation in LS than in SS for bilateral inferior frontal and parietal regions when rested. And, after SD, brain activation in SS increased in right prefrontal and bilateral parahippocampal regions, whereas brain activation in LS did not change.
Conclusion: The habitual sleep duration difference between SS and LS has been established but waking performance differences between these 2 groups are essentially unstudied and unknown. Interestingly, LS showed greater brain activation than SS in the rested condition – and in areas sensitive to SD – suggesting LS show signs of SD 12 hours after waking. SS, on the other hand, showed an increase in activation after 36 hours SD, suggesting a different impact of SD between these 2 groups on cognitive resources required to maintain performance.
Support (optional): ONR Stress Physiology Program Work Order N00014-04-AF-00002
UCSD GCRC RR00827

0359

ADAPTING TO SLEEP LOSS: DYNAMIC PROPERTIES OF COGNITIVE PERFORMANCE PREDICTIONS BASED ON THE TWO-PROCESS MODEL

McCauley P, Smith A, Belenky G, Van Dongen H
Washington State University, Spokane, WA, USA

Introduction: The two-process model (TPM) of sleep regulation has been used to predict cognitive performance over time. Recently, an expansion of the model was proposed, modifying its asymptotes in response to sleep loss in order to capture the cumulative performance deficits from chronic sleep restriction (SLEEP 2005;28:A130/A133). Here we compare dynamic properties (steady states and stability) of the homeostatic drive in the original and the expanded TPM.
Methods: For both models, homeostatic drive was expressed as a set of ordinary differential equations. Requiring continuity from one sleep/wake cycle (n) to the next ($n+1$), a system of linear inhomogeneous difference equations was derived for the homeostatic drive during sleep (s_n) and wakefulness (w_n). Conditions for steady states were investigated by solving $w_{n+1}=wn$. For the expanded model, this was a function of the upper asymptote (u_n), necessitating also solving $u_{n+1}=un$. Stability was determined from the eigenvalues of the system.
Results: The original TPM converged to a steady state regardless of the amount of daily sleep, including total sleep deprivation. For the expanded TPM, a steady state existed when $u_n=(\&mu_w W+u_n-1)\exp(-\&mu_s S)+1$, where W and S are daily amounts of wake and sleep ($\&mu_w$ and $\&mu_s$ are constants). It follows that the expanded model tended to a steady state for chronic sleep restriction, but not for total sleep deprivation (S=0). For all steady states, stability was confirmed.
Conclusion: Our recent expansion of the TPM resulted in loss of convergence for total sleep deprivation. However, convergence to steady (albeit elevated) homeostatic states was still present under conditions of chronic sleep restriction. Moreover, these states were found to be stable under temporary changes in the amount of sleep. To the extent that the expanded TPM reflects sleep/wake physiology, these findings suggest that physiologically sustainable quantities of sleep reduction should eventually lead to an elevated state of homeostatic adaptation.
Support (optional): AFOSR grant FA9550-05-1-0086; DURIP grant FA9550-06-1-0281; congressionally directed funding W81XWH-01-0099.

0360

RACIAL DIFFERENCES IN SELF-REPORTS OF SLEEP DURATION IN A POPULATION-BASED STUDY

Hale L,[1] Do D[2]
(1) State University of New York at Stony Brook, Stony Brook, NY, USA, (2) University of Michigan, MI, USA

Introduction: Racial and ethnic differences in sleep duration are not well understood. Research shows that short (<6.5 hours) and long (>8.5 hours) sleepers have higher mortality risks than mid-range sleepers. We investigate whether sleep duration varies by racial and ethnic characteristics and if some of this effect may be explained by residential context.
Methods: Using a 1990 subsample (n=32,184) of the National Health Interview Survey of non-institutionalized adults living in the US, we estimate a multinomial logistic regression that predicts short (<6.5 hours), mid-range (6.5-8.5 hours), and long sleep (>8.5 hours) duration including covariates for race/ethnicity, among other demographic, health, and neighborhood characteristics.

Results: Black respondents have an increased risk of being short and long sleepers (OR=1.66, p<.001 and OR=1.42, p<.05, respectively) relative to white respondents. Hispanics (excluding Mexican Americans) and non-Hispanic 'Others' are also associated with increased risk of short sleeping (OR=1.27, p<.01 and OR=1.34, p<.01, respectively). Living in an inner city is associated with increased risks of short sleeping and reduced risks of long sleeping, compared to non-urban areas. Some of the higher risk of short and long sleeping among blacks can be explained by higher prevalence of blacks living in the inner city.
Conclusion: Blacks and other racial minorities have sleep durations that are associated with increased mortality. The results are consistent with the hypothesis that unhealthy sleep patterns among minorities may contribute to health differentials.
Support (optional): The authors have no financial interests to disclose.

0361

WINSCAT TEST BATTERY IS PARTIALLY SENSITIVE TO CHRONIC SLEEP RESTRICTION

Erickson J,[1] Banks S,[2] Dinges D[1]
(1) University of Pennsylvania School of Medicine, Philadelphia, PA, USA, (2) University of Pennsylvania, Philadelphia, PA, USA

Introduction: The Spaceflight Cognitive Assessment Tool for Windows (WinSCAT) was designed to detect neurocognitive deficits resulting from head trauma, drug effects, environmental factors and/or fatigue in the performance of astronauts. We sought to determine if WinSCAT testing was sensitive to chronic sleep restriction, which is commonly experienced by astronauts in space flight.
Methods: N = 41 healthy adults (22-44y; M=28.9y ± 6.8; 20 females) participated in a 16-day laboratory protocol consisting of 2 nights of baseline sleep (B1-B2, both 10h TIB); then 5 nights of sleep restriction (SR1-SR5, all 4h TIB); then 1 night of condition-recovery (CR1, randomized to 0h, 2h, 4h, 6h, 8h, 10h, or 12h); then 5 additional nights of sleep restriction (SR6-SR10, all 4h TIB); and finally, 2 recovery nights (R1 and R2, both 10h TIB). WinSCAT testing took place daily at 19:00h on B1, B2, SR5, CR1, SR6, SR10 and R1. For the four WinSCAT tasks, % correct and response time were calculated. The number of lapses (responses >700ms) was used for the running memory task.
Results: Significant improvements in response times of all WinSCAT tasks were found across protocol days: code substitution (p=0.001), running memory (p=0.001), match to sample (p=0.001), and mathematics (p=0.001). Match to sample accuracy was the only performance measure that was adversely affected by sleep restriction (B2 to SR5, p=0.018), and code substitution accuracy (p=0.048) and match to sample accuracy (p=0.003) were improved as recovery sleep time increased following sleep restriction.
Conclusion: WinSCAT response times on all task showed continued learning over 8 days, even when sleep was restricted. Only match to sample accuracy was sensitive to both sleep restriction and varying degrees of recovery sleep. Since these conditions are common in space flight, it appears that WinSCAT is not ideally suited to identify fatigue from inadequate sleep in space.
Support (optional): Supported by NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute and NIH RR00040.

0362

REM EXPRESSION INCREASES OVER A 5-DAY PERIOD OF SLEEP RESTRICTION

Kalra G,[1] Banks S,[1] Van Dongen H,[2] Dinges D[1]
(1) University of Pennsylvania School of Medicine, Philadelphia, PA, USA, (2) Washington State University, Spokane, WA, USA

Introduction: It is controversial whether sleep restriction can result in REM sleep homeostasis. We used a chronic sleep restriction paradigm to examine this issue.
Methods: N=58 healthy subjects (22-44y) participated in an 11-day controlled laboratory protocol that included 2 nights of baseline sleep (TIB=10h) followed by 5 nights of sleep restriction (TIB=4h) at 04:00-08:00 hours. PSG data from the first and fifth sleep restriction nights (SR1 and SR5) were analyzed for latency to NREM and REM sleep, and minutes of stages 2, SWS and REM sleep.
Results: Paired t-tests revealed no significant difference between SR1 and SR5 in the following sleep latency measures: latency to sleep onset, latency from stage 1 to 2, latency from wake to SWS, latency from stage 1 to SWS, and latency from stage 2 to SWS. In contrast, REM onset latency was shortened on SR5 relative to SR1 (mean difference = 8.62min, t = 2.28, p = 0.026). The amount of REM sleep also increased significantly (mean difference = 7.88min, t = 3.48, p = 0.001), as did the amount of stage 2 time (mean difference = 9.06min, t = 3.04, p = 0.004).
Conclusion: The reduction in REM latency in the absence of a change in NREM latency, as well as an increase in REM time on the fifth night of sleep restriction relative to first night of sleep restriction, suggests the possibility of elevated homeostatic pressure for REM sleep engendered by sleep restriction. It is unlikely that REM latency shortened because of circadian phase advancement since circadian delay (not advance), accompanies late night sleep restriction. These data suggest that REM sleep homeostasis may play a role in the neurobehavioral effects of late night sleep restriction.
Support (optional): NIH NR004281 and RR00040

0363

REPRODUCIBILITY OF CHANGES IN BEHAVIOR AND FMRI ACTIVATION ASSOCIATED WITH SLEEP DEPRIVATION IN A WORKING MEMORY TASK

Lim J,[1] Choo W,[2] Chee M[3]
(1) University of Pennsylvania, Philadelphia, PA, USA, (2) SingHealth, Singapore, (3) Duke-NUS Graduate Medical School, Singapore, Singapore

Introduction: Although the stability of inter-individual differences in vulnerability to sleep deprivation have been well established behaviorally, there is less clarity regarding the functional imaging counterparts of these differences. In this study, we assessed the reproducibility of fMRI activation and performance on a working memory task before and after 24 hours of sleep deprivation (SD).
Methods: 19 subjects (mean age = 21.37 ± 1.54 years) underwent scans at rested wakefulness (RW) and after SD. Each volunteer underwent four scans- two pairs of RW-SD, or SD-RW scans. The order of scans (RW or SD first) was counterbalanced across participants, but consistent across the duplicate studies within individuals. Subjects performed a Sternberg-like working memory task involving consonant letters. Intra-class correlation coefficients (ICCs) of behavioral metrics and parameter estimates of activation were computed to estimate interindividual variability.
Results: Brain activation was highly correlated across sessions in a fronto-parietal network previously implicated in working memory

function. ICC values in these regions ranged from 0.58 to 0.69. The magnitude of decline in activation after SD was most reliably reproduced in bilateral parietal regions. Among several behavioral metrics investigated, the most reproducible one was the change in the intra-individual coefficient of variation of reaction times following SD. This was shown to be both stable over time and to correlate with the drop in left parietal activation from RW to SD in both experimental sessions.
Conclusion: Our results suggest that parietal lobe activation tracks behavioral deficits in a working memory task following SD in reproducible manner. The correlation between variation in response time and activation indicates that deficits in attention may underlie declines in working memory task performance following SD.
Support (optional): DSO National Laboratories, Singapore (No. DSOCL05141), SingHealth Foundation and the Shaw Foundation

0364

BRAIN ACTIVITY FOLLOWING NORMAL SLEEP PREDICTS PERFORMANCE IMPAIRMENTS FOLLOWING SLEEP DEPRIVATION AND SUBSEQUENT SLEEP RECOVERY

Mander B,[1] Reid K,[1] Tjoa T,[2] Parrish T,[2] Johnson N,[2] Weintraub S,[2] Mesulam M,[2] Gitelman D,[2] Zee P[2]
(1) Northwestern University, Chicago, IL, USA, (2) Northwestern University, IL, USA

Introduction: Performance changes following sleep deprivation (SD) are highly variable across individuals. In the current study, functional magnetic resonance imaging was used to examine whether brain activity after normal sleep (NS) predicted performance impairments following SD and sleep recovery (SR).
Methods: Nine subjects (26.0±3.6 years) underwent MRI scanning at 3T while performing a go/no-go task after 9 hours of NS, after 33-35 hours of SD, and after 10 hours of SR. NS and SD order was counterbalanced. Subjects saw a stream of target and foil symbols. Subjects had to inhibit responses during stop trials defined as those with either foil symbols or where a target symbol was repeated. The percentage of trials in which subjects correctly inhibited a response was compared across sleep states and used as a regressor against brain activity during stop trials. Data were analyzed using SPM2 (http://www.fil.ion.ucl.ac.uk/spm). Small volume correction was used for predetermined middle frontal gyrus (mFG) regions. Results are reported at $p<0.05$ corrected.
Results: Greater anterior cingulate cortex (ACC) activation after NS predicted a greater performance drop following SD and SR. Subjects with more left middle frontal gyrus (mFG) activity following SD and greater left mFG and right amygdala activity following SR showed lesser declines in performance. Greater bilateral parietal activity after NS was associated with a smaller performance drop following SR.
Conclusion: Greater impairment of inhibitory control following SD and SR is predicted by greater ACC activity following NS. ACC Activity during inhibitory events has been associated with impulsivity. The ability to preserve performance following SD and SR depends on the ability to compensate by recruiting more left mFG activity than following NS. These data suggest that performance on an inhibitory task following SD and subsequent SR may reflect differential patterns of brain activity that are observed even when subjects are rested.
Support (optional): Supported by P01 AG11412, M01 RR-00048, R01 HL67604, AG1385, F31 MH074291, and the Northwestern University Cross-School Initiative.

0365

EFFECTS OF INADEQUATE RECOVERY FROM SLEEP RESTRICTION ON THE INFLAMMATORY MARKER C-REACTIVE PROTEIN

Simpson N, Arroyo S, Banks S, Dinges D
University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: Short sleep durations are associated with increased cardiovascular morbidity. One inflammatory marker associated with cardiovascular risk is high-sensitivity C-reactive protein (hs-CRP), which has also been found to increase significantly in response to severe sleep debt. However, it remains unclear if milder sleep deprivation has similar effects on hs-CRP.
Methods: 64 healthy adults (29 men and 35 women; 30.0+6.6 years) were randomized to either a sleep deprivation or control group following two nights of baseline sleep. In the deprivation condition, participants underwent 5 nights of partial sleep restriction (4h time in bed [TIB]), followed by one night of randomly assigned recovery sleep and a final night of 10h TIB. The recovery night conditions were categorized as either “high recovery” (6-10h TIB) or “low recovery” (0-4h TIB). Control participants spent 10h TIB/night. Blood samples were collected prior to sleep restriction (BD1), following the fifth night of 4h TIB (BD2), and following the final 10h night of sleep (BD3).
Results: There was no statistical effect of the 5-night partial sleep deprivation on hs-CRP levels (comparison of BD1 and BD2); however, “low-recovery” sleep was associated with increased hs-CRP levels. Data analyses on log-transformed hs-CRP values revealed a significant increase in hs-CRP levels between BD1 and BD3 ($t=-2.14$, $p=0.042$, effect size = -0.22), as well as BD2 and BD3 ($t=-2.71$, $p=.012$) in the “low-recovery” group." No comparisons within the control condition or the "high recovery” partial sleep deprivation groups reached statistical significance.
Conclusion: Although a five-day period of partial sleep deprivation was not sufficient to produce a significant increase in hs-CRP levels in healthy adults, an additional night of sleep restriction (as occurred in the “low recovery group”) resulted elevated hs-CRP levels even after a subsequent recovery night of sleep. These findings suggest that even modest sleep restriction may potentiate inflammatory processes.
Support (optional): National Institutes of Health/NINR: R01 NR04281-1, RR 00040

0366

ARE SIMPLE AND COMPLEX TASKS EQUIVALENT IN MEASURING DRIVER PERFORMANCE DURING EXTENDED WAKEFULNESS?

Baulk S,[1] Biggs S,[1] Reid K,[2] Van Den Heuvel C,[3] Dawson D[1]
(1) University of South Australia, Adelaide, South Australia, Australia, (2) Northwestern University, Chicago, IL, USA, (3) University of Adelaide, Adelaide, South Australia, Australia

Introduction: Driver fatigue remains a significant cause of motor vehicle accidents worldwide. While new technologies are utilised to improve road safety, there are no effective on-road measures for fatigue. Simulated driving tasks are shown to be sensitive, and simple performance tasks have been used in industrial settings to quantify risk, but little is known about the relationship between such measures. This study aimed to measure fatigue-related performance decrements using simple and complex tasks, and to determine the potential for a link between such measures, to improve fatigue management systems.
Methods: Fifteen volunteer participants (7m, 8f) aged 22-56yrs (mean 33.6y), underwent 26 hours of supervised wakefulness before an 8-hour recovery sleep opportunity. Participants were tested using a 30-minute

interactive driving simulation test, bracketed by a 10-minute PVT at 4, 8, 18 and 24hrs of wakefulness, and following recovery sleep.
Results: Performance varied with extended wakefulness. Significant increases were found in lane drifting ($F[3,36]=11.54$, $p=0.002$) and mean reaction time ($F[3,36]=10.52$, $p=0.006$) as fatigue increased. As predicted, lane drifting was significantly correlated to both RT ($R2 = 0.92$; $p = 0.01$) and lapses ($R2 = 0.93$; $p <0.01$). A Bland-Altman plot was constructed for paired comparisons between these measures, showing a bias of 43.79 (95%CI, 14.7-72.9). The square of the difference between the two performance scores was tested for association with the mean incident score using regression analysis, and found to be statistically significant ($p<0.001$), indicating a systematic error within the measures.
Conclusion: Extended wakefulness caused significant decrements in PVT and driving performance. Although these measures are clearly linked, our analyses suggest that driving simulation cannot be replaced by a simple PVT. Further research is needed to closely examine links between performance measures, and to facilitate accurate management of fitness to drive, which requires more complex assessments of performance than RT alone.
Support (optional): This study was supported by the Australian Transport Safety Bureau.

0367

THE DISCREPANCY BETWEEN OBJECTIVE PERFORMANCE IMPAIRMENT AND SUBJECTIVE SLEEPINESS DURING SLEEP DEPRIVATION IS NOT SOLELY DUE TO REPORT BIAS

Grant D,[1] Dinges D,[2] Van Dongen H[1]
(1) Washington State University, Spokane, WA, USA, (2) University of Pennsylvania, Philadelphia, PA, USA

Introduction: Several studies have shown that differences among individuals in objectively measured performance impairment during sleep deprivation do not coincide with differences in self-reported sleepiness. The reason for this discrepancy remains unclear.
Methods: 21 healthy adults (11f, 10m, ages 22–40y) spent eleven consecutive days in a sleep laboratory. They were exposed to three 36h total sleep deprivation periods, each preceded and followed by two recovery nights (12h TIB). Throughout scheduled wakefulness, neurobehavioral performance and subjective sleepiness were tested every 2h. Tests included the Karolinska Sleepiness Scale (KSS), yielding a self-reported score of sleepiness; and the Psychomotor Vigilance Test (PVT), for which the number of lapses was determined. Within subjects, grand averages across the last 24h of sleep deprivation were assessed. Z-transformations were applied to allow comparison of PVT and KSS results across the sample. Subtracting each subject´s KSS Z-score from his/her PVT Z-score produced an overall discrepancy score. Prior to the experiment, subjects completed the Marlowe-Crowne Social Desirability Scale, yielding a social desirability response bias score; and the Minnesota Multiphasic Personality Inventory (MMPI-2), for which T-scores were calculated of the three validity scales F, K and L. These scales measure response bias from intentional or unintentional infrequent response patterns, overcorrection, and defensiveness, respectively. Social Desirability Scale and MMPI-2 scores were correlated with subjects´ objective/subjective discrepancy scores.
Results: The MMPI-2 F scale correlated with the objective/subjective discrepancy ($r=0.49$; $P=0.025$), but this correlation was in the wrong direction to provide a meaningful explanation for the objective/subjective discrepancy scores. Correlations for the other scales were non-significant ($|r|<0.31$; $P>0.17$).
Conclusion: There was no evidence that the discrepancy between objective performance impairment and subjective sleepiness during sleep deprivation was a function of trait psychological tendencies for biased self-reporting. The discrepancy may therefore be physiological in nature—sleep deprivation may impair the ability to self-evaluate.
Support (optional): NIH grants HL70154 and RR00040

0368

SLEEP HOMEOSTATIC REGULATION AND RESTORATIVE PROCESSES FOLLOWING SLEEP DEPRIVATION AND RECOVERY SLEEP

Trksak G,[1] Dorsey C,[2] Jensen J,[3] Tartarini W,[4] Juliano T,[4] Su Z,[5] Cuadra B,[4] Kaufman M,[3] Renshaw P,[3] Lukas S[6]
(1) Behavioral Pharmacology Research Laboratory, Mclean Hospiatal/Harvard Medical School, Belmont, MA, USA, (2) SleepHealth Centers, Sleep Research Program, Mclean Hospital/Harvard Medical School, MA, USA, (3) Brain Imaging Center, Mclean Hospital/Harvard Medical School, MA, USA, (4) Sleep Research Program, McLean Hospital, MA, USA, (5) Behavioral Pharmacology Research Laboratory, McLean Hospital, MA, USA, (6) Behavioral Pharmacology Research Laboratory, McLean Hospital, Harvard Medical School, MA, USA

Introduction: Sleep deprivation (SD) is a principal research tool used for studying sleep-regulating mechanisms and sleep homeostasis. Increases in slow wave activity (SWA) have been demonstrated during recovery sleep following SD. Adenosine has been implicated to promote slow EEG potentials and that prior wakefulness results in an accumulation of adenosine. This may reflect a SD-induced disruption of restorative sleep, as adenosine is a degradation product of adenosine triphosphate (ATP) that is transported in response to enhanced metabolic demands. A greater understanding of SWA and its relationship to brain high-energy phosphates may be crucial in elucidating homeostatic sleep processes and the function of sleep.
Methods: We examined 11 control, 8 short-term, and 6 long-term methadone-maintained subjects in a SD paradigm that consisted of baseline, SD (36 hours), and two nights of recovery sleep. Sleep was recorded polysomnographically and phosphorous MRS scans performed each morning using a Varian INOVA 4 Tesla MR system with a dual proton/phosphorus head-coil.
Results: All subjects experienced significant ($p<.05$) increases in slow wave sleep during the first recovery night. MRS data demonstrated that control subjects exhibited significant ($p<.05$) increases in beta-NTP and phosphocreatine during SD and a more pronounced increase following recovery sleep. A similar profile of beta-NTP during SD and following recovery sleep was observed in methadone subjects, with the largest effects in short-term subjects, while long-term subjects were more similar to controls.
Conclusion: Results suggest that brain chemistry is indeed altered in normal sleepers following SD, but homeostatic processes appear to regulate ATP over the course of recovery sleep. The restoration of brain energy metabolism may be central to sleep function. The enhanced SD-induced effects in brain ATP in methadone subjects may reflect an altered ability, particularly in short-term methadone subjects to respond to insults on the homeostatic sleep process.
Support (optional): NIDA grants DA016542, T32DA15036, KO2DA017324, K24DA15116, and KO5DA00343.

0369

AVIAN SLOW-WAVE SLEEP HOMEOSTASIS

Rattenborg N, Martinez-Gonzalez D
Max Planck Institute for Ornithology - Seewiesen, Starnberg, Bavaria, Germany

Introduction: Like mammals, birds exhibit slow-wave sleep (SWS) and rapid eye-movement (REM) sleep. Unlike mammals, however, previous studies did not find an increase in EEG slow-wave activity (SWA) following sleep deprivation (SD) in birds. Herein we show an increase in SWS-related SWA at night following short-term SD during the day in pigeons (Columba livia).
Methods: Six bipolar EEG channels were recorded from five pigeons during two consecutive 24-hour periods under a 12:12 LD photoperiod. The first 24 hours served as a baseline. On the second day, the pigeons were kept awake for the last 8 hours of the light phase using gentle handling. At lights out, the birds were allowed to sleep undisturbed. Wakefulness, SWS and REM sleep were scored visually for each 4-second epoch using EEG and video recordings. FFTs were used to calculate spectral power. SWS-related SWA (0.4-4.0 Hz) was averaged for each quartile of each night, and expressed as a percentage of the average for the entire baseline night.
Results: Daytime sleep was reduced from 51.26±3.20% (mean±SD) during baseline to 8.42±7.42% during SD ($P<0.001$; two-tailed paired t-test). Although SD did not affect time spent in each state during the recovery night ($P>0.05$), SWA increased significantly during SWS. In contrast to the baseline night, where SWA deviated little from the nighttime average, SWA during recovery was highest in the first quartile and then declined across the night. SWA during the first quartile of recovery was elevated by 12.48±7.85% to 27.33±15.50% ($P=0.06$ to 0.004). The increase in SWA was most pronounced in the hyperpallium and similar between hemispheres.
Conclusion: The comparatively short duration of SD employed herein may explain why SWA increased in this, but not previous studies. Although the increase in SWA was markedly less than in mammals, the general pattern is consistent with the notion that birds exhibit SWS homeostasis.
Support (optional): Max Planck Society

0370

COCAINE-INDUCED GENITAL REFLEXES IN PARADOXICAL SLEEP DEPRIVED RATS: INDICATIONS OF MEDIATION BY SEROTONIN RECEPTORS

Andersen M, Antunes I, Tufik S
Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil

Introduction: As paradoxical sleep deprivation (PSD) modifies cocaine-induced genital reflexes (penile erection [PE] and ejaculation [EJ]) and since cocaine is a serotonin (5-HT) reuptake inhibitor, we hypothesized that 5-HT also plays a role in these genital reflexes in PSD male rats.
Methods: After a four-day period of PSD each group was administered with serotonergic drugs prior to cocaine and placed in observation cages for genital reflexes evaluation.
Results: The selective 5-HT1 agonist (8-OH-DPAT) completely abolished PE events whereas the antagonist (pindolol) did not produce significant effects in the number of animals displaying PE. It was found that both drugs reduce the frequency of PE. There were not significant effects on the number of animals that ejaculated or in its frequency after pindolol although both parameters were reduced by the agonist at the highest doses (2 and 4 mg/kg, SC). Pretreatment with the 5-HT2 agonist 1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI) (0.12; 0.5 and 1 mg/kg, SC) significantly reduced the number of rats displaying PE and all doses reduced both PE and EJ frequencies. The number of animals displaying PE after 5-HT2 antagonist (ketanserin) pretreatment at 1 and 2.5 mg/kg doses was significantly decreased in relation to vehicle rats and all doses reduced PE frequency. 5-HT2 compounds at any dose did not affect the number of animals ejaculating, but the frequency was significantly reduced by all doses of DOI and by 1 to 5 mg/kg doses of ketanserin.
Conclusion: Taken together, the results suggest that serotonergic receptors play an important role in genital reflexes induced by cocaine in sleep deprived males.
Support (optional): AFIP andFAPESP

0371

PROGESTERONE REDUCES ERECTILE DYSFUNCTION IN SLEEP-DEPRIVED SPONTANEOUSLY HYPERTENSIVE RATS

Andersen M,[1] Martins R,[2] Alvarenga T,[2] Antunes I,[2] Papale L,[2] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil

Introduction: Paradoxical sleep deprivation (PSD) associated with cocaine has been shown to enhance genital reflexes, specifically penile erection (PE) and ejaculation (EJ) in rats. Since hypertension predisposes men to erectile dysfunction, the present study investigated the effects of PSD on genital reflexes induced by saline and cocaine in the spontaneously hypertensive rat (SHR) compared to the Wistar strain. We also examined how PSD affected steroid hormone concentrations in both strains.
Methods: After a four-day period of PSD each group was administered with saline or cocaine and placed in observation cages for genital reflexes evaluation.
Results: Four-day period of sleep deprivation induced PE in 50% of the Wistar rats against 10% for the SHR. This effect was potentiated by cocaine; but the SHR still showed significantly fewer PE and EJ events than the Wistar strain. Ejaculatory behavior was shown by 20% of both SHR and Wistar rats. As for hormone concentrations, both sleep-deprived Wistar and SHR showed lower testosterone concentrations than their controls. Progesterone concentrations were higher in PSD-Wistar rats than in controls, whereas no significant alterations were found after PSD in the SHR strain. In order to explore the role of progesterone in the occurrence of genital reflexes, PSD-SHR were treated daily with progesterone; there was a significant increase in erectile events compared with the SHR+vehicle+cocaine-challenged group.
Conclusion: Our data showed that the low frequency of genital reflexes found in SHR may be attributed to the absence of high concentrations of progesterone in PSD rats, since progesterone replacement was found to reduce this inhibitory effect.
Support (optional): AFIP and FAPESP

0372

EFFECTS OF LONG-TERM FOOD RESTRICTION ON GENITAL REFLEXES IN MALE PARADOXICALLY SLEEP DEPRIVED RATS

Alvarenga T,[1] Andersen M,[2] Papale L,[1] Tufik S[2]
(1) Univ Fed Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil

Introduction: The purpose was to ascertain whether the different schedules of long-term food restriction (FR) exert influence on genital reflexes (penile erection-PE and ejaculation-EJ) induced by paradoxical sleep deprivation (PSD) in male rats.
Methods: Diet restriction began at weaning with 6g/day and food was increased by 1 g per week until reaching 15g/day by adulthood. Rats

submitted to FR and those fed ad libitum were distributed into PSD (96 hours) or maintained as control groups and challenged with saline or cocaine, and placed in observation cages.
Results: PSD+saline induced PE and EJ in both ad libitum and FR groups, but cocaine only potentiated reflexes in ad libitum group. In an attempt to revert the effects of FR on genital reflexes, we provided food ad libitum to the restricted group during the PSD period (4 days). When compared to FR rats, an increase in the frequency of PE was observed in the FR group fed ad libitum during PSD (both groups were challenged with cocaine). Further, we sought to investigate motivational behavior by placing food within the behavioral cage during the evaluation of genital reflexes. The FR PSD+saline group challenged with food did not display genital reflexes but when injected with cocaine the responses were similar to those observed in FR PSD+cocaine rats not challenged with food.
Conclusion: Our data suggest that the facilitatory effect of PSD on genital reflexes did not override the inhibitory effect of FR on erectile function, but different schedules of FR produce distinct effects on genital reflexes.
Support (optional): AFIP and FAPESP

0373

EFFECTS OF COX-2 INHIBITOR IN ACUTE INFLAMMATION OF THE TEMPOROMANDIBULAR JOINTS (TMJ) OF RATS

Schutz T, Andersen M, Tufik S
Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil

Introduction: Freund´s adjuvant (FA) into the temporomandibular joint (TMJ) of rats induce an experimental orofacial pain (OFP) model. The objective of this study was to determine whether the Cyclooxygenase-2 enzyme (COX-2) and prostaglandins were involved in the altered sleep-wake pattern and in the TMJ pain.
Methods: Animals were injected with saline and recorded to obtain the SHAM values. In another group, the animals (OFP group) were injected with FA in TMJ and then the sleep was monitored during two consecutive days. In other phase of the study, after injection the FA or saline, COX-2 inhibitor, etoricoxib (Arcoxia), was administered (90 mg/kg p.o.) at 0700 a.m. on the first day.
Results: The OFP group showed a reduction in sleep efficiency, in non-rapid eye movement (nREM) sleep and in rapid eye movement (REM) sleep, and an increase in sleep latency and in REM sleep latency only in the light periods compared with SHAM group, reaffirming that this orofacial pain model altered sleep patterns in rats. The p.o. administration of etoricoxib to OFP group increased sleep efficiency, nREM and REM sleep. The levels of these parameters returned progressively to those found in the SHAM group. The COX-2 inhibitor also reduced sleep latency and REM sleep latency in OFP animals treated with this drug. The isolated COX-2 inhibitor specifically enhanced the REM sleep in relation to animals injected with saline (SHAM group).
Conclusion: Treatment with etoricoxib improved the sleep parameters suggesting the involvement of COX-2 enzyme in painful TMJ conditions and, specifically, in REM sleep.
Support (optional): AFIP and FAPESP

0374

EFFECTS OF SLEEP LOSS ON SLEEP ARCHITECTURE IN WISTAR RATS: GENDER-SPECIFIC COPING STRATEGIES FOR REBOUND SLEEP

Antunes I,[1] Andersen M,[1] Baracat E,[2] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, SP

Introduction: There is an increasing concern about risks related to sleepiness in our society. Although sleep deprivation has a dramatic impact on multiple physiological process, it is not yet clear which factors contribute the most to the sleep disturbances reported in the female organism. The purpose of the study was to examine whether gender exerts influence upon sleep rebound architecture after a 4-day paradoxical sleep deprivation (PSD) period in rats.
Methods: After five days of baseline sleep recording, male and female Wistar rats were submitted to 96h PSD according to the phase of the estrous cycle (proestrus, estrus and diestrus). Immediately after the PSD period, all rats returned to their home-cage for sleep recording during a five-day recovery period (equivalent to one estrous cycle).
Results: Our results demonstrated that the estrous cycle had undetectable influence in the sleep pattern during baseline recording. Although PSD provoked a significant increase in PS on the first day of the rebound dark period in all groups, proestrous, estrous and constant diestrus (Da), in contrast to cyclic diestrus (Dc) and males, maintained this increase until the second day of the rebound dark period. Of note, Da was the only group in which PS remained enhanced on the second day of the rebound period but not enough to be considered statistically different from the first day.
Conclusion: Our findings indicate that Da females, which presented prolonged diestrus induced by PSD, are as susceptible to PSD as females in proestrous because in both phases alterations in sleep pattern increased the time needed to return to baseline values. It seems that females have a distinct sleep mechanism that might be regulated by hormonal factors that influence the duration of the sleep recovery.
Support (optional): AFIP, FAPESP and CEPID

0375

EFFECTS OF SLEEP DEPRIVATION OR SLEEP REBOUND ON MEMORY OF FEMALE RATS: INFLUENCE OF AGE

Antunes I,[1] Andersen M,[1] Alvarenga T,[2] Patti C,[3] Calzavara M,[3] Lopez G,[3] Silva R,[3] Frussa-Filho R,[3] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil, (3) Univ Fed Sao Paulo, SP

Introduction: It is widely accepted that cognitive ability steadily declines while sleep disturbances increase with advanced age. Sleep disorders, such as insomnia, are often reported by women in perimenopause and postmenopausal period. The present purpose was to investigate possible differences in age-related memory ability, by utilizing the plus-maze discriminative avoidance task in sleep-deprived female rats.
Methods: Female rats at different ages (5-, 7- and 15-month-old) were submitted to the plus-maze discriminative avoidance task. In the training session, each animal was placed in the center of the apparatus and, over a period of 10 min, every time the animal entered the aversive enclosed arm (containing a lamp), an aversive situation was produced until the animal left the arm. In the test session, the animal was again placed in the apparatus, for 3 min, without receiving the aversive stimulation. After the training session, the animals were returned to their home-cage for 96h (control group), while the remaining rats were submitted to paradoxical sleep deprivation (PSD) for 96h. Immediately after this

period, half of sleep-deprived rats were submitted to the test session while the other half returned to their home-cages and were allowed to sleep for 24h (rebound group) before being tested.
Results: In control (non-sleep-deprived) rats no memory deficits was verified irrespective from age. Paradoxical sleep-deprived rats at the age of 15 months (but not 5 or 7 months) presented a memory deficit. In addition, a memory deficit was observed in the rebound period regardless the age.
Conclusion: Paradoxical sleep deprivation and advanced age combine mutually to produce memory deficits in female rats. Paradoxical sleep rebound was more effective than sleep deprivation to produce memory deficits in female rats, ocurring irrespectively from the age group of the animals.
Support (optional): AFIP, FAPESP and CAPES

0376

RENAL SYMPATHETIC ACTIVATION INDUCED BY PARADOXICAL SLEEP DEPRIVATION IN RATS

Perry J,[1] Carvalho R,[2] Carillo B,[2] Campos R,[2] Bergamaschi C,[2] Andersen M,[1] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil

Introduction: It has been proposed that both hypoxia and sleep fragmentation are implicated in cardiovascular risk associated to obstructive sleep apnea. Thus, the present study was designed to determine the effects of acute and subchronic exposure to sleep deprivation in heart rate, blood pressure, splancnic sympathetic nerve activity and renal sympathetic nerve activity in rats. Moreover, we evaluated the effects of sleep deprivation in serum creatinine concentration.
Methods: Wistar-Hannover male rats (n=6-8/group) were randomly assigned to three treatment groups: 1) control, 2) acute paradoxical sleep deprivation for 24 hours (PSD24h), 3) subchronic paradoxical sleep deprivation for 96 hours (PSD96h) using the single platform method.
Results: Subchronic PSD96h increases heart rate compared to control group (control 394±51 vs. PSD96h 475±20; $p<0.05$). No significant statistical differences were observed on blood pressure and splancnic sympathetic nerve activity among groups. However, renal sympathetic nerve activity was increased in all treated groups (control 103 ± 29; PSD24h 147±19; PSD96h 147±40; Hz; $p<0.05$). Acute and subchronic PSD increases serum creatinine compared to control group ($p<0.01$).
Conclusion: The results suggest that both acute and subchronic exposure to PSD may produce an increase in sympathetic activity, preferentially in the kidney. These results may be related to increases of serum creatinine.
Support (optional): AFIP, FAPESP, CEPID, CNPq

0377

SHORT SLEEP DURATION AND OBESITY: EVIDENCE FROM POPULATION-BASED STUDIES IN CHILDREN, ADOLESCENTS AND ADULTS ACROSS THE WORLD

Cappuccio F
University of Warwick, Coventry, England, United Kingdom

Introduction: Night-time sleep duration may be a risk factor for the development of obesity. We performed a meta-analysis of population-based studies to assess the evidence and to obtain a quantitative estimate of the risk of obesity in short sleepers.
Methods: We searched publications using MEDLINE, EMBASE, CINHAL and PsycINFO without language restrictions. Inclusion criteria were: duration of sleep as exposure, BMI or obesity as outcomes. We used a random effect model. Influence analysis, heterogeneity and publication bias were checked.
Results: Of 285 studies identified, 26 met the inclusion criteria (9 in children and adolescents and 17 in adults) and 17 (9 and 8, respectively) provided suitable data. They included 537,299 participants (28,337 children and adolescents and 508,912 adults) worldwide. Age ranged from 2 to 102 years and included boys, girls, men and women. In children and adolescents the pooled OR was 1.90 (95% CIs 1.41 to 2.55; $p<0.001$). Publication bias was detected by the Egger's test ($p=0.024$) but not by the Begg's test ($p=0.175$). Heterogeneity was significant ($p<0.001$) and attenuated by stratification by study's size ($p=0.019$). In adults the pooled OR was 1.84 (1.44 to 2.35; $p<0.0001$). There was no evidence of publication bias. Heterogeneity was significant ($p=0.004$) and attenuated by stratification by age, study's size and the cut-off for short sleep duration. The &beta coefficient for short sleep duration was -0.40h (-0.56 to -0.24) for unit increase in BMI. In four prospective studies those sleeping less than 5h per night were more likely to develop obesity over time.
Conclusion: Population-based studies show a consistent association between short sleep duration and obesity in children, adolescents and adults worldwide and a two-fold increased risk of obesity amongst short sleepers. Causal inference is difficult due to lack of control for important confounders. There is scientific evidence for temporal sequence and biological mechanisms.

0378

CAFFEINE MAINTAINS VIGILANCE DURING A 74-HOUR FIELD TEST WITH LIMITED SLEEP

Kamimori G,[1] Reichart R,[1] Voss D,[2] Tate C,[3] Mclellan T,[4] Smith S,[5] Lieberman H[6]
(1) Walter Reed Army Institute of Research, Silver Spring, MD, USA, (2) New Zealand Defence Force, Kohimarama, Auckland, New Zealand, (3) New Zealand Defence Force, Papkura, Auckland, New Zealand, (4) University of Toronto, Toronto, Ontario, Canada, (5) Defence Science & Technology Laboratories, Salisbury, United Kingdom, (6) Natick, MA, USA

Introduction: We have previously reported that caffeine gum had a significant positive affect on vigilance during 73-hr period without sleep. This study examined the ability of caffeine gum to sustain vigilance during a 74 hr simulated military field operation in which only a limited amount of sleep was available.
Methods: Twenty soldiers were randomly assigned to placebo (PLA) or caffeine (CAF) treatment. After completing a normal duty day (Day 1) with full nights sleep period, volunteers reported for duty at 0700 (Day 2) and trained until 1600 when the field exercise began. They completed a variety of field tasks during the night with no sleep permitted until the following day (Day 3) when they were allowed a 4 hr sleep period (1330-1730). This sleep period was repeated on Day 4. During Nights 2, 3 & 4 volunteers chewed two sticks of gum containing placebo or 200 mg of caffeine (100 mg/piece) at 2200, 0115, 0400, and 0700. Performance was assessed with a 120 min field vigilance task (FVT) administered seven times; on the evening of Day 1 (baseline control) and at 0130 and 0415 on Night 2, 3 and 4. The FVT presented a brief, < 5 sec duration, visual stimulus to which the soldier responded as rapidly as possible. A stimulus was presented randomly once in each 20 min time interval.
Results: Data were analyzed with a 2x3 factorial ANOVA with session as a within-subject factor. The caffeine gum improved performance on the FVT on all 3 test nights, with the CAF group performing significantly better ($p < 0.05$) on Nights 3 and 4 compared to the PLA group.

Conclusion: This study demonstrates that caffeine significantly improves performance of a monotonous field vigilance task during night operations when only limited opportunities for sleep are available.

0379

AIRCRAFT NOISE EFFECTS ON SLEEP: DLR RESEARCH RESULTS AND THEIR APPLICATION

Samel A,[1] Basner M,[2] Isermann U[3]
(1) DLR - Institute for Aerospace Medicine, Köln, Germany, (2) Deutsches Zentrum für Luft- und Raumfahrt, Köln, Germany, (3) Deutsches Zentrum für Luft- und Raumfahrt, Göttingen, Niedersachsen, Germany

Introduction: DLR studied nocturnal aircraft noise effects in laboratory and field experiments for developing sound criteria for protecting residents living near airports.
Methods: In the laboratory, 128 subjects (18-65 years, 53 male) were polysomnographically examined during 13 consecutive nights. 4 to 128 aircraft noise events (ANEs) were applied per night with maximum sound pressure levels (maxSPLs) between 45 and 80 dBA. Results were validated in the field with 64 subjects (19-61 years, 29 male) living near Cologne airport during 9 consecutive nights.
Results: In the laboratory and based on TIB, aircraft noise lead to sleep fragmentation, as amounts of Stage 1 (+2.2 min, p<.001) and number of awakenings (+3.5, p<.001) increased with noise exposure. SWS decreased by 5.3 min (p<.001). Unexpectedly, TST increased on average by 2.5 min (p=.354), most probably caused by reduction of sleep onset latency (-3.1 min, p=.002) and decrements in the duration of spontaneous awakenings in exposure nights. Both may be attributed to minor partial sleep deprivation accumulated during previous exposure nights. Dose-response relationships with both increasing number and maxSPL of ANEs were observed as well as a prominent first-exposure-night effect. In the field, aircraft noise obviously did not change sleep structure. Additionally, at the same maxSPL awakening probability was much lower compared to the laboratory.
Conclusion: Based on the field results, new criteria for protecting residents against nocturnal aircraft noise were developed for the extension of Airport Leipzig/Halle. The protection plan indicates: (1) on average, less than one additional awakening should be induced by aircraft noise, (2) awakenings recalled in the morning should be avoided, (3) aircraft noise should interfere with the process of falling asleep again as little as possible.
Support (optional): Financially supported within the DLR/HGF-project "Quiet Air Traffic" and within the HGF Virtual Institute "Transportation Noise Effects on Sleep and Performance" (grant VH-VI-111).

0380

ENDOCRINE ORCHESTRATION FOR BODY WEIGHT CONTROL DURING SLEEP DEPRIVATION IN RATS

Martins P, D'Almeida V, Tufik S
Universidade Federal de São Paulo, São Paulo, Brazil

Introduction: Epidemiological studies have shown a negative relationship between daily sleep hours and body mass index. However, rats differ from humans, since their weight does not increase with sleep deprivation. In the present study our aim was to investigate the body weight homeostatic control of rats, assessing their feeding behavior, hormones and glycogen storage responses to sleep deprivation. Recently we have shown that sleep deprived rats receiving chow pellets have impairment in food access and therefore a liquid diet have been offered in order to solve this inconvenience.
Methods: The protocol was accomplished by sleep depriving rats for 24 up to 96 hours by platform method or 96 hours of sleep deprivation followed by 24 hours of recovery.
Results: We found a mild body weight reduction despite an increased food intake during 96h of sleep deprivation by platform technique. Furthermore, liver glycogen, blood leptin and insulin were reduced while glucagon and norepinephrine concentrations were increased in this condition. After 24h of sleep recovery the majority of these changes was restored despite of low food intake.
Conclusion: These data suggest that sleep deprivation increases the energy demand and consequently decreases body weight. Body weight decrease triggers hormonal changes to activate catabolism and increase food intake. The failure in recovering weight under hyperphagic behavior led us to propose that factors such as sleep seek or stress overlap the feeding drive avoiding the equilibrium in energy balance during sleep deprivation.
Support (optional): FAPESP CNPq and AFIP.

0381

INCREASE OF CIRCULATING CATECHOLAMINES AFTER 21 DAYS OF SLEEP RESTRICTION IN RATS

D'Almeida V, Martins P, Tufik S
Universidade Federal de São Paulo, São Paulo, Brazil

Introduction: The platform technique is the strategy most widely used to deprive rats of sleep and thoroughly characterized. Likewise by others techniques, a hyperphagia-weight loss paradox have been established in rats chronically sleep deprived by platforms. However, recent studies have proposed that sleep restriction protocols would be more reliable to investigate consequences of chronic sleep loss. In humans, restriction or reduction of sleep has been associated to hormonal changes compatible to increased hunger supporting a negative relationship between sleep hours and body mass index.Our aim was to study hormonal and metabolic responses of rats submitted to sleep restriction receiving a liquid diet.
Methods: The protocol was accomplished by sleep depriving rats for 18 h everyday for 21 days by platform method and allowing them to sleep from 10:00 to 16:00.
Results: In opposition to others sleep deprivation protocols, no compensatory hyperfagia was found during 21 days of sleep restriction in rats receiving a liquid diet. Sleep restricted rats showed no changes in parameters such as body weight, glycogen, ghrelin or glucagon, despite of insulin and leptin reductions and norepinephrine and epinephrine significant increases.
Conclusion: In conclusion, sleep restriction increases sympathetic activity and decrease leptin as described in some clinical studies, which suggest this protocol as more reliable to study metabolic consequences of sleep loss.
Support (optional): Supported by FAPESP, CNPq and AFIP.

0382

PHENOTYPING NEUROBEHAVIORAL AND COGNITIVE RESPONSES TO PARTIAL SLEEP DEPRIVATION

Goel N, Lakhtman L, Basner M, Banks S, Dinges D
University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: Differential vulnerability to sleep loss assayed by cognitive and behavioral responses has been demonstrated in subjects undergoing total sleep deprivation, but has not been quantified in partial sleep restriction protocols. This study defined such heterogeneity by phenotyping responses to chronic partial sleep loss.
Methods: N = 120 healthy adults (M=29.9y ± 6.8y; 60 females) completed 2 baseline sleep nights (TIB=10h) followed by 5 sleep

restriction nights (TIB=4h). N = 13 subjects were controls (M=29.0y) completing 7 nights of 10h TIB. The 10-min Psychomotor Vigilance Test (PVT), Digit Symbol Substitution Task (DSST), Karolinska Sleepiness Scale (KSS) and "Fresh-Tired" visual analog scale (VAS) were administered every 2h on all days. PVT responses (baseline to day 5 of sleep restriction) were used to identify three groups: Type 1 responders (n=24) were 1+ standard deviations (SD) below the mean; Type 3 responders (n=22) were 1+ SD above the mean; and Type 2 responders (n=74) were within 1 SD of the mean. ANOVA compared differences in DSST, KSS, and VAS outcomes to sleep restriction among PVT response types.
Results: Baseline DSST, VAS and KSS measures did not differ among the PVT response groups. Compared with Type 1 PVT responders, Type 3 responders had fewer correct DSST responses (p=0.007) during sleep restriction, and higher KSS (p=0.02) and VAS fatigue scores (p=0.003). By contrast, Type 1 PVT responders and control subjects showed no differences between baseline and sleep restriction on DSST, KSS, and VAS measures.
Conclusion: Type 3 responders categorized for their PVT vulnerability to sleep restriction, also showed consistent differential vulnerability in cognitive (DSST) performance and subjective sleepiness and fatigue. By contrast, Type 1 responders were similar to control subjects, showing neither cognitive nor subjective responses to partial sleep loss. These data suggest that stable inter-individual differences exist in neurobehavioral vulnerability to partial sleep loss.
Support (optional): Supported by NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute and by NIH NR004281 and RR00040.

0383

MSLT DEFINED SLEEPINESS PREDICTS VERIFIED AUTOMOTIVE CRASHES IN THE GENERAL POPULATION

Drake C,[1] Scofield H,[1] Jefferson C,[2] Roehrs T,[1] Breslau N,[3] Johnson E,[4] Myers E,[5] Roth T[1]
(1) Henry Ford Hospital Sleep Disorders and Research Center, Detroit, MI, USA, (2) MI, USA, (3) Michigan State University, East Lansing, MI, USA, (4) RTI International, NC, USA, (5) Henry Ford Hospital Sleep Disorders and Research Center, MI, USA

Introduction: The Multiple Sleep Latency Test (MSLT) is the most widely used and validated measure of physiologic sleep tendency. However, the direct relationship between the MSLT and risk for documented traffic accidents has never been quantified in the general population. The present study was aimed at determining the risk for verified automotive crashes at standard MSLT cutoffs in a large representative sample.
Methods: A total of 618 individuals (mean age = 41.6 ± 12.8; 48.5% male) were recruited from the general population of southeastern Michigan using random-digit dialing techniques. Individuals completed a ~24-hr sleep laboratory visit including an 8.5 hour polysomnogram and a 5-nap MSLT that were administered and scored according to standard criteria. Police report data on traffic accidents was obtained from the state police for each individual for the period from 1995 to 2005. Subjects were divided into three groups based on their average MSLT latency in minutes (excessively sleepy ≤ 5[n =69]; borderline >5 to ≤ 10[n=204]; and alert > 10[n=345]). Cochran-Armitage Trend Test was used to determine the relationship between MSLT and accidents across the groups.
Results: The prevalence rates for accidents in the 3 MSLT groups were: excessively sleepy=59.4%, borderline=52.5%, alert=47.3%. Subjects with lower MSLTs were at significantly greater risk for all accidents compared to individuals with higher MSLTs (p=.048). A similar relationship was present for severe injury accidents (sleepy=4.3%, borderline=0.5%, alert=0.6%; p=.028). Finally, for single occupant accidents subjects in the lowest MSLT group had the greatest risk for crashes compared with alert individuals (sleepy=52.2%, borderline=42.2%, alert=37.4%; p=.022).
Conclusion: These are the first data to demonstrate a greater risk for objectively verified automotive accidents in individuals identified as excessively sleepy using standard laboratory assessed MSLT values in a population-based sample. These findings provide evidence for the relationship between objectively determined sleepiness and an important real world outcome, automotive crashes.
Support (optional): NIMH grants: 59338 and 68372

0384

NEUROBEHAVIORAL AND COGNITIVE DIFFERENCES DURING TOTAL VERSUS PARTIAL SLEEP DEPRIVATION

Goel N, Lakhtman L, Basner M, Banks S, Dinges D
University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: Because subjects show varying neurobehavioral and cognitive responses to sleep loss, we examined the same individuals in repeated studies to systematically assess the differential impact of partial sleep deprivation (PSD) versus total sleep deprivation (TSD).
Methods: N=19 healthy adults (30.5y ± 6.9y; 11 females) completed 2 separate laboratory protocols: a PSD study (2 nights of baseline sleep [TIB=10h] followed by 5 nights of sleep restriction [TIB=4h]), and a TSD study (one night of baseline sleep [TIB=8h] followed by 40h without sleep). In both studies, the 10-min Psychomotor Vigilance Test (PVT), Digit Symbol Substitution Task (DSST), and Karolinska Sleepiness Scale (KSS) were administered every 2h while awake. Paired t-tests examined differences in measures between studies.
Results: Baseline values for the three outcomes did not differ significantly between studies. TSD produced significantly greater changes in all three outcomes than 5 nights of 4h PSD (PVT lapses were more frequent with TSD [p=0.02]; DSST correct responses were fewer with TSD [p<0.001]; and KSS ratings were higher with TSD [p<0.001]). Despite TSD producing greater neurobehavioral impairment than PSD, changes in PVT reaction times induced by TSD and PSD were highly correlated (r=0.95, p<0.001).
Conclusion: Forty hours of total sleep loss is more debilitating than 5 nights of 4h sleep on neurobehavioral, cognitive and self-rated measures in the same subjects undergoing both protocols.
Support (optional): Supported by the Department of Homeland Security´s Transportation Security Laboratory Human Factors Program (FAA #04-G-010), NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute and NIH NR004281 and RR00040.

0385

EFFECT OF SLEEP DEPRIVATION ON COGNITIVE INHIBITION TASK AND NEURAL ACTIVATION IN YOUNG AND OLD ADULTS

Meloy M,[1] Wetherell L,[2] Salamat J,[3] Drummond S[4]
(1) University of California San Diego and Veterans Affairs San Diego Healthcare System, San Diego, CA, USA, (2) University of California, San Diego and Veterans Affairs SanDiego Healthcare System, CA, USA, (3) Veterans Affairs San Diego Healthcare System, Research Service, San Diego, CA, USA, (4) University of California, San Diego and Veterans Affairs San Diego Healthcare System, San Diego, CA, USA

Introduction: Studies have used functional magnetic resonance imaging (fMRI) to examine neural correlates of inhibition in young adults,

including during total sleep deprivation (TSD). No studies have examined inhibition during TSD in older adults. Here, we examined cerebral activation before and after 36hrs TSD in younger and older adults, and hypothesized that after TSD older adults would demonstrate increased activation with relatively intact performance, relative to younger adults.
Methods: Participants performed a go-nogo task while in the fMRI scanner after 12 and 36 hours of wakefulness. Task performance was analyzed for 11 old/8 young (age=68.0 +/-5.0; 27.6 +/-5.9); fMRI data was analyzed for 9 old/9 young (age=68.3 +/-5.5 ; 27.6 +/-6.2). Analyses focused on inhibition (i.e., "nogo") trials.
Results: Older adults showed smaller increases in errors during TSD relative to younger adults (Older: 9.4% +/-6.4% vs 9.9% +/-5.9% ; Younger: 8.1% +/-6.7% vs 24.6% +/-25.3%). Imaging results showed an interaction between group and night with increased activation in the older compared to young adults after TSD. Increased regions of activation for the older adults during inhibition trials included bilateral anterior cingulate (ACC), left superior and middle frontal gyri (SFG, MFG), right precuneus (PC) and right superior and inferior parietal lobules (SPL, IPL). Two regions in the bilateral paracentral lobule (PCL) showed decreased activation for older adults after TSD.
Conclusion: A non-significant decline in older adult performance was accompanied by increased activation, suggesting compensatory processes, in regions associated with response conflict, motor inhibition, and cortical attention. Findings suggest two types of compensatory responses: 1) greater activation in regions typically involved in inhibitory processes (ACC, SPL, IPL); and 2) recruitment of left hemisphere homologues of right hemisphere regions (SFG and MFG) typically utilized during task performance. Older adults appear to maintain performance levels during inhibition through compensatory recruitment processes after 36hrs TSD.
Support (optional): R01AG24506
UCSD GCRC M01 RR00827

0386

DIGIT SYMBOL SUBSTITUTION TASK PERFORMANCE IN A CHRONIC SLEEP RESTRICTION EXPERIMENT WITH AND WITHOUT NAPS

Mollicone D,[1] Van Dongen H,[2] Dinges D[1]
(1) University of Pennsylvania School of Medicine, Philadelphia, PA, USA, (2) Washington State University, Spokane, WA, USA

Introduction: This study investigated the effect of a range of restricted nocturnal sleep schedules with and without diurnal naps on Digit Symbol Substitution Task (DSST) performance, a measure of cognitive throughput well established to be sensitive to sleep loss. The objective was to determine whether split sleep schedules with reduced TST could increase total wake time without reductions in performance.
Methods: N=90 healthy adults (21–49y; 38 females) participated in a 10-night sleep restriction protocol where they were randomized to 1 of 18 sleep schedules that involved restricted nocturnal anchor sleep (4.2h, 5.2h, 6.2h or 8.2h TIB) and a diurnal nap (0.4h, 0.8h, 1.2h, 1.6h, 2.0h or 2.4h TIB) or no nap. Neurobehavioral performance was tested at 2h intervals during scheduled wakefulness. Total DSST correct responses (sleep inertia bouts excluded) were averaged within each subject on each day. Response surface maps (RSMs) with increasing degrees of freedom were fitted to examine the rate of degradation of DSST performance across the 10 sleep-restriction days for each of the 18 conditions.
Results: A linear RSM of daily total TIB (i.e., anchor + nap) was found to explain 67% of the variance in DSST performance across days, with greater total TIB per 24h resulting in more correct answers ($\chi^2[1]=5.6$, $p=0.045$). An RSM differentiating between each anchor and nap sleep duration resulted in significantly improved goodness-of-fit ($\chi^2[8]=20.5$, $p=0.009$), but the additional model complexity (8 more parameters) only explained an additional 2% of variance.
Conclusion: During chronic nocturnal sleep restriction with and without diurnal naps, DSST performance was primarily a function of total TIB per 24h. Differentiating between anchor and nap sleep duration provided marginal improvement in explained variance, suggesting a more complex relationship possibly including learning effects.
Support (optional): This work is supported by the National Space Biomedical Research Institute through NASA NCC 9-58 and the Institute for Experimental Psychiatry Research Foundation.

0387

PSYCHOPHYSIOLOGICAL PROFILES OF SLEEP DEPRIVATION AND STRESS DURING MARINE CORPS TRAINING

Berka C,[1] Davis G,[1] Johnson R,[1] Levendowski D,[1] Whitmoyer M,[1] Fatch R,[1] Murray S,[2] Ensign W,[3] Yanagi M,[4] Olmstead R[5]
(1) Advanced Brain Monitoring, Carlsbad, CA, USA, (2) SPAWAR Systems Center, San Diego, CA, USA, (3) Space and Naval Warfare Systems Center, San Diego, CA, USA, (4) SPAWAR Systems Center, San Diego, San Diego, CA, USA, (5) VA Greater Los Angeles Healthcare System, CA, USA

Introduction: U.S. Marine Corps troops experience combined stressors including sleep deprivation, physical exertion and threat of enemy fire that can impair vigilance and decision-making with potentially dangerous consequences. This study explored the utility of psychophysiological assessment of fatigue in a USMC operational environment.
Methods: USMC battalion/platoon leaders (n=17) were evaluated with continuous actigraphy during 28-day, live-fire training exercises and weekly with wireless EEG and heartrate(HR/HRV) acquired during performance of a 20-minute, 3-Choice-Vigilance-Test(3C-VT). Self-reported stress, fatigue and mood were assessed with Profile of Mood States, Stanford/Karolinska sleepiness scales, Brief Fatigue Inventory and Perceived Stress Scale.
Results: B-Alert® algorithms classified one-second EEG epochs as High-Engagement, Low-Engagement, Distracted or Drowsy. The total percentage of epochs in each class was calculated for each 5-minute segment of the 3C-VT. Reaction-time(RT), percent-correct and percent-missed(lapses) were computed by 3C-VT segment.
Mean sleep duration measured by actigraphy was 5.3 hours/day(SEM=20mins). A 4(Week)x4(Quartile) RMANOVA revealed significant interaction effects ($p<.0001$) across quartiles over time in the 3C-VT for all EEG classes with increasing Distraction/Drowsiness and decreasing High-Engagement across weeks of training accompanied by increasingly impaired 3C-VT performance. A 1(HR)x4(Week) RMANOVA showed HR decreased significantly ($p<.0001$) across weeks of training. These data indicate that EEG and HR measures were able to assess the fatigue indicated by the significantly increased errors and inattention ($p<.0001$) found during 3C-VT. Significant changes in self-report measures included only decreased POMS-Vigor. POMS-Anger scores>60th percentile suggested greater anger in Marines than the average population.
Conclusion: EEG/HR/HRV assessed during the 20-minute-3C-VT provided quantitative measures of fatigue easily obtained in operational environments. Fatigue is a serious problem during USMC convoy operations, and with 35%-50% of US casualties in Iraq occurring during attacks on convoys, assessment of fatigue coupled with appropriate interventions could save lives. These data indicate that Marines do not

self-report issues related to fatigue, thus more objective measures would be highly beneficial.
Support (optional): This research was supported by the DARPA program "Preventing Sleep Deprivation", and by the Office of Naval Research via the Space and Naval Warfare Systems Command (SPAWAR).

0388

A PSYCHOMOTOR TRACKING TASK FOR FITNESS-FOR-DUTY TESTING FOR SLEEP DEPRIVED PERSONNEL

Park G,[1] Rosenthal T,[1] Guibert M,[1] Allen R,[1] May J,[2] Ware J[3]
(1) Systems Technology, Inc., Hawthorne, CA, USA, (2) Eastern Virginia Medical School, VA, USA, (3) Eastern Virginia Medical School, Norfolk, VA, USA

Introduction: A sleep deprivation (SD) study was conducted to determine simple, efficient measures of fitness-for-duty for sleep deprived personnel using a series of psychomotor, subjective, and physiological measures.
Methods: A total of 14 healthy participants (19-57 years, 7 females) completed 3 separate 24-hour counterbalanced visits sleeping for either 8, 4, or 0hrs. In the morning, participants completed a 60-minute driving simulator (DS) task involving a rural drive (Risser et al 2000), the Critical Tracking Task (CTT) (Allen *et al.*, 1999), the Psychomotor Vigilance Task (PVT), the Epworth Sleepiness Scale (ESS), Visual Analogue Scale (VAS), the Stanford Sleepiness Scale (SSS), and a one-nap sleep latency (ONSLT) trial.
Results: DS measures of average lateral lane deviations showed the best discrimination between 8, 4, and 0hr conditions but required utilizing the full 60 minutes of data. Reaction times for the 10 min PVT were only significant between the 8 and 0hr conditions. Averaging at 4-5 mins, the CTT data provided significant differences between the 8 and 0hr ($p = .002$) and 4 and 0hr ($p = .032$) conditions; 8hr: $M = 3.40$, $SD = .428$, 4hr: $M = 3.40$, $SD = .383$, 0hr: $M = 3.40$, $SD = .362$. Sleep questionnaires VAS and SSS provided good discrimination between all three SD conditions. The ESS, similar to the CTT was not sensitive between the 8 and 4hr conditions. The ONSLT, similar to the PVT results was sensitive only between the 8 and 0hr conditions.
Conclusion: Taking into account testing sensitivity and efficiency, the CTT provided the most potential as a fitness-for-duty measure for sleep deprived personnel in realworld applications. However, sensitivity differences between SD conditions suggest the CTT to have an alerting effect and to be more sensitive as SD becomes more severe.
Support (optional): This study was funded by the National Center for Injury Prevention and Control, 1 R43 CE00049-01A1.

0389

THE INFLUENCE OF SLEEP DEPRIVATION ON PSYCHOMOTOR PERFORMANCE IN NURSES WHO WORK THE NIGHT SHIFT

Johnson A, Umlauf M, Brown K, Weaver M
University of Alabama at Birmingham, Birmingham, AL, USA

Introduction: Reduction in the amount of sleep predisposes individuals to sleep deprivation, resulting in poor psychomotor performance. Nurses who work the night shift may be particularly subject to sleep deprivation because of irregularity of sleep hours and disruptions in the circadian cycle. Few studies discuss the influence of sleep deprivation among nurses and how sleep deprivation influences psychomotor performance. Poor psychomotor performance has been associated with an increase in error. Increased error can be translated into an unsafe work environment. The identification of sleep deprivation in nurses is essential for maintaining a safe work environment.
Methods: The d2 test of attention, a timed pencil and paper letter recognition psychomotor performance test was administered with the Profile of Mood States, the Pittsburgh Sleep Quality index, and a demographic questionnaire to nurses while they were working on the night shift in the hospital setting. The sample was classified as sleep deprived or not sleep deprived.
Results: The sample of 289-licensed nurses was predominantly female. Fifty six percent of the sample was sleep deprived. While there was no significant difference in psychomotor performance scores between the sleep deprived and the non-sleep deprived groups, the mean psychomotor performance scores in both groups were above than the normative mean (26.6 male, 11.4 female) for male (44.4) and female (41.03). There was also a significant ($p<0.0001$) inverse relationship between psychomotor performance and hours of sleep.
Conclusion: The total sample of night shift nurses revealed poor psychomotor performance scores. Sleep deprived nurses who worked the night shift had poorer sleep quality ($p=0.0006$) and lower mood states ($p=0.0094$). As the hours of sleep decreased the psychomotor performance declined.
Support (optional): Completed Research Support, NIOSH T42 CCT410429 Oestenstad (PI) 2005, National Institute of Occupational Safety and Health, Occupational Health and Safety Training NORA funding. The major goal of this award was to support the dissertation research effort related to sleep deprivation, performance and the occurrence of error in nurses who the night shift.
Role: Award Recipient

0390

CHANGES IN EYE-STEERING COORDINATION OF SLEEP-DEPRIVED DRIVERS COULD HELP AVOID ACCIDENTS DUE TO FALLING ASLEEP AT THE WHEEL

Chattington M, Wilson M, Marple-Horvat D
Manchester Metropolitan University, Alsager, Cheshire, United Kingdom

Introduction: Driving requires coordination of horizontal eye movements and steering. This study analyses the change in coordination when drivers have been sleep-deprived for one night. These changes could be detected before a driver falls asleep, and a warning given so as to avoid the impending accident.
Methods: Local ethical committee approval and written informed consent were obtained prior to testing. Six participants (3 male, 3 female, mean age 21.1 years) drove a winding route on a driving simulator. On day 1 (control) they drove for 1 hour starting at 5pm. They were kept awake the following night, and on day 2 (test) drove again from 5pm for up to two and a half hours. Their eye movements were monitored using a dashboard mounted eye tracker (ASL 5000 pan-tilt camera), and steering wheel movement was monitored through a precision potentiometer attached to the steering column. Cross-correlation signal analysis of successive 1 minute epochs of driving yielded degree of covariation and relative timing of eye and steering movements.
Results: In all drivers, sleep deprivation impacted their ability to coordinate eye movements with steering. There were instances of both acute and chronic reductions ($P<0.05$) in degree of coordination and in time lead of eye movements over steering. Acute drops were correlation coefficient or time lead values in any 1 minute period of driving that fell below the (mean-2SD) limit defined by 45 minutes of normal driving. Chronic reductions were identified by paired t-test comparison of 45 minutes of normal and sleep-deprived driving.
Conclusion: Changes in eye-steering coordination were identified

before drivers fell asleep; analysis of eye-steering coordination may therefore provide a useful method of detecting when a driver is in danger of losing control of a vehicle due to fatigue, before the driver actually falls asleep.

0391

SIZING THE EFFECT OF SELECTIVE SWS/SWA DISRUPTION ON OBJECTIVE AND SUBJECTIVE DAYTIME SLEEP PROPENSITY, MOOD, EXECUTIVE FUNCTION, SUSTAINED ATTENTION, WORKING MEMORY AND OVERNIGHT MEMORY CONSOLIDATION

Groeger J,[1] Deacon S,[2] Stanley N,[3] Snyder E,[4] Legters A,[5] Dijk D[6]
(1) University of Surrey, Guildford, United Kingdom, (2) Lundbeck Ltd., Milton Keynes, United Kingdom, (3) University of Surrey, United Kingdom, (4) Merck Research Laboratories, Upper Gwynedd, PA, PA, USA, (5) Lundbeck B.V., Netherlands, (6) University of Surrey, Guildford, United Kingdom

Introduction: The objective of the study was to address SWS/SWA´s functional role by selectively depriving healthy subjects of SWS/SWA and observing the subsequent effects on daytime sleepiness, mood, performance and overnight memory consolidation.
Methods: Healthy young (20-30y, n=44), middle-aged (40-55y, n=35) and older (66-83y, n=31) subjects, without sleep complaints, received 2 nights of selective SWS/SWA disruption or no disruption, following a baseline assessment, in a parallel group design. SWS/SWA disruption was achieved through acoustic stimulation contingent upon appearance of delta waves in the ongoing sleep EEG. Polysomnography (PSG) was performed on all laboratory nights (23:00-07:00h). The primary endpoint was the multiple sleep latency test (MSLT; composed of 5 sleep latency tests [SLT]) on Day 2. Secondary outcome measures included assessments of daytime function, which preceded each SLT, and overnight memory assessments, including Texture Discrimination. Effect size estimates (Cohen´s d) were used to compare the sensitivity of measures to SWS/SWA disruption.
Results: Compared with controls, the disruption group showed significant reductions in both SWS and SWA, significant increases in stages 1 and 2, but no change in total sleep time or REM duration. Large negative effect sizes (≥ 0.8, $p<0.005$) were observed for MSLT (1.27), Karolinska Sleepiness Scale (0.8) and VAS:tiredness (0.88). Statistically reliable ($p<0.05$) moderate and small negative effect sizes (≥ 0.5 & ≥ 0.2) were obtained for VAS:energy (0.63), VAS:sleep quality (0.77), VAS:freshness on waking (0.49), VAS:ability to function (0.42), Positive Affect (0.51), Critical Flicker Fusion (0.57), Motor Tracking (0.41) and Sustained Attention Response Task (0.39). Texture Discrimination showed improvement overnight but no effect of SWS/SWA disruption.
Conclusion: The primary effect of acute SWS/SWA disruption appears to be a significant increase in daytime sleepiness, with reliable negative effects on subjective alertness and tasks that require sustained attention, and smaller or no effects on tasks which reflect executive or memory function.
Support (optional): H. Lundbeck A/S, Copenhagen, Denmark.

0392

EFFECTS OF FATIGUE FROM NIGHT WORK AND SLEEP LOSS ON SIMULATED THREAT DETECTION PERFORMANCE

Dinges D,[1] Basner M,[1] Fomberstein K,[2] Ecker A,[1] Coble M,[2] Avinash D,[1] Goel N,[1] Banks S[1]
(1) University of Pennsylvania School of Medicine, Philadelphia, PA, USA, (2) University of Pennsylvania School of Medicine, PA, USA

Introduction: Fatigue from night work and sleep loss can increase the risk of human error during critical visual search tasks in the real world. This study is the first to investigate the effects of night work and sleep loss on threat detection performance.
Methods: We developed a simulated luggage search task (SLST), consisting of 6,000 unique simulated X-ray images of luggage, organized into 30 stimulus sets of 200 bags each. 25% of the bags contained either a gun or a knife. N=24 healthy volunteer subjects performed a 200-bag search every 2 hours during a 34-hour period of prolonged wakefulness, starting at 8 am. Based on hits and false alarms, d´—the standard measure of signal detection theory— was calculated, with high values of d´ indicating good threat detection performance. Night work (9 pm to 7 am, 13h-23h awake) and sleep loss (9 am to 5 pm, 25h-34h awake) performance were compared to nonsleep-deprived daytime performance (1h-11h awake).
Results: During night work, hit rate (HR) decreased on average by 2.8% ($p=0.002$), while false alarm rate (FAR) increased by 1.6% ($p<0.001$), leading to a significant decrease in d´ of 10.9% ($p<0.001$). Response latency decreased significantly by 181 ms per bag ($p<0.001$). During sleep loss, HR decreased on average by 2.6% ($p=0.010$), while FAR increased on average by 1.6% ($p=0.004$), leading to a significant decrease in d´ of 10.8% ($p=0.002$). Response latency decreased significantly by 250 ms per bag ($p<0.001$). There were also prominent time on task effects on HR and FAR, not affecting d´.
Conclusion: Fatigue from night work and sleep loss adversely affects performance on a task that simulates threat detection demands. Thus, fatigue may pose a risk for errors in tasks involving detection of threats, unless countermeasures for fatigue are deployed.
Support (optional): This investigation was sponsored by the Department of Homeland Security´s Transportation Security Laboratory Human Factors Program (FAA #04-G-010), and by NIH grant M01-RR00040.

0393

EFFECTS OF SLEEP DEPRIVATION ON SLOW EYELID CLOSURES (PERCLOS) DURING SIMULATED THREAT DETECTION PERFORMANCE

Dinges D, Basner M, Fomberstein K, Ecker A, Coble M, Avinash D, Goel N, Banks S
University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: We have found that night work and sleep loss reduce threat detection performance on a simulated luggage screening task (SLST). In an effort to find a reliable, valid, unobtrusive method for online monitoring of declining threat detection performance due to sleepiness, we evaluated the percentage of slow eyelid closures (PERCLOS), which we originally validated to be sensitive to lapses of attention on the Psychomotor Vigilance Test (PVT).
Methods: Intra-individual coherence coefficients between PERCLOS and SLST performance were calculated from SLST testing (every 2h) across a 34h period of prolonged wakefulness in N=24 volunteer healthy subjects. d´—the standard measure of signal detection theory—was calculated for SLST performance at each 2h test bout, and PERCLOS

was measured throughout each SLST test bout using FaceLABTM. Within each subject, covariation (coherence) between d´ and PERCLOS was calculated for the 17 test bouts (across 34h period).
Results: PERCLOS as well as d´ showed deterioration in the majority of subjects after 16 hours of wakefulness. PERCLOS values were negatively linearly correlated with SLST performance within subjects (average r=-0.39, range –0.87 to 0.20). SLST performance decreased markedly in trials with average PERCLOS >6%. Therefore, alert subjects (PERCLOS <1%) were contrasted to sleepy subjects (PERCLOS >6%): From 100 threats that would have been detected by an alert subject, 9 were missed because of sleepiness. Simultaneously, from 100 safe bags that would have passed if the subject was alert, 5 were declared as threats because of sleepiness.
Conclusion: These data show that PERCLOS and threat detection performance are negatively correlated. PERCLOS may serve as a useful tool for online monitoring of people engaged in threat detection tasks, but proof for this will require validation in the field.
Support (optional): This investigation was sponsored by the Department of Homeland Security´s Transportation Security Laboratory Human Factors Program (FAA #04-G-010), and by NIH grant M01-RR00040.

0394

EXTENDING SLEEP OPPORTUNITIES FROM ~6 TO ~8 HOURS PER NIGHT IMPROVES SELECTIVE ATTENTION AND EXECUTIVE FUNCTION

Wright K, Frey D, Moritz M, Jung C, Nguyen J, Rodgers J, Wertz A
University of Colorado at Boulder, Boulder, CO, USA

Introduction: Short sleep durations of <7h have been reported to impair daytime alertness and cognitive function while extending sleep opportunities from 7/8h up to 10h per night has been reported to improve alertness and vigilance performance. However, to date, no study has tested the hypothesis that extending sleep from ~6h up to the "recommended" ~8h per night produces significant improvements in higher order cognitive functions.
Methods: Twenty-six healthy subjects (11 women, 15 men), aged 22.4±4.0 (Mean±SD), who reported habitual sleep schedules of <6.5h during the work/school week completed a month long protocol. Habitual sleep schedules were first monitored for two weeks at home using actigraphy, diaries, and time-stamped call-ins. Subjects lived in the lab for ~24h for baseline performance and sleep assessments. Following this lab visit, sleep schedules were monitored for two more weeks. Twelve subjects were randomized to a sleep maintenance condition and were asked to maintain their habitual sleep schedules. Fourteen subjects were randomized to a sleep extension condition which required subjects to increase time in bed by ~2h per night. Performance and sleep were reassessed during a second ~24h lab visit. Selective attention (visual search) and executive function (Stroop Color Word) were assessed every 2h across the day and analyzed with repeated measures ANOVA.
Results: Subjects who maintained their habitual sleep schedule spent on average 6.0±0.6h and 6.1±0.5h per night in bed during the first two and second two weeks of the protocol, respectively. Subjects in the sleep extension condition spent 6.0±0.6h and 8.2±0.7h per night in bed during the first two and second two weeks, respectively. We observed a significantly greater improvement in selective attention and executive function in the sleep extension compared to the sleep maintenance condition ($p<0.05$).
Conclusion: Extending sleep of subjects who chronically obtain "inadequate" sleep to the "recommended" ~8h per night improves higher order cognitive functions.
Support (optional): Research Supported by the American Sleep Medicine Foundation and by grants from the Undergraduate Research Opportunities Program and the Howard Hughes Medical Institute in collaboration with the Biological Sciences Initiative at the University of Colorado at Boulder.

0395

SLEEP DEPRIVATION AND STRESS HAVE ADDITIVE EFFECTS ON NEGATIVE MOOD STATES

Minkel J,[1] McGlinchey E,[1] Caruso H,[1] Ecker A,[1] William J,[1] Banks S,[1] Dinges D[2]
(1) University of Pennsylvania School of Medicine, Philadelphia, PA, USA, (2) University of Pennsylvania, Philadelphia, PA, USA

Introduction: Inadequate sleep frequently co-occurs with stress making it difficult for researchers to understand the unique influence of each on affective processes. The following study was designed to provide novel data for the effects of stress in interaction with sleep deprivation in a controlled setting.
Methods: Healthy adult volunteers (N=29, age range: 22-45, female = 15) were randomly assigned to a night of sleep deprivation (n=14 deprivation condition) or 9h TIB (n=15 control condition). Subjects were tested under low and high stressor conditions once on day 1, before the experimental manipulation and again on day 2, after the experimental manipulation. The low-stressor condition included relatively easy cognitive tasks and positive feedback on performance. The high-stressor condition included more difficult cognitive tasks and negative feedback on performance. After each bout of testing, subjects completed the Profile of Mood States (POMS). All subjects received 10 hours of sleep opportunity on the second night of the study. Within and between group differences were compared using repeated measures ANOVA and t-tests.
Results: The high-stressor bouts were associated with greater reports of total mood disturbance (TMD) on the POMS than the low-stressor bouts. This was found on day 1 ($t=-5.06$, $p<0.01$, effect size $d=0.68$) before the sleep manipulation and on day 2 for both the sleep deprived ($t=-2.86$, $p=0.01$, $d=0.68$) and control subjects ($t=-3.01$, $p<0.01$, $d=0.68$). The sleep deprived subjects reported greater levels of TMD than control subjects. This was found after both the low-stressor bout ($t=-2.67$, $p=0.01$, $d=1.06$) and the high-stressor bout ($t=-2.25$, $p<0.05$, $d=0.87$). There was not a significant interaction of stressor-level and sleep condition ($F=0.07$, $p=0.79$).
Conclusion: These data suggest that sleep deprivation and stress each have negative effects on mood which are additive rather than interactive.
Support (optional): NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute.

0396

ODOR IDENTIFICATION ACCURACY PREDICTS RESISTANCE TO SLEEP LOSS

McBride S, Brian L, Kamimori G, Killgore W
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: Although there are individual differences in vulnerability to the effects of sleep deprivation, the basis for these differences remains relatively unexplored. Because prolonged wakefulness reduces brain activity in the prefrontal and orbitofrontal cortices, it is possible that the individual level of brain activity at rested baseline may be predictive of resistance to sleep loss. Evidence suggests that ability to identify odors is a reliable measure of the functional integrity of the orbitofrontal cortex. Therefore, we hypothesized that individuals with better olfactory discrimination at rested baseline would be less susceptible to the adverse effects of sleep deprivation.

Methods: Twenty healthy volunteers (16 men; M age=24.9, SD=3.9) obtained a full night of sleep (8 hours time in bed). Volunteers were awakened at 0700 the following morning and remained awake continuously for 77 hours. At baseline, participants completed 20 items from the University of Pennsylvania Smell Identification Test (UPSIT), a reliable and valid, self-administered test of odor discrimination. For the next three nights, participants completed psychomotor vigilance testing (PVT) at 10-25 minute intervals from 0015 to 0845. Half of the sample also received caffeinated gum (200mg) every two hours. Speed (1/Reaction Time*100) was calculated for each PVT, converted to percent of baseline (PVT%) for each subject, and averaged across all administrations for each night. Baseline UPSIT scores were correlated with these performances.
Results: Rested UPSIT performance was not significantly correlated with PVT% scores on Night 1 (r=.42, p=.06), but was significantly predictive of performance on Night 2 (r=.67, p=.001), and Night 3 (r=.46, p=.04), and all PVT% performances averaged across the 3 days (r=.59, p=.007).
Conclusion: Olfactory discrimination at rested baseline, a measure of orbitofrontal system integrity, was predictive of the ability to resist sleep loss following two to three nights awake, supporting a "prefrontal reserve" theory of vulnerability to sleep loss.

0397

INDIVIDUAL DIFFERENCES IN ODOR DISCRIMINATION PREDICT MOOD DYSREGULATION FOLLOWING 56 HOURS OF SLEEP DEPRIVATION

Smith K, McBride S, Kamimori G, Killgore W
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: Individuals differ in their vulnerability to the effects of sleep deprivation, but the neurobiological basis for these differences is largely unknown. Because sleep loss has a detrimental effect on the metabolism and functioning of the prefrontal cortex, particularly the ventral and orbitofrontal regions important for affective processing, it is conceivable that the functional integrity of these regions may account for some of these differences. Interestingly, olfactory discrimination appears to be a reliable measure of orbitofrontal functioning. Accordingly, we hypothesized that the quality of olfactory discrimination when an individual was well rested would predict changes in affective symptoms of psychopathology following sleep deprivation.
Methods: Following a full night of sleep (8 hours time in bed), twenty-three healthy volunteers (18 men; M age=25.0, SD=3.9) remained awake continuously for 77 hours. When rested, participants completed 20 items from the University of Pennsylvania Smell Identification Test (UPSIT) and the Personality Assessment Inventory (PAI). Participants completed the PAI again following 56 hours of continuous wakefulness, and change scores from baseline to sleep deprived conditions were calculated for each scale. Baseline performance on the UPSIT was used to predict these change scores.
Results: Baseline UPSIT performances were significantly correlated with PAI change scores for several scales, including Affective symptoms of Anxiety (r=-.42, p=.05), Affective symptoms of Depression (r=-.44, p=.03), Psychotic Experiences of Schizophrenia (r=-.61, p=.002), Borderline Features (r=-.42, p=.05), Borderline Negative Relationships (r=-.52, p=.01), and Aggression (r=-.45, p=.03).
Conclusion: Poorer olfactory discrimination at rested baseline predicted the severity of affective dysregulation and worsening of psychopathological symptoms following 56 hours of sleep loss. Assuming that olfactory discrimination is a valid measure of orbitofrontal system integrity, these results suggest that individuals with the most intact prefrontal cortices and associated functions (i.e., those with the greatest "prefrontal reserve") are also least susceptible to affective changes during sleep deprivation.

0398

CHANGES IN ODOR DISCRIMINATION PREDICT EXECUTIVE FUNCTION DEFICITS FOLLOWING 45 HOURS OF WAKEFULNESS

Killgore D,[1] McBride S,[1] Balkin T,[1] Grugle N,[2] Killgore W[1]
(1) Walter Reed Army Institute of Research, Silver Spring, MD, USA,
(2) Walter Reed Army Institute of Research, MD, USA

Introduction: As little as 24 hours of continuous wakefulness is associated with a significant decline in cerebral metabolism within the prefrontal cortex, the region most critical for higher-order executive functions. We recently showed that 24 hours of sleep loss was associated with a significant decline in olfactory discrimination, an ability that is highly indicative of the integrity of the orbitofrontal cortex. Here, we examined whether the degree of decline in olfactory discrimination at 24 hours awake would be predictive of deficits in higher-order executive functioning after 45 hours of sleep deprivation.
Methods: Fifty four healthy volunteers (29 males) were tested 6 hours after waking from a full night of sleep (baseline) and then following 24 hours awake with the UPSIT, a reliable test of olfactory discrimination consisting of 40 "scratch and sniff" items. Twenty items were administered at baseline and another 20 when sleep deprived, with order counterbalanced across sessions. Change scores from baseline to 24 hours were calculated for the UPSIT. Participants received a single dose of dextroamphetamine 20mg, modafinil 400mg, caffeine 600mg, or placebo following 44 hours of wakefulness. At 45 hours, participants completed the 64-item Wisconsin Card Sorting Test (WCST). UPSIT change scores were used to predict performance on the WCST.
Results: WCST was unaffected by stimulants (p>.05), so groups were collapsed across drugs. UPSIT change scores at 24 hours were significantly associated with performance on WCST Total Correct (r=.35, p=.01), Nonperseverative Errors (r=-.47, p=.001), Conceptual Level Responses (r=.35, p=.01), and number of Completed Categories (r=.31, p = .03).
Conclusion: Declines in olfactory discrimination after 24 hours awake were significantly predictive of poorer performance on the WCST, a well-validated measure of executive functioning, at 45 hours awake. Findings suggest that changes in a measure sensitive to orbitofrontal dysfunction are predictive of the magnitude of executive function deficits produced by two nights of sleep loss.

0399

MORNINGNESS-EVENINGNESS AFFECTS RISK-TAKING PROPENSITY DURING SLEEP DEPRIVATION

Lipizzi E,[1] Richards J,[1] Balkin T,[1] Grugle N,[2] Killgore W[1]
(1) Walter Reed Army Institute of Research, Silver Spring, MD, USA,
(2) Walter Reed Army Institute of Research, MD, USA

Introduction: Individuals differ in their preferred time of day for awakening, sleeping, and engaging in demanding activities, a construct known as Morningness-Eveningness (M-E). This construct has recently been linked to specific personality traits, including novelty-seeking and impulsivity, but it is not clear whether this trait affects risk-taking and sensation seeking in response to sleep deprivation.
Methods: Fifty-four healthy volunteers (29 men; Mage = 23.5 years, SD = 4.0) completed the Morningness-Eveningness Questionnaire. Based on a median split (Median=52), participants were categorized as showing Morning Traits or Evening Traits. Participants were

administered the Evaluation of Risks Scale (EVAR) and Brief Sensation Seeking Scale (BSSS) at rested baseline and again following 23 hours awake.
Results: At baseline, significant negative correlations were found between M-E and Impulsiveness (r=-.55), Invincibility (r=-.26), and Total Risk Propensity (r=-.30). When sleep deprived, significant negative correlations were found between M-E and Danger Seeking (r=-.28), Impulsiveness (r=-.52), Invincibility (r=-.40), and Total Risk Propensity (TRP) (r=-.39). M-E was not correlated with BSSS at baseline or sleep deprived state. Repeated measures ANOVA showed that both groups declined in Self-Control (p<.001), but Morning types declined more severely than evening types (p=.04), both groups declined on self-reported Danger Seeking (p=.001) and Energy (p<.001). Evening types reported significantly higher scores on Impulsiveness (p-.001) and Invincibility (p=.02), but this was not affected by sleep deprivation. Overall Evening types scored higher on TRP (p=.004), regardless of condition. Sleep deprivation reduced scores on TRP (p<.001). BSSS scores declined as a result of sleep loss (p<.001), but there was no difference between M-E types.
Conclusion: M-E is correlated with several dimensions of risk-taking propensity but not sensation-seeking, with higher Eveningness traits associated with greater risk-propensity. This relationship appears to be only minimally enhanced by sleep loss.

0400

ODOR IDENTIFICATION ABILITY PREDICTS VULNERABILITY TO ATTENTIONAL LAPSES DURING 77 HOURS OF SLEEP DEPRIVATION

McBride S,[1] Ganesan G,[2] Kamimori G,[1] Killgore W[1]
(1) Walter Reed Army Institute of Research, Silver Spring, MD, USA, (2) Walter Reed Army Institute of Research, MD, USA

Introduction: The basis for individual differences in the resistance/vulnerability to sleep loss is poorly understood. Given that brain activity in the prefrontal cortex (PFC) is particularly affected by prolonged wakefulness, it is possible that individual differences in the baseline functioning of the PFC may identify persons more prone to succumbing to attentional lapses when fatigued. A reliable indicator of the functional integrity of the orbitofrontal cortex is the ability to discriminate among various odors. We hypothesized that poorer scores on a measure of olfactory discrimination at rested baseline would identify individuals most vulnerable to attentional lapses during three nights of sleep deprivation.
Methods: Twenty-one healthy volunteers (17 men; M age=24.9, SD=3.8) were provided 8 hours time in bed and then awakened at 0700 the following morning. Participants were deprived of sleep continuously for 77 hours. Participants completed 20 items from the University of Pennsylvania Smell Identification Test (UPSIT) at baseline. A series of five minute psychomotor vigilance tests (PVT), taken at 10-25 minute intervals from 0015 to 0845 was completed each night. Eleven participants received caffeinated gum (200mg) every two hours each night. The number of 1-, 3-, and 5-second lapses, relative to baseline, was calculated and averaged across each night. UPSIT scores were then correlated with lapses.
Results: On Night 1, higher baseline UPSIT scores predicted fewer 1-second (r=-.55, p=.004) and 3-second lapses (r=-.41, p=.03). On Night 2, UPSIT correlated with 3-second (r=-.59, p=.002) and 5-second lapses (r=-.66, p=.001). By Night 3, baseline UPSIT scores were only predictive of 5-second lapses (r=-.45, p=.02). With all lapses combined the findings remained significant, even after controlling for caffeine group.
Conclusion: Poorer baseline olfactory discrimination, a gauge of prefrontal cortex integrity, was predictive of vulnerability to attentional lapses following sleep deprivation, consistent with a "prefrontal reserve" theory of resistance to sleep deprivation.

0401

EXTROVERSION PREDICTS INCREASED ATTENTIONAL LAPSES DURING SLEEP DEPRIVATION

Richards J, Lipizzi E, Kamimori G, Killgore W
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: Eysenck´s 1990 theory of Introversion-Extroversion (I-E Theory) suggests that introverts have higher levels of basal arousal in the reticulo-thalamo-cortical pathway than extroverts. Therefore, introverts need low intensities of stimulation to reach their optimal level of functioning, while extroverts need higher intensities of stimulation to function optimally. Based on Eysenck´s theory, we hypothesized that introverts (those with high basal arousal) would be more resistant to sleep loss, resulting in fewer attentional lapses than extroverts.
Methods: Twenty-three healthy volunteers (19 men; M age = 25.3, SD = 4.1) completed the Revised NEO Personality Inventory (NEO PI-R) on Day 0, followed by 8 hours of sleep that night. Volunteers awoke at 0700 on Day 1 and remained awake for 77 hours. Over the next three nights, psychomotor vigilance tests (PVT) were administered every 10-25 minutes from 0015 to 0845. Half the volunteers (n=12) received caffeine gum (200mg) every two hours during testing sessions. The number of 1-, 3-, and 5-second attentional lapses were tabulated for each overnight testing session. The mean number of lapses for each session was subtracted from the mean number of baseline lapses to find the average change score for each session. We ran a Pearson´s r one-tailed test predicting a positive correlation between change scores and the 5 NEO factors.
Results: A partial correlation, controlling for drug group, revealed that 1-second lapses correlated significantly with Extraversion (r=.517, p=.007). Of the six sub-traits of Extraversion, higher Gregariousness and Activity were most predictive of increases in 1- and 3-second lapses in Night 1 only (p´s.032). Gregariousness was significantly positively correlated with 5-second lapses all three nights (p´s≤.033).
Conclusion: Individual differences in Extroversion predicted change in attentional lapses during sleep deprivation. Consistent with Eysenck´s theory, extroverts were less resistant to sleep deprivation, showing an increase in attentional lapses relative to baseline.

0402

BRAIN RESPONSE ON A WORKING MEMORY TASK FOLLOWING TOTAL SLEEP DEPRIVATION IN OLDER ADULTS

McKenna B,[1] Meloy M,[2] Salamat J,[3] Drummond S[4]
(1) SDSU/UCSD Joint Doctoral Program in Clinical Psychology and Veterans Affairs San Diego Healthcare System, Research Service, San Diego, CA, USA, (2) University of California, San Diego, Department of Psychiatry, San Diego, CA, USA, (3) Veterans Affairs San Diego Healthcare System, Research Service, San Diego, CA, USA, (4) University of California, San Diego, Department of Psychiatry and Veterans Affairs San Diego Healthcare System, Psychology Service, San Diego, CA, USA

Introduction: Working memory is a temporary storage system for the maintenance and manipulation of information. In older adults this ability is compromised when the memory system is overloaded by increasing demands, generally due to a failure to activate task-related neural areas. Here, we examine the neural and behavioral changes on an n-back task in older adults following total sleep deprivation (TSD).

Methods: Twelve subjects (age=68 ± 6.5yrs; 10F; education=16.1 ± 2.1yrs) performed n-back during FMRI, both while well-rested (WR) and after 36 hours TSD. A night (WR vs. TSD) by load (1-back vs. 2-back vs. 3-back) ANOVA revealed significant clusters of activation related to performance on n-back. The same ANOVA was used to analyze behavioral performance.
Results: Clusters of activation in areas associated with the main effect of night included right orbitofrontal/dorsolateral prefrontal cortices (BA32/8), right premotor area (BA6), left dorsolateral prefrontal/anterior-polar prefrontal cortices (BA9/10), and left paracentral lobule/cingulate gyrus. Clusters of activation in areas associated with the night by load interaction included right precuneus/superior parietal lobe/cingulate gyrus (BA7), right cerebellum, right dorsolateral prefrontal cortex (BA46), and left premotor area (BA6). Behaviorally, a main effect of n-back load was found for accuracy (WR: 1-back=94%, 2-back=70%, 3-back=52%; TSD: 1-back=90%, 2-back=58%, 3-back=54%; p=0.001).
Conclusion: Overall, older adults performed well on n-back when task demands were low (e.g. 94% correct on 1-back), but declined in accuracy as the working memory system was taxed. When sleep deprived, older adults were able to maintain performance on n-back by increasing activation in areas associated with reorganization and updating of remembered material, executive processes, and maintenance of visuospatial attention. These findings suggest that while aging may cause a reorganization of neural resources, the brain is still able to recruit task-related areas to preserve at least some types of working memory performance when sleep deprived.
Support (optional): UCSD General Clincal Research Center
UCSD Laboratory for Sleep and Chronobiology
UCSD Office of Graduate Student Research, San Diego Fellowship
R01AG24506

0403

CHANGES IN STATE AND TRAIT ANGER FOLLOWING 56 HOURS OF SLEEP DEPRIVATION

Newman R, Krugler A, Kamimori G, Killgore W
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: It is well established that sleep loss produces significant changes in mood state. However, such changes have typically been assessed by global indices that assess general mood states and which do not allow a refined analysis of specific cognitive and affective sub-components that may be affected. To clarify the effects of sleep deprivation on State and Trait anger and the associated expression or suppression of aggressive behavior, we administered the Spielberger State-Trait Anger Expression Inventory (STAXI) as rested baseline and again following 56 hours of continuous wakefulness.
Methods: Twenty-six healthy volunteers (21 men; M age = 25.3 years) were given 8 hours time in bed, followed by 77 hours of continuous wakefulness. The State-Trait Anxiety Inventory (STAXI-2) was administered twice, once at rested baseline, and again at the same time of day (1500 hrs) following 56 hours of sleep deprivation. Each night, 12 participants also received caffeine gum 200mg every two hours from 0100 to 0700, while the others received an identical placebo (n=14).
Results: Each scale was evaluated with a mixed-model ANOVA. As expected, overnight caffeine had no effect on mid-day reports of anger. Sleep loss did, however, produce a significant increase in State- (p=.029) but not Trait-Anger. This was particularly true for angry feelings (S-Ang/F; p=.008), but not for the desire to express anger through verbal or physical aggression. Sleep loss also reduced the behavioral tendency to express anger via verbally or physically aggressive behavior (AX-O; p=.048) and reduced the tendency to ruminate on angry feelings (AX-I; p=.013). There was no change in the energy expended toward control of these feelings or behaviors.
Conclusion: Sleep loss was associated with increased State-Anger, particularly angry feelings and emotions, and a simultaneous reduction in the propensity to act on these feelings via physical or verbally aggressive behavior.

0404

SLEEP DEPRIVATION IMPAIRS ACCURATE ESTIMATION OF PERFORMANCE ON A TEMPORAL MEMORY TEST

Pace-Schott E,[1] Hutcherson C,[2] Bemporad B,[3] Kumar A,[4] Hobson A,[4] Stickgold R[5]
(1) Boston, MA, USA, (2) Stanford University, CA, USA, (3) Boston University, MA, USA, (4) Harvard University, MA, USA, (5) Harvard University, Boston, MA, USA

Introduction: Harrison *et al.* (Sleep 23:1067-73) showed sleep deprivation (TSD) impairs young adults' estimates of performance on the Parkin Temporal Memory test (PTM). We replicate and extend this finding.
Methods: Male college students, aged 19-25, were semi-randomly assigned to control (N=14) or TSD (N=10) protocols (Sleep 25:A446). TSD spanned Day 1 rising until Day 2 late evening. Ordinal position of the PTM was counterbalanced between subjects within an extended battery (presented 18:30-23:00 Day 2). Two sets of 12 face photographs were presented (1 minute/photograph, 5 minutes between sets). After another 5 minutes, photographs were re-presented with 24 novel faces. Subjects were asked if they previously saw a face (recognition memory) and in which set it occurred (temporal memory). Subjects rated confidence (1-5, 5=highest) for answers to both questions combined. Rating style differences were controlled by dividing each subject's absolute responses by their mean rating for all stimuli ("relative ratings"), and by subtracting mean confidence ratings of incorrect from correct temporal memory responses.
Results: Recognition: Repeated measures ANOVA showed hits and correct rejections had higher absolute and relative confidence than misses and false recognition ($p < .0001$) but without TSD effects. Hits plus correct rejections analyzed separately trended toward higher relative confidence for TSD (p=.06). Temporal memory: Absolute and relative confidence was higher for correct than incorrect responses ($p<.0001$), an effect greater in controls (interaction p=.05). TSD subjects had overall higher temporal memory relative confidence ratings (trend p=.07). TSD subjects gave higher relative confidence ratings for incorrect ($p<.05$, t- and U-tests) but not correct answers. Controls showed significantly higher absolute and relative confidence differences between correct and incorrect responses (p=.05).
Conclusion: Despite our previously reported lack of group differences in temporal memory accuracy, TSD subjects significantly over-estimated the accuracy of incorrect responses. Recognition memory confidence estimates were less impacted.
Support (optional): NIDA DA11744

0405

INDIVIDUAL DIFFERENCES IN SLEEP PHYSIOLOGY AND THE MAGNITUDE OF WAKING NEUROBEHAVIORAL IMPAIRMENT DURING SLEEP DEPRIVATION

Tucker A,[1] Dinges D,[2] Van Dongen H[1]
(1) Washington State University, Spokane, WA, USA, (2) University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: Individual differences in normal human sleep physiology may involve multiple traits. In a repeated sleep deprivation paradigm,

trait individual differences were reported to cluster in three dimensions, which were interpreted as reflecting duration, intensity and discontinuity of sleep. The current study explored whether these sleep trait dimensions were correlated with the magnitude of neurobehavioral impairment during sleep deprivation, which has also been shown to involve trait individual differences.
Methods: 20 healthy adults (age 29.4 ± 5.3; 11 females) spent eleven consecutive days in the laboratory. They completed three 36h sleep deprivation periods, each preceded by baseline and followed by recovery sleep (12h TIB). Polysomnographic sleep parameters and EEG delta power were linearly combined to yield overall scores for the three sleep trait dimensions. These scores were averaged within subjects over the baseline nights and over the recovery nights (baseline data were missing for one subject). During two of the sleep deprivation periods, every 2h subjects completed a 30min neurobehavioral test battery including a 10min PVT and the Karolinska Sleepiness Scale (KSS). PVT lapse counts (RT≥500ms) and KSS sleepiness scores were averaged within subjects across the final 24h of both sleep deprivations. The PVT and KSS results were correlated with the sleep trait scores, subject to Bonferroni correction for multiple comparisons.
Results: Trait sleep discontinuity (sleep stage transitions, movement time, stage 1 sleep) correlated negatively with KSS scores (baseline: r=–0.69, P=0.002; recovery: r=–0.62, P=0.004). No other correlations were significant after Bonferroni correction.
Conclusion: In this study, there were no significant relationships between trait individual differences in psychomotor vigilance impairment from sleep loss and trait individual differences in sleep physiology. However, individuals experiencing greater subjective sleepiness during sleep deprivation also exhibited greater continuity of baseline and recovery sleep. This could result from individual differences in the strength of a persistent underlying sleep drive.
Support (optional): NIH grants HL70154 and RR00040.

0406

TOTAL SLEEP DEPRIVATION FOLLOWING EXTENDED DECLARATIVE LEARNING DOES NOT AFFECT RETENTION FOLLOWING THREE NIGHTS RECOVERY SLEEP IN HEALTHY YOUNG ADULTS

Pace-Schott E,[1] Morgan A,[2] Stickgold R[2]
(1) Boston, MA, USA, (2) Harvard University, MA, USA

Introduction: Sleep deprivation (TSD) can impair declarative memory consolidation, although such effects are not seen in all studies. We examined the effects of TSD on retention of English meanings for Chinese characters following self-paced learning.
Methods: Half of 48 subjects (aged 18-24, Harvard undergraduates, 54% female) studied Chinese characters for 1 or 6 hours on Day 1. Deep encoding was encouraged by having subjects write descriptions of studied characters. After initial recall testing, half the subjects underwent TSD until 21:00 hours on Day 2. Further testing occurred on Days 2 and 5. Only half of the studied characters were tested on Day 2. Percent of initial performance retained on Day-5 was analyzed for total items, and those tested ("old") or not tested ("new") on Day-2. ANOVAs compared Day-5 retention between TSD and control subjects. ANCOVAs controlled for subjects' (i) initial performance, (ii) sleep the night before study (Day 0), (iii) total sleep Days 2-4, and (iv) descriptions' median word count.
Results: Collapsed across groups, immediate recall averaged 89% of studied words, indicating highly efficient encoding. Recall on Day 2 was nearly as good, averaging 96% of recall on Day 1, while recall on Day 5 averaged 79% of Day-1 values. Among 6-hour study subjects, controls showed a very small advantage (5-8% for total, new and old) that became a trend ($p < .1$) when Day-0 sleep was covaried, but which became insignificant (2-4% advantage) when considering only subjects whose initial performance was >80%. No other ANOVA or ANCOVA showed control group advantage.
Conclusion: In this young, intelligent, highly motivated population, one night's TSD has little effect on retention of naturalistic declarative learning following recovery sleep. This may reflect a ceiling effect, due to the over-learning reflected in the near-perfect recall in all groups the day after training.

0407

RAPID EYE MOVEMENT SLEEP DEPRIVATION IN MICE WITH DISC TREADMILL METHOD

Fang J, Guan Z
Pennsylvania State University, Hershey, PA, USA

Introduction: Rapid eye movement sleep (REMS) is thought to play important roles in brain functions during development and adulthood. Current methods for REMS deprivation (RSD) are not satisfactory for various reasons. The present study was aimed to develop a new RSD method in mice with an automatic disc treadmill system developed in our lab.
Methods: Male C57BL/6 mice (n=8) were implanted with EEG and EMG electrodes. RSD was performed with a disc treadmill system, in which each animal cage was made of a round pan as the bottom and a suspended Plexiglas tube with a divider at the bottom. The animal was awakened by the rotation of the pan. The pan rotation was triggered by REMS (high EEG power between 6-10Hz and low EMG) under the control of a computer program (SleepWave). Baseline EEG and EMG were recorded for 1 day. In the next day, 4 mice received RSD during the first 8 hours of the light period. The disc rotated in 1-sec pulses until the animal was awake. Each RDS animal was matched with a control animal, which received the same amounts of stimuli with all disc rotations occurring in the last 10-min of each 120-min block.
Results: REMS during the RSD period was reduced by 85% compared to the baseline ($F(4,16)=17.434$, $p<0.025$). This was followed by a REMS rebound during the subsequent light and dark periods ($p<0.05$). Non-NREMS (NREMS) was not significantly altered in the RSD group. Wake, NREMS and REMS were not significantly altered during the RSD period or the entire RSD day.
Conclusion: REMS in mice can be selectively deprived with disc treadmill method without significant influences on sleep in the control mice that received similar physical stimulation as the RSD mice. Our data is promising. Additional studies are needed to extend the observations to rats and longer RSD duration.

0408

EFFECTS OF EXPERIMENTAL SLEEP FRAGMENTATION ON GLUCOSE METABOLISM IN NORMAL SUBJECTS

Stamatakis K, Punjabi N
Johns Hopkins University, Baltimore, MD, USA

Introduction: Sleep-disordered breathing (SDB) is associated with impaired glucose metabolism, although its causative role has yet to be established. Intermittent hypoxemia and frequent arousals from sleep are often observed in SDB and are considered as pathophysiologic triggers of a cascade of physiologic responses that may lead to alterations in glucose metabolism. To segregate the metabolic effects of sleep fragmentation from hypoxemia, an experimental approach was used to investigate the independent impact of sleep fragmentation on glucose metabolism in normal subjects.
Methods: Nine non-smoking non-obese healthy volunteers were

screened for prevalent medical condition (no diabetes, SDB, obesity, etc.), health behaviors (alcohol or caffeine consumption <=2 drinks/day), and sleep habits (sleep duration 7-8 hours) before entry into a pre-post study of sleep fragmentation on glucose metabolism. Subjects were admitted to the GCRC for three nights and sleep was monitored every night. Assessment of glucose metabolism was performed with the intravenous glucose tolerance test (IVGTT) at baseline and after two-nights of sleep fragmentation with recurrent auditory and mechanical stimuli. The minimal model was used to quantify insulin sensitivity (SI) from the IVGTT.
Results: The average ASDA arousal index during sleep fragmentation was 37.2 and 34.1 events/hour on nights 2 and 3, respectively. SI after sleep fragmentation decreased from 4.71 to 3.81 (mU/L)-1 min-1 ($p < 0.001$), representing a 20.4% change from baseline. No significant changes in body weight or fat were observed over the follow-up period.
Conclusion: Sleep fragmentation for two nights in normal subjects decreases insulin sensitivity. While these findings describe acute metabolic alterations with sleep fragmentation, they are also relevant to understanding the long-term metabolic derangements that may result from chronic exposure to sleep fragmentation. This model of sleep fragmentation may be representative of disrupted sleep occurring in conditions such as SDB, periodic leg movement disorder, and sleep maintenance insomnia.
Support (optional): Supported by NIH grants HL083640, HL07578, and AG025553.

0409

PHYSIOLOGIC MANIFESTATIONS OF EXPERIMENTAL SLEEP FRAGMENTATION IN NORMAL SUBJECTS

Stamatakis K, Punjabi N
Johns Hopkins University, Baltimore, MD, USA

Introduction: Sleep fragmentation is characterized by brief arousals that are defined using ASDA criteria. However, alterations in EEG activity not meeting ASDA criteria and alterations in autonomic activity with experimental sleep fragmentation are not well defined. The objective of this investigation was to characterize various EEG and autonomic responses induced by sleep fragmentation in normal subjects.
Methods: Seven healthy, non-obese, volunteers were enrolled in a three-night protocol. Subjects were admitted to the GCRC for four days and sleep was monitored for three nights. On nights 2 and 3 auditory and mechanical stimuli were used to induce brief arousals. Visual scoring was used to describe the heterogeneity in cortical and autonomic responses using: conventional ASDA arousals, delta-wave bursts, and increases in autonomic activity with heart rate or peripheral vascular tone. The discrete Fast Fourier Transform was used to compute spectral EEG power and to quantify full-night, stage-specific, and event-specific variations in sleep microstructure.
Results: The average number of stimuli applied during fragmentation, nights 2 and 3, was 74.2 and 79.6 per hour, respectively. The average arousal index was 37.2 and 34.1 events/hour, the average delta-wave burst index was 13.6 and 17.0 events/hour, and the average number of autonomic responses was 20.8 and 26.3/hour. Delta power in the EEG was reduced during fragmentation relative to the baseline night, while alpha and beta EEG power were increased. Patterns of altered sleep microstructure were dependent on time of night, sleep stage, and proximity to stimuli.
Conclusion: Descriptions of sleep fragmentation that rely on ASDA arousal indices and conventional sleep stages overlook several important variations in EEG activity and autonomic responses. Such characteristics of fragmented sleep are likely to be important in understanding mechanisms underlying cognitive and physiologic consequences of sleep fragmentation.
Support (optional): Supported by NIH grants HL083640, HL07578, and AG025553.

0410

NEUROBEHAVIORAL OUTCOMES FOLLOWING SLEEP DEPRIVATION: SLEEPINESS, AFFECTIVE AND COGNITIVE DOMAINS

Franzen P, Siegle G, Buysse D
University of Pittsburgh, Pittsburgh, PA, USA

Introduction: Impairments in vigilance and cognition are among the most well-documented neurobehavioral effects of sleep deprivation (SD). The impact of SD on affect, and associations among different neurobehavioral outcome domains, has been less thoroughly explored. To examine this, we compared subjective and objective measures of sleepiness, affect, and attention following SD.
Methods: Using a parallel group design, 21–30y.o. adults were randomly assigned to one night of total SD (n=15) or normal sleep (NS; n=14). A multiple sleep latency test was performed the following day. Prior to each nap, participants completed mood and sleepiness visual analog scale (VAS) ratings and a 10-minute psychomotor vigilance task (PVT). In the afternoon, pupillary instability (quantified during the Pupil Sleepiness Test; PST) and affect reactivity (mean pupil dilation response to negatively-valenced picture stimuli) were assessed. All outcomes were analyzed with multivariate analysis of variance (MANOVA) and their effect sizes compared. Associations among the outcomes were compared with Pearson correlations.
Results: The overall multivariate test of group was significant, $F(6,20)=13.25$, $p<.001$ (partial Eta-square effect size, PESES=.799), as were univariate tests for each outcome: VAS-sleepiness ($p<.001$, PESES=.938), Pupil Sleepiness Test ($p<.001$, PESES=.784), MSLT ($p<.001$, PESES=.742); affect outcomes: VAS-mood ($p=.039$, PESES=.159), affect reactivity ($p=.006$, PESES=.265); and slowest 10% of PVT responses ($p=.040$, PESES=.160). A mixed pattern of correlation among the outcomes was found. Within the SD group, PST was associated with MSLT ($r=-.76$, $p=.001$) and affect reactivity ($r=.56$, $p=.031$), and negative mood was associated with subjective sleepiness ($r=.586$, $p=.022$).
Conclusion: SD significantly affected affect, cognition, and sleepiness-related outcomes. Affect-related outcomes had effect sizes smaller than sleepiness outcomes, but similar in magnitude to the PVT, the gold-standard neurobehavioral outcome measure. Relationships among outcomes showed various patterns, indicating that the effects of SD are not uniform across these domains.
Support (optional): MH030915, MH016804, RR0000056, National Sleep Foundation

0411

YOUNGER VERSUS OLDER ADULT COGNITIVE PERFORMANCE DURING 36 HOURS OF TOTAL SLEEP DEPRIVATION

Salamat J,[1] Morshedabbasi M,[2] Drummond S[3]
(1) Veterans Affairs San Diego Healthcare System, Research Service, San Diego, CA, USA, (2) Veterans Affairs San Diego Healthcare System, CA, USA, (3) University of California, San Diego, San Diego, CA, USA

Introduction: Sleep deprivation impacts many different aspects of cognitive and behavioral functioning in young adults (YA). Whether these functions are affected in older adults (OA) undergoing sleep deprivation is less clear. We examined performance across 36-hours total

sleep deprivation (TSD) comparing YA and OA hypothesizing that OA would show smaller deficits in performance relative to YA throughout TSD.
Methods: Ten YA (6F, range=19-36, age=27.1±6.0 and education=15.1±1.3) and 16 OA (13F, range: 60-82, age=68.4±6.2 and education=16.4±2.0) healthy subjects participated in a 36-hour TSD protocol. Subjects completed the psychomotor vigilance task (PVT) and a spatial working memory task (SWM) during 5 different testing sessions. Repeated measures ANOVA was run for all tasks.
Results: Generally, YA performed better than OA at baseline and both groups showed decrements in performance throughout TSD. PVT measures showed a main effect of Time for number of lapses ($p=.003$), median reaction time ($p<.001$), and the slowest responses ($p\leq.001$), and a marginally significant GroupxTime interaction in the middle of the night (22 & 26 hrs TSD), with greater decrements compared to baseline in YA relative to OA ($p=.08$). SWM did not show any significant effects, but performance on SWM did appear to show a circadian influence with OA showing a delayed profile with respect to time/TSD effects.
Conclusion: Overall, YA perform better on the PVT and SWM than OA while well-rested. While performance declined in both groups during TSD, OA experienced smaller decrements on sustained attention in the early morning hours. We did not expect null findings on SWM, although this may have been due to differences in circadian influences between the groups and/or insufficient sample sizes. These preliminary analyses provide evidence that OA may be less vulnerable to TSD in some cognitive domains, but larger samples are needed in this ongoing study to make more definitive conclusions.
Support (optional): 1. R01AG24506
2. UCSD GCRC M01 RR00827

0412

SELF REPORTED SLEEP HABITS OF FIREFIGHTERS IMPROVE AFTER SWITCHING TO 48-96 WORK SCHEDULE (48 HOURS ON - 96 HOURS OFF)

Lange N,[1] Hawkes A,[2] Vellman W[2]
(1) St Anthony Central Hospital, Denver, Denver, CO, USA, (2) St Anthony Central Hospital, Denver, CO, USA

Introduction: Many firefighting departments nationwide are changing to a work schedule of 48 hours on shift followed by 96 hours off shift (48-96) without knowing the effect it has on sleep. We had an opportunity to study the effect of this schedule change on sleep with one large Denver metro department that changed to the 48-96 schedule from the Cal-Berkley Schedule (24 on – 24 off for 3 cycles followed by 72 off).
Methods: On-line personnel (n=269) were asked to complete questionnaires, including the Epworth Sleepiness Scale (ESS), and sleep diaries prior to the shift change (pre) and six months after the change. Data regarding call volume was obtained from the firefighting department. Statistical significance was assessed using the Wilcoxon ranked sum test for hours slept, paired t test for ESS, and t test for two samples for call volume.
Results: 122 personnel (45%) returned the pre-questionnaire, 13 (42%) the six-month. For sleep diaries, 102 (38%) returned the "pre" and 97 (36%) the six-month. Complete data were available for 69 firefighters (26%). The average total hours slept per week pre- change was 46.1 compared to 49.7 at six-months ($p<0.01$). The average number of hours slept per night increased both on and off shift. There was a slight decrease in the mean ESS from 8.8 pre to 8.3 at six months (not statistically significant). Monthly call volume did not change significantly (from 2997 to 2898).
Conclusion: In general, duration of self reported sleep of firefighters is reasonable. Following the change to the 48-96 work schedule, firefighters on average reported sleeping 3.6 more hours per week, and did not report a significant change in daytime sleepiness. The observed changes can not be attributed to a significant change in call volume.

0413

SLEEP RESTRICTION DECREASED ERP BRAINWAVES IN DIRECTIONAL STROOP TASK

Wu J,[1] Dykman R,[2] Molfese D[1]
(1) University of Louisville, Louisville, KY, USA, (2) University of Louisville, KY, USA

Introduction: Previous research on sleep time reduction showed that even small changes of sleep length could lead to cognitive deficits in school-age children (Gozal, 2005). The present study extended this line of investigation to assess the influence of minor sleep loss on cognitive and functional tasks using electrophysiological brain recordings.
Methods: Event-related potentials (ERPs) were obtained from 128-electrode high-density arrays before and after a week of one-hour sleep length change in three experimental groups: one more hour for the extended group; one less hour for the restricted group and no change for the control group. Forty-eight children (age range 6-7 years old) participated in a functional Sroop task. Factor analysis followed by varimax rotation reduced data on both the electrode and time dimensions. Nine electrode clusters (89.57% of the total variance) across the scalp and four time regions across 900 ms (containing 87.463% of the total variance) were identified. Repeated measured ANOVAs were subsequently applied to each selected electrode cluster and peak.
Results: A significant Week by Group interaction was found over the left occipital-temporal region approximately 136 ms after stimulus onset, $F(2,45)=5.421$, $p=.008$, obs. power=.821. Further analysis identified a reduction in brainwave amplitude following sleep time reduction in the restricted group compared to the extended group. A significant Week by Group interaction also occurred over the right occipital lobe approximately 636 ms after stimulus onset, $F(2,45)=5.497$, $p=.007$, obs.power=.826. Further analysis indicated a reduction in ERP amplitude over the two weeks in only the restricted group.
Conclusion: Even a one-hour in sleep duration over a week changes brainwave activity during cognition. Compared to the extended group, the restricted sleep group exhibited decreased brainwaves at different brain areas, at both early and late time period after stimulus onset, suggesting changes on both perceptual and cognitive abilities.
Support (optional): Grant 19T

0414

PERCEIVED SLEEP DEBT: COGNITIVE, EMOTIONAL AND BEHAVIORAL CORRELATES IN YOUNG ADULTS

Vela-Bueno A,[1] Fernandez-Mendoza J,[2] Olavarrieta-Bernardino S,[2] Rodriguez-MuñOz A,[2] De La Cruz-Troca J,[2] Bixler E[3]
(1) Universidad Autonoma Madrid, Madrid, Spain, (2) Universidad Autonoma Madrid, Spain, (3) Pennsylvania State University, Hershey, PA, USA

Introduction: The aim was to examine the relationship between perceived sleep debt (difference between desired and actual sleep time during the weekdays; PSD) and self-reported mood, sleepiness and cognitive and academic performance.
Methods: Self-reported information was obtained from anonymous questionnaires administered to first year students of the Universidad Autonoma, Madrid, Spain. The ethical committee of the University

granted the fulfillment of international ethical standards. The final sample consisted of 1,276 (response rate 74.5%). Mean age was 18.74 (±1.24) years, range 16-23. The survey package included: (1) a Self-Developed Questionnaire (SDQ) that included sections to assess 1) Sleep habits and sleep duration (Cronbach's $\alpha = 0.67$), 2) Health status including mood (Cronbach's $\alpha = 0.81$), and 3) Academic and cognitive performance (Cronbach's $\alpha = 0.57$); (2) the Spanish version of the Epworth Sleepiness Scale (ESS). All information was referred to the last 12 months, unless otherwise stated. To study the relationship between PSD and self-reported health status, sleepiness and cognitive and academic consequences due to sleep, t Student tests were used. The significance level was stated at $p<0.05$.
Results: PSD was significantly associated with excessive daytime sleepiness (ESS>10, $p<0.05$; missing classes due to sleepiness, $p<0.001$; and due to tiredness, $p<0.05$; fall asleep in class, $p<0.05$; daytime sleep attacks, $p<0.001$); negative affect (sadness, $p<0.001$; crying, $p<0.001$; indecision, $p<0.05$; irritability, $p<0.001$; aggressiveness, $p<0.001$; violence, $p<0.001$); and poor memory ($p<0.05$) and restlessness in class ($p<0.001$).
Conclusion: The subjective perception of sleep debt during weekdays in young adults is associated with marked negative consequences on cognition, emotion and behavior.

0415

ACADEMIC PERFORMANCE IN COLLEGE STUDENTS, PROCRASTINATION, AND USE OF A SINGLE NIGHT OF TOTAL SLEEP DEPRIVATION: IS THE "ALL-NIGHTER" A GOOD IDEA?

Thacher P,[1] Kelly K[2]
(1) St. Lawrence University, Canton, NY, USA, (2) St. Lawrence University, NY, USA

Introduction: Sleep in college students is generally inadequate, irregular, and of poor quality. As sleep quality and quantity decrease, academic performance worsens. One practice in which many college students engage includes "pulling all-nighters," or a single night of total sleep deprivation (SN-TSD). Previous studies have reported that about 60% of a small sample of college students had engaged in one or more SN-TSD. The use of SN-TSD was associated with lower grade point average (GPA), "evening" preference, and later bedtimes. This study examined whether procrastination might represent a "third variable" underlying the correlation between poorer academic performance and engagement in SN-TSD.
Methods: 111students (Ps) (68% female) completed measures of procrastination, morningness/eveningness, and use of SN-TSD. Of the sample, 85% of Ps consented to release cumulative GPA from the University registrar. Students who reported that they used one or more SN-TSD were more likely to refuse consent than were those who did not.
Results: Procrastination scores were not associated with use of SN-TSD ($r = .08$, ns), although procrastination scores and GPA were negatively correlated ($r = -.32$, $p < .01$). Full sample mean GPA was 3.0 on a 4.0 scale. Use of SN-TSD was associated with lower GPAs compared to those who did not use SN-TSD (GPA = 2.9 in those who do versus 3.1 in those who do not, $r = -.20$, $p < .06$). However, a minority of students who reported that they use multiple SN-TSDs maintain excellent GPAs.
Conclusion: Our data suggest that for most students, "pulling all-nighters" is not reliably associated with procrastination. These data also indicate that use of SN-TSD is not an effective practice for achieving academic goals. Use of SN-TSD may be effective for a small proportion of students. These data should be considered preliminary until a more extensive, prospective study can be completed.

0416

STANDING STILL WHILE FALLING INTO SLEEPINESS; HOW SLEEP DEPRIVATION AFFECTS POSTURAL CONTROL IN YOUNG ADULTS (PRELIMINARY RESULTS)

Robillard R,[1] Boissonneault M,[2] Filipini D,[2] Prince F,[3] Carrier J[2]
(1) Centre d'étude du sommeil et des rythmes biologiques,, Montreal, Quebec, Canada, (2) Centre du sommeil et des rythmes biologiques, Hôpital du Sacré-Cœur de Montréal, Quebec, Canada, (3) Department of Kinesiology, University of Montreal, Quebec, Canada

Introduction: Postural control (PC), even in simple quiet standing, seems to require attention. Because of its effect on attention, sleep deprivation (SD) might decrease attentional resources available for PC. Recent results have suggested that SD may affect PC directly, or may impinge on PC only when attentional resources are mobilized by a concurrent cognitive task. Moreover, by decreasing attentional resources, SD may also alter integration of visual information in PC. The aim of this study was to determine how sleep deprivation, restricted attentional resources and withdrawal of visual input intermingle to influence PC.
Methods: Six young healthy adults (mean age=24,2±1,8) performed quiet standing on a force plate in two counterbalanced sleep conditions: after a night of sleep (baseline) and after 25h of SD. In both sleep conditions, center of pressure (CoP) displacements were measured 2h after habitual wake time in six conditions: eyes open and eyes closed while doing an interference task, a control task, and no task. T-tests were executed on CoP range and speed with a significance threshold of 0.05.
Results: In our baseline sleep condition, the absence of visual information increased CoP range in the anterio-posterior (AP) direction ($p=0.013$), whereas the interference task increased medio-lateral (ML) CoP speed ($p=0.045$).
While no significant difference between sleep and SD conditions was found when the control task was done with closed eyes, SD decreased ML CoP speed when subjects did the interference task without visual input ($p=0.018$).
Conclusion: SD interfered with postural sway in the most challenging condition. The central nervous system has been shown to prevent disrupted motor performance by increasing muscle stiffness when exposed to stressors. It is therefore possible that under SD, when attentional resources are mobilized elsewhere and visual information is absent, stiffness is increased to reduce sway speed.
Support (optional): This study was supported by the Canadian Institutes of Health Research, the Fonds québécois de la recherche sur la nature et les technologies and the Institut de recherche Robert-Sauvé en santé et en sécurité du travail.

0417

PERIPHERAL VASCULAR REACTIVITY TO FOREARM OCCLUSION IN HEALTHY ADULTS DURING TOTAL SLEEP DEPRIVATION

Toth M,[1] Serrador J,[2] Haack M,[2] Gilmartin G,[2] Cohen D,[2] Gopalakrishnan G,[2] Meier-Ewert H,[3] Mullington J[2]
(1) Beth Israel Deaconess Medical Center, Boston, MA, USA, (2) Beth Israel Deaconess Medical Center, MA, USA, (3) Boston University, MA, USA

Introduction: Blood pressure increases during sleep deprivation (DEP) suggest peripheral arterial vasoconstriction, which may be the result of increased sympathetic outflow due to autonomic activation or altered local peripheral control mechanisms. We investigated the peripheral

vascular response of the brachial artery to occlusion during acute total sleep deprivation.
Methods: During the study, five participants stayed awake continuously for up to 88 hours (5 female, age 39.4±4.8 years) and two participants slept at night (1 female, 1 male, age 26.0±1.0). The arterial blood flow response after 5 minutes of forearm occlusion was recorded every afternoon on the left brachial artery with a pulsed Doppler ultrasound (HDI 5000, ATL Ultrasound). Diameter and flow were analyzed from B-Mode images. Blood pressure was measured on the right finger via photoplethysmography (Portapres).
Results: Peak flow showed a decreasing trend throughout the sleep deprivation period and the comparison between the baseline day (BL) and 58 hours DEP was significant (p=0.01); (mean peak flow, ml/min±SE at BL: 490.4±41.0; 34 hours DEP: 317.9±82.4; 58 hours DEP: 275.3±29.4; 82 hours DEP: 363.5±190.4). There was a statistical trend for an increase in the pre-occlusion mean arterial pressure throughout the days in the sleep deprivation group (mean arterial pressure, mmHg±SE at BL: 73±5.1; 34 hours DEP: 81±9.4; 58 hours DEP: 90±8.9 and 82 hours DEP: 101±16.7). There were no changes in peak flow or blood pressure in the control group. The diameter of the brachial artery did not change during the study in the groups (mean diameter, cm±SE, in DEP vs. control at BL: 0.31±0.01 vs. 0.36±0.04; at 82 hours DEP: 0.31±0.03 vs. 0.34±0.03).
Conclusion: Our preliminary data suggest that acute total sleep deprivation leads to alterations in the peripheral vascular response to occlusion, possibly due to an increasing peripheral sympathetic vasoconstriction associated with sleep loss.
Support (optional): National Institutes of Health (HL075501, and GCRC grant RR01032)

0418

EFFECTS OF RECOVERY SLEEP FOLLOWING PARTIAL SLEEP DEPRIVATION ON DAYTIME SLEEPINESS AND PERFORMANCE

Basta M,[1] Lin H,[2] Bixler E,[1] Tsaoussoglou M,[1] Vgontzas A[1]
(1) Pennsylvania State University, Hershey, PA, USA, (2) Pennsylvania State University, PA, USA

Introduction: It has been shown that one week of modest sleep restriction (from 8h to 6h of sleep/night for 1 wk) impacts adversely sleepiness, performance and inflammatory cytokines. Many individuals in modern societies try to overcome these adverse effects by extending their sleep during the non-work days. The aim of this study was to assess objectively this common practice, i.e. two days of extended ("recovery") sleep following one week of sleep curtailment.
Methods: Ten young, healthy, normal sleepers, mean age ± SE 24.9±1.3 years, were studied for 13 consecutive nights in the sleep laboratory. The first 4 nights served as baseline nights (8 h/night), followed by 6 nights of partial sleep restriction (6h/night), followed by 3 recovery nights (10h/night). Daytime sleepiness [Multiple Sleep Latency Test (MSLT)] and daytime performance [Psychomotor Vigilance Test (PVT)] and serial plasma cytokines´ levels were measured on days 4 (baseline), 10 (after one week of sleep restriction) and 13(after 2 nights of recovery sleep).
Results: Preliminary analysis showed that sleep latency in MSLT was significantly decreased after restriction, compared to baseline overall (p=0.001). Sleep latency improved significantly after recovery sleep, compared to restriction overall (p<0.0001). Interestingly, sleep latencies in recovery tended to be higher compared to baseline (p=0.1).
All 4 PVT variables tended to be worse during restriction compared to baseline, and did not show any improvement during the recovery period; particularly during the evening period for the median RT and mean SRT (p<0.1).
Conclusion: Extended "recovery" sleep of two days appears to reverse the impact of one work-week of mild sleep restriction on daytime sleepiness and fatigue. However, there seems to be a lag on performance´s improvement during the recovery period. Improvement of alertness on recovery compared to baseline may imply that 8h of sleep are not adequate for young, healthy adults.
Support (optional): NIH RO1 HL-64415

0419

SLEEP RESTRICTION DEGRADES PERFORMANCE IN A DRIVING SIMULATOR IN A SLEEP-DOSE DEPENDENT MANNER

Belenky G,[1] Thorne D,[2] Wesensten N,[2] Van Dongen H,[1] Balkin T[2]
(1) Washington State University, Spokane, WA, USA, (2) Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: In real-world operations, multiple days of sleep restriction are more common than acute total sleep deprivation. To characterize the effects of chronic sleep restriction on a task relevant to real-world performance we conducted a sleep dose response study using a driving simulator.
Methods: Sixty-six healthy adults (ages 24–55y; 16 women) spent fourteen consecutive days in a sleep laboratory. They were allowed 8h time in bed (TIB) each night for 3 baseline days. They were then randomized to one of four sleep dose conditions—3h, 5h, 7h or 9h TIB per night—for 7 experimental days. They were again allowed 8h TIB each night for 4 recovery nights. Subjects drove a PC-based driving simulator (STISIM®) four times a day (07:40, 10:40, 13:40, 19:40) for 45min. For the purposes of analysis, the 45min of driving were divided into 7 equal segments. Lane tracking variability (root mean square of lane position) was measured for each segment. Results were analyzed with repeated-measures ANOVA across the experimental and recovery days.
Results: All main effects were significant: sleep dose condition ($F_{3,62}=3.74$, $P=0.001$); day ($F_{10,620}=10.44$, $P<0.001$); time of day ($F_{3,186}=7.96$, $P<0.001$); and segment ($F_{6,372}=57.14$, $P<0.001$). All two-way interactions except time of day by condition were significant: day by condition ($F_{30,620}=6.57$, $P<0.001$); segment by condition ($F_{18,372}=4.08$, $P<0.001$); day by time of day ($F_{30,1860}=1.93$, $P=0.034$); segment by time of day ($F_{18,1116}=2.92$, $P=0.014$); and day by segment ($F_{50,3720}=1.68$, $P=0.044$).
Conclusion: Lane tracking variability exhibited clear sleep dose dependency, with increasing performance degradation from mild to severe daily sleep restriction. Lane tracking variability also showed time-on-task (segment) effects which increased hand in hand with overall levels of performance impairment. These results mimic observations for other performance measures such as the PVT. The findings suggest the effect of chronic sleep loss on performance is similarly potent for tasks relevant to real-world performance.
Support (optional): The U.S. Army Medical Research and Materiel Command and the U.S. Department of Transportation, Federal Motor Carrier Administration.

0420

EFFECTS OF SLEEP DEPRIVATION ON LEARNING AND MEMORY IN MICE AFTER ECSTASY TREATMENT

TeráN G,[1] Andersen M,[2] Ruiz F,[2] Lima M,[3] Takatsu A,[2] Niigaki S,[2] Zaguer A,[2] Frussa-Filho R,[2] VeláZquez J,[4] Tufik S[2]
(1) Autonomy Metropolitan University, D.F., Mexico, (2) Universidade Federal de São Paulo, São Paulo, Sao Paulo, Brazil, (3) Universidade Federal de Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (4) Autonomy Metropolitan University, D.F, Mexico

Introduction: Few studies have directly compared the effects of methylenedioxymethamphetamine (MDMA) and sleep deprivation (SD) on learning and memory. Several lines of experimental evidence suggest that sleep, particularly paradoxical SD plays a role in learning/memory process. The study was designed to examine the effects of SD on learning/memory in mice after ecstasy treatment using the plus-maze discriminative avoidance task (PMDAT as an animal model of learning/memory).
Methods: Mice were treated with saline, 1.25, 2.50 or 5.0 mg/kg of ecstasy (ip) and were submitted to 24h SD or maintained as home-cage control (CTRL) group. All groups were submitted to PMDAT conditioning (training session). During the test session, performed 24h later, mice were again placed in the apparatus for 3 min, without receiving the aversive stimulation (test session).
Results: No differences were found between CTRL and SD mice treated with ecstasy or saline in the training session, indicating that SD associated with ecstasy treatment did not promote deficit learning. The higher doses of ecstasy (5 mg/kg) induced a memory deficit, evaluated in the test session, in both control and SD mice. The lower doses of ecstasy induced such a deficit only in SD mice.
Conclusion: SD can potentiate memory deficit induced by ecstasy in mice.

0421

ADVANTAGES OF CAFFEINE GUM USE FOR PVT PERFORMANCE IN A SLEEP RESTRICTED FIELD ENVIRONMENT

Reichardt R, Leavitt B, Kamimori G
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: We have previously reported that caffeine gum significantly improves performance over placebo on the Psychomotor Vigilance Task (PVT) during sleep deprivation in a laboratory setting. This study examined the ability of repeated dosing of caffeine gum in sustaining PVT performance during a 74-hr simulated military field operation under sleep restriction.
Methods: Twenty soldiers were randomly assigned to placebo (PLA; n=10) or caffeine (CAF; n=10) treatment. After completing a normal duty day (Day 1) with a full night of sleep, volunteers reported for duty at 0700 (Day 2) and trained until 1600 when the field exercise began. Starting at approximately 2200 each evening, field and performance tasks were completed during four 2-hr testing blocks. During these testing sessions volunteers chewed gum containing either placebo or 200 mg of caffeine at 2200, 0115, 0400, and 0700. On Day 3 & 4, a four hour sleep period was allowed from 1330-1730. Psychomotor vigilance was assessed using a palm pilot version of the 5-minute PVT that was administered prior to and following gum administration.
Results: Data were analyzed with a 3-way mixed model ANOVA. A significant group x session interaction ($p < .05$) indicated that the CAF group was significantly faster on the PVT than the PLA group across sessions over the course of the night. Tukey´s post hoc comparisons indicated that within the CAF group speed was maintained through the night, but within the PLA group speed significantly declined in the later testing sessions.
Conclusion: This study demonstrates the effectiveness of caffeine at sustaining simple alertness and vigilance under continuous operations in an actual field environment.

0422

HABITUAL LONG VERSUS HABITUAL SHORT SLEEPERS: CORTISOL SECRETION IN RESPONSE TO 36 HOURS OF TOTAL SLEEP DEPRIVATION

De Valck E,[1] Mairesse O,[2] Quanten S,[3] Berckmans D,[3] Cluydts R[1]
(1) University of Brussels, Brussels, Belgium, (2) University of Brussels, Belgium, (3) Catholic University of Louvain, Belgium

Introduction: In this study we studied the cortisol response of habitual long versus habitual short sleepers during 36 hours of total sleep deprivation.
Methods: Seven male, five female habitual short sleepers and four male, seven female habitual long sleepers participated in the study. Sleep diary assessment two weeks prior to the experiment showed that the habitual short sleepers slept an average of 5.86 hrs per night (SD=.86), whereas habitual long sleepers report an average sleep length of 8.92 hrs per night (SD=.53). During a period of 36 hrs of total sleep deprivation, salivary cortisol levels were sampled every two hours.
Results: A significant difference between short versus long sleepers was found [$F(1,18) = 4.51$; $p<0.05$]: cortisol levels were significantly higher in habitual short sleepers (M = 5.39 µg/l saliva; SE = 0.45 µg/l saliva) than in habitual long sleepers (M = 4.03 µg/l saliva; SE = 0.45 µg/l saliva). The effect of time was also significant ($F(17,306) = 7.55$; $p<0.001$) and post hoc tests suggested both circadian and homeostatic factors are involved. There was no significant interaction effect between the factors habitual sleep duration and time. ($F(17,306) = 0.55$; ns).
Conclusion: Present findings suggest that short sleepers have a higher cortisol secretion in comparison with long sleepers. Future studies are needed to explore whether this represents a potential long term health risk for short sleepers.

0423

SLEEP COMPLAINTS IN HEALTHY WOMEN ARE ASSOCIATED WITH INCREASES IN C-REACTIVE PROTEIN

Okun M,[1] Coussons-Read M,[2] Hall M[1]
(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) University of Colorado at Denver, CO, USA

Introduction: Increased C-Reactive Protein (CRP) is associated with risk of cardiovascular disease (CVD) and rheumatoid arthritis in women. Sleep disturbances have been shown to increase levels of CRP. Little data exists regarding the association between sleep and CRP in women. We evaluated self-reported sleep in a sample of women to evaluate whether the relationship between disturbed sleep and CRP extends beyond clinical populations. This information could identify sleep disturbances as a risk factor in healthy women.
Methods: Nonpregnant women (N = 43, average age 28.2 ± 5.2 years) recruited as a comparison group completed the PSQI, gave a sample of blood and completed a sleep diary for 2-weeks. CRP was detected via EIA (DSL, Webster, TX) with the use of antiserum and the data were log-transformed for analysis.
Results: Pearson correlations indicated that women with greater subjective sleep complaints had increased levels of CRP ($r = .46$, $p < .01$). This relationship was dependent on menstrual phase. Women in the luteal phase with higher PSQI scores had increased levels of CRP ($r = .57$, $p < .05$). This relationship was not observed for women in the

follicular phase (r = .21, p = .29). Data from the sleep diaries revealed no differences in sleep continuity or duration between women in the luteal or follicular phases.
Conclusion: Our data corroborate previous reports that sleep complaints are greater during the luteal phase (Baker *et al.*, 2001) and that poor sleep is associated with elevated CRP (Meier-Ewert *et al.*, 2004). We provide evidence of a relationship between sleep complaints and CRP in a healthy, nonpregnant sample. These data warrant further examination of sleep complaints in non-clinical populations, particularly healthy, menstruating women, due to the epidemiological evidence suggesting increased levels of CRP are associated with increased medical morbidity in women (Everett *et al.*, 2006; Shadick *et al.*, 2006).
Support (optional): None

0424

SLEEP RESTRICTION AND EVENT-RELATED POTENTIALS: DEVELOPMENTAL IMPLICATIONS

Barnes M,[1] Warren C,[1] Millis B,[1] Gozal D,[1] Molfese V,[2] Molfese D[1]
(1) University of Louisville, Louisville, KY, USA, (2) University of Louisville, KY, USA

Introduction: Sleep deprivation affects children at very young ages. Children in the US routinely receive less than the recommended nine hours of sleep. The impact of sleep deprivation on the development of cognition, language, attention, and neurological functioning remains poorly understood. We investigated whether age mediated the effects of a one-hour reduction in sleep on patterns of brain activity in young children.
Methods: Differences in auditory processing and event-related potentials (ERPs) as an outcome of age and sleep assignment were investigated in 81 children (mean age 6.51 years, 44 females) using 128-electrode nets during a speech discrimination task. Children participated in overnight polysomnography and ERP testing after a week of normal sleep established baseline (Week 1). During Week 2, sleep time was reduced by 1 hour and another ERP session conducted. Sleep/wake cycles were confirmed by actigraphy across all weeks.
Results: Factor scores from Principal Component Analysis scores served as dependent measures in a mixed-factorial ANOVA. The omnibus ANOVA revealed a significant week*hemisphere*age (F=3.676, p=0.016) interaction for Factor 1 (372 to 676 ms), accounting for 60.7% of total variance. Post-hoc one-way ANOVA and Tukey´s HSD identified increased activation in 5-year-olds relative to 6-year-olds (F=3.888, p=0.012) over the left hemisphere at Week 1. This could reflect more effortful processing of speech stimuli in younger children. Although it contributed a smaller proportion of variance, a significant week*group interaction (F=4.493, p=0.017) was identified for Factor 4 (260 to 420 ms). Post-hoc tests indicated increased activity in the sleep-restricted children (F=3.221, p=0.039) relative to controls during Week 2.
Conclusion: These results supported our hypotheses that sleep-restricted children expend more effort during processing than control participants and that sleep restriction effects are mediated by age. Sleep restriction impaired speech discrimination in young children. Subsequent analysis indicated a protective effect of sleep on auditory processing.
Support (optional): Research was funded by the following NIH grants: R01HL070911 and R41HD47083.

0425

AGING ATTENUATES THE UNFOLDED PROTEIN RESPONSE TO SLEEP DEPRIVATION IN MICE

Naidoo N, Master M, Pack A
University of Pennsylvania, Philadelphia, PA, USA

Introduction: Earlier studies from our group indicated that acute sleep deprivation in mice leads to up regulation of BiP and induction of the unfolded protein response (UPR). We have now extended the study to examine the effect of acute sleep deprivation on the BiP response and UPR in aged mice.
Methods: Aged (24 month old) C57/BL6 mice were sleep deprived for 3, 6, 9 and 12 hours (n=8/timepoint) starting at lights on (7AM) and were sacrificed at the end of the deprivation period. Mice that had been left undisturbed and sacrificed at the same time points were used as diurnal controls (n=8/timepoint). Expression of BiP, the key cellular marker of the UPR, was determined by western blots. We also determined the phosphorylation status of PERK a sensor of the UPR and regulator of protein translation. Expression of ubiquitin and the pro-apoptotic protein CHOP (C/EBP homologous protein) were also determined.
Results: Unlike in young sleep deprived animals BiP protein levels remained unchanged in the cerebral cortex of sleep deprived aged animals compared to control animals sacrificed at the same diurnal time. We also observed no phosphorylation of PERK in the old sleep deprived mice suggesting that protein translation was not attenuated. Both control and sleep deprived mice displayed an increase in the level of ubiquitination compared to young mice. CHOP levels were also increased in both control and sleep deprived old mice.
Conclusion: The lack of BiP up regulation and the absence of PERK phosphorylation suggest that the UPR is attenuated or not induced in mouse cerebral cortex following sleep deprivation. Increased ubiquitination and in the old animals suggests that more proteins are misfolded and are being targeted for degradation while the increased expression of CHOP suggests that cell death/apoptotic pathways are being activated.
Support (optional): Supported by NIH grant AG025353.

0426

LYMPHOCYTE PHENOTYPE CHANGES IN RESPONSE TO LOSS AND RECOVERY OF SLEEP

Everson C
Milwaukee, WI, USA

Introduction: Sleep deprivation in rats produces a paradoxical combination of proinflammatory status and decreased resistance to bacterial infections, resembling systemic inflammatory response syndrome in humans. The proinflammatory markers mostly are considered nonspecific and produced by a variety of cells other than by T lymphocytes. Recovery sleep arrests pathogenic changes and restores physical health, but by unknown mechanisms. Defects in cellular immunity mediated by T lymphocytes are known to result in decreased resistance to microbial infections, thereby implicating changes to the T lymphocyte phenotype in the reversal of pathophysiology by recovery sleep.
Methods: Total and partial sleep deprivation were produced by the Rechtschaffen-Bergmann method for 5 or 10 days by a brief ambulatory requirement contingent or noncontingent on sleep onset, respectively. Recovery rats were allowed 2 days of sleep after 10 days of sleep deprivation. Baseline control rats were studied after 7 days of ad libitum sleep. There typically were 6 or more rats per group. Leukocytes isolated from blood, spleen, and mesenteric lymph nodes

(MLN) were counted, tested for viability, and tagged by antibody binding to identify T lymphocytes (CD3+) and coreceptors for the recognition of class II and class I MHC antigens: CD4 (helper) and CD8α (cytotoxic). Backgating analyses of flow cytometry data were performed to determine the proportion of CD3+ cells that were double positive. Time points were tested for statistical significance by planned comparison analyses.
Results: The proportion of leukocytes that was composed of T lymphocytes was not different between baseline and recovery sleep. The proportion of CD3+ cells that were double positive (CD4+CD8+) remained unchanged or decreased by 10 days of total or partial sleep deprivation in each tissue studied. In contrast to the proportion of single positive T cells (CD3+CD4+ and CD3+CD8+), which were less strikingly affected, double positive T cells increased markedly and significantly above basal levels by 22% in the spleen and by 108 and 173% in the blood and MLN, respectively.
Conclusion: Regulation of CD4 and CD8 expression generally results in non-overlapping populations T cells, restricted for the type of cell with which the T cell can interact. During sleep recovery after sleep deprivation or restriction, the dramatic increase in the proportion of T cells that were double positive is an unusual phenotype and suggests an increase proportion of recent thymic emigrants. Double positive T cells have been shown by others to be immunologically activated, displaying a variety of functions, such as cytotoxicity, help for humoral immunity, and immunologic memory. These data suggest that one recuperative function of sleep may be recompensatory priming and replenishment of the T cell pool and related functions in response to inadequate sleep.

0427

SLEEP DEPRIVATION IN THE RAT USING MOTION DETECTION

Newman S,[1] Paletz E,[2] Feit E,[3] Obermeyer W,[1] Benca R[1]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) Madison, WI, USA, (3) University of Wisconsin-Madison, WI, USA

Introduction: Extensive work has been done using the disk-over-water method (DOW) for sleep deprivation in rats. We have developed a new apparatus, the conveyor-over-water (COW), which can be used to induce sleep loss via motion detection. The purpose of this study is to determine if the use of motion detection alone is sufficient to induce sleep deprivation. Validation of motion detection for sleep deprivation will allow for selective sleep deprivation and sleep restriction studies on a larger number of animals than is currently feasible.
Methods: The COW operates similarly to the original DOW, but a treadmill suspended over water replaces the disk. Rats (n=3 deprived, 3 controls) were implanted with recording electrodes to allow EEG scoring of behavioral state. Weight, food, water consumption and temperature were recorded daily. A video-based motion detection system recorded the data and triggered belt rotation. Rats were deprived of sleep on two separate occasions, once for seven days, and once for up to 21 days; each deprivation was followed by recovery.
Results: Total sleep time across a seven day deprivation was reduced to an average of 50% of baseline. REM sleep was reduced to an average of 30% of baseline. Recovery sleep showed increases in REM sleep exceeding 300% of baseline and total sleep of 118% of baseline amounts. Energy expenditure and temperature showed increasing and decreasing trend, respectively, among deprived rats.
Conclusion: Sleep deprivation by motion detection is feasible, and results in similar development of the well-documented sleep deprivation syndrome that is seen with the DOW. Procedure refinements (e.g., adjustments of camera sensitivities) may provide a more effective sleep deprivation than is seen in this pilot study.

0428

CONTROLLED ATTENTION THEORY: EFFECT OF SLEEP DEPRIVATION ON ONE-CHOICE AND FOUR-CHOICE RESPONSE TASKS

Pilcher J,[1] Poole P,[2] McCubbin J[2]
(1) Clemson University, Clemson, SC, USA, (2) Clemson University, SC, USA

Introduction: Several theories have been suggested to explain the effects of sleep deprivation. The purpose of the current study was to use a 1-choice response task, requiring controlled attention, and a 4-choice response task, requiring little controlled attention, to examine a recent theory proposing that controlled attention could be an underlying mechanism in decrements in performance due to sleep deprivation.
Methods: Twenty-five participants (age: 21.1 ± 2.6) completed a number of tasks under sleep deprivation conditions. One task, a 5-minute computerized version of the Psychomotor Vigilance Task (PVT), provided a single-choice response task. Another task, the Clemson Diamond Task (CDT) provided a 5-minute four-choice response task. The CDT used 4 directional arrows, corresponding to the 4 arrows on the keyboard, at 3 distances around a center diamond. The participants had to respond by pressing the corresponding arrow key on the keyboard when each arrow appeared on the monitor. Both tasks were administered four times during 30 hours of sleep deprivation, once in each testing session (6:30 – 10:30PM, 11:00PM – 3:00AM, 3:30 – 7:30AM, and 8:00 – 12:00PM). All tasks were counter-balanced across participants.
Results: Repeated-measures ANOVAs indicated that reaction time on the computerized PVT ($p=.003$) and on the CDT ($p<.001$) increased significantly across the testing sessions. The change in reaction time on the CDT; however, was during session 3 with a return to normal levels in session 4. Furthermore, the magnitude of the change in reaction time was greater on the PVT (z-scores ranged from 0.35 to -0.4) than the CDT (z-scores ranged from 0.05 to -0.1).
Conclusion: These findings indicate that although sleep deprivation negatively affected reaction time on both tasks, the effect on PVT performance was more profound. This suggests that the task requiring controlled attention to complete was more susceptible to the effects of sleep deprivation.
Support (optional): This research was funded by the Department of Defense and the Center for Advance Study of Language at the University of Maryland.

0429

EFFECTS OF 36-HR SLEEP DEPRIVATION ON COMMON VOICE MEASURES

Lajambe C,[1] Brown F,[1] Reichardt R,[2] Prosek R[1]
(1) Pennsylvania State University, University Park, PA, USA, (2) Towson University, Baltimore, MD, USA

Introduction: Discrepancies exist between subjective measures of sleepiness and objective measures of sleepiness-impaired performance. Identification and development of non-obtrusive objective measures of sleepiness are imperative. Voice analysis may have potential as a sleepiness-induced fatigue monitoring method.
Methods: Twenty-eight participants (age: 20.5+1.9), 15 sleep deprived for 36 hours (SD, female=7) and 13 non-SD control (CTRL, female=10) produced four voice recordings including on Day 1 practice recording session at 1830h and session 1 at 2030h, on Day 2 session 2 at 0830h and session 3 at 2030h. The CTRL group slept between recordings 1 and 2 while the SD group remained awake throughout. Voice tasks were

rapid counting from 90-99 (COUNT) and reading a standard clinical prose "rainbow passage" (RBOW). Voice measures included fundamental frequency (F0) in Hz, speaking response-time latency (LAT) in msec, syllables-per-second speaking rate (SPS), db Intensity/loudness (INT), perturbations in cycle-to-cycle F0 (JITTER) and Intensity (SHIMMER), misarticulations (MISART), and speaking errors (ERR).
Results: Repeated-measures ANOVA across test sessions indicated for the SD group an increase in F0 means for both COUNT [F(2,28)=3.76, p=.041, session 1<3] and for RBOW [F(2,28)=5.62, p=.010, session 2<3]. No other SD voice changes occurred. In contrast, for COUNT the CTRL group decreased LAT [F(2,24)=4.92, p=.018, session 2,3<1], increased INT [F(2,24)=6.72, p=.012, session 1<2,3] and decreased JIT [F(2,24)=4.16, p=.049, session 3<1,2]. For RBOW the CTRL group tended toward decreased LAT [F(2,24)=2.98, p=.071, session 3<1], increased INT [F(2,24)=7.71, p=.005, session 3>2], and marginally increased SPS [F(2,24)=2.96, p=.087, session 3>2]. No other voice measures changed over sessions.
Conclusion: The SD group progressively increased some in F0, consistent with previous findings. The CTRL group apparently increased in vocal efficiency, a possible learning effect attenuated by fatigue in the SD group. Voice measure sensitivity to SD appears related to both choice of task and measure. Design implications are discussed.

0430

EFFECT OF SLEEP DEPRIVATION ON SPATIAL SKILLS: USE OF A STANDARDIZED TASK

Pilcher J,[1] Pierce T,[2] McCubbin J[2]
(1) Clemson University, Clemson, SC, USA, (2) Clemson University, SC, USA

Introduction: Although our ability to properly process our spatial world is important in virtually every aspect of our lives, little research has examined the effects of sleep deprivation on spatial skills. The purpose of this study was to determine whether short-term sleep deprivation had an effect on spatial skills.
Methods: Twenty-five participants (age: 21.1 ± 2.6) were paid to complete a number of tasks under sleep deprivation conditions. One task was the Perceptual Ability Test (PAT) portion of the Dental Admission Test. The PAT contained 6 different sections, 4 of which were used in the current study (angle discrimination, cubes, aperture, and paper folding). Angle discrimination required participants to distinguish between 2-D angles. Cubes required participants to count the cubes in a stack based on specific characteristics of the cubes. Aperture required participants to mentally pass a 3-D object through a 2-D aperture. Paper folding required participants to mentally fold up a 2-D representation of a paper into a 3-D form. The PAT was administered four times during 30 hours of sleep deprivation, once in each testing session (6:30 – 10:30PM, 11:00PM – 3:00AM, 3:30 – 7:30AM, and 8:00 – 12:00PM). All tasks were counter-balanced across participants.
Results: Repeated-measures ANOVAs were conducted to determine if performance changed across the testing sessions. When collapsing across the four subtests, performance on the PAT decreased significantly (p=.026). Of the subtests of the PAT, performance on only the aperture section decreased (p=.040).
Conclusion: These findings indicate that sleep deprivation negatively affects spatial skills as measured in a standardized test. Skills that require multiple complex spatial strategies, such as the aperture section, seem to be particularly susceptible to sleep deprivation. This result is relevant in our on-going effort to better understand the effects of short-term sleep deprivation on cognitive processing used in a wide range of daily settings.
Support (optional): This research was funded by the Department of Defense and the Center for Advance Study of Language at the University of Maryland.

0431

ETHNICITY, SOCIOECONOMIC STATUS AND SLEEP DURATION IN A SOUTHEASTERN VIRGINIA PRIMARY CARE POPULATION

Vorona R, Thorpe B, Ware C
Eastern Virginia Medical School, Norfolk, VA, USA

Introduction: Increasing evidence links restricted sleep with enhanced risk of obesity. Socioeconomic status might also influence sleep duration and obesity likelihood. The investigators hypothesized that lower socioeconomic status would associate with reduced sleep in a large/diverse primary care population.
Methods: A trained research associate (RA) or clinician presented an anonymous survey to patients at 5 primary care practices. A health professional aided patients in survey completion if needed. Surveys collected demographics, sleep duration, sleep quality (Likert scale), medical and sleep problems, diet, exercise, sleep hygiene, shift work, educational level and income (3 categories). After patients placed surveys in an envelope, medical professionals measured and recorded height and weight on the envelopes and placed them in locked containers. A biostatistician analyzed survey information from the survey results database.
Results: To date, N=861: 549 Caucasian (63.8%), 249 African-American (28.9%), 9 Asian (1%), 5 Hispanic (0.6%). Women 557 (64.7%), men 286 (33%). Mean age 54.6 years (18-95) S.D. 16.2. Mean BMI 29.7 SD 7.1, mean TST 51.8 hr./week SD 17.
Education level: 7.7% < High School, 27.2% High School/GED, 9.7% Associates/Vocational, 27.1% Some College, 14.9% Bachelors, 11.4% Post-Graduate.
Income: <$19,350 10.8%, $19,351-42,000 22.9%, >$42, 000 35.8%, not listed 30.5%.
TST: African-Americans < Caucasians, 49.9 hr./wk vs. 52.2 hrs./wk (95% CI .272, 6.348). Caucasian women reported most sleep: 52.7 hr > Caucasian men 51.8 > Black men 51.3 > Black women 48.4 hr/wk.
BMI: African-American (30.8 kg/m2) > Caucasian (29.2. kg/m2), (95% CI 0.503, 2.742).
Education: A non significant positive trend indicated more sleep with more education, i.e., less than High School = 50.3 hr. (SE 2.0) vs. graduate/Post-graduate = 54.8 hr./wk (SE 2.1).
Conclusion: African-American primary care patients report less sleep than Caucasians. Socioeconomic status as measured by education demonstrates a non-statistically
significant trend towards more sleep in those with greater education.

0432

AGE DIFFERENCES IN ADAPTATION TO AND RECOVERY FROM A SLEEP DEBT

Nedeltcheva A, Penev P, Whitmore H, Buxton O, Spiegel K, Pannain S, Leproult R, Van Cauter E
University of Chicago, Chicago, IL, USA

Introduction: Bedtime curtailment affects adults from all ages. It is not known whether the amount and quality of sleep during sleep restriction and sleep recovery differs in young and older adults.
Methods: Nine middle-aged (35-55 yr) and 17 young (18-27 yr) healthy lean adults spent 16 consecutive nights in the laboratory, including 3 baseline nights with 8-h bedtimes (B1-B3), 6 short nights with 4-h bedtimes (D1-D6), and 7 recovery nights with 12-h bedtime (R1-R6). Blood was sampled during the last night of each condition. The impact of age was therefore examined at B2, D5, R1 and R5.
Results: Total sleep time on B2 (437 ± 17 vs. 425 ± 25 min; mean ± SD) and R5 (233 ± 6 vs. 234 ± 3 min) was similar for both groups, but younger subjects had more recovery sleep both on R1 (675 ± 18 vs. 586 ± 74 min; $p<0.0002$) and R5 (585 ± 49 vs. 470 ± 63 min; $p<0.0001$). REM sleep was similar in both age groups on B2 and D5 but the rebound on R1 was larger in young adults (R1: 201± 39 vs 147 ± 58 min; $p<0.02$). In the older group, SWS remained constant across all bedtime conditions whereas young adults lost ± 20 min of SWS in D5 as compared to B2 ($p<0.01$) and rebounded by ± 30 min in R1 as compared to D5 ($p<0.001$).
Conclusion: Age differences in sleep duration and quality during adaptation to and recovery from a sleep debt are already detectable in midlife.
Support (optional): This work was supported by NIH grants PO1 AG11412

0433

EFFECTS OF SLEEP LOSS ON ENDOTOXIN BINDING PROTEIN AND ENDOTOXIN CLEARANCE IN HEALTHY HUMAN PARTICIPANTS

Lee E,[1] Haack M,[1] Balachandran D,[2] Mullington J[1]
(1) Beth Israel Deaconess Medical Center, Boston, MA, USA, (2) Beth Israel Deaconess Medical Center, TX, USA

Introduction: To investigate the effects of prolonged partial sleep deprivation on human host response, we used a model of purified endotoxin challenge in healthy human participants. Here we investigate changes in endotoxin binding protein (LPS-BP) due to sleep loss and endotoxin clearance in participants following challenge.
Methods: 40 healthy volunteers, ages 21-40 years, stayed in the General Clinical Research Center (GCRC) for 16 days. Participants were allowed to sleep 8hr for the first two nights (baseline). Following this, participants were randomized into one of two sleep conditions, 8hr-sleep condition (N=18), where subjects continued to sleep between 11pm-7am or a 4hr-sleep condition (N=22), where subjects slept between 11pm and 3am for 12 nights. Subjects were also randomized to an endotoxin or placebo condition where on the 11th night they received a double blind injection of endotoxin or placebo. Participants in the endotoxin group received 2ng/kg of endotoxin derived from Salmonella abortus equi just prior to lights out at 11pm. LPS-BP levels were analyzed (N=40) at 1035h, 1435h, and 1835h in serum collected at baseline and at the same times after 10 nights of sleeping 4hr or 8hr/night, and prior to endotoxin/placebo challenge. LPS-BP measurements were made in the GCRC Core Lab via the DPC Immulite system. Endotoxin levels were measured (N=23) at baseline (pre-injection) and in increments of three minutes post-injection for a total of 30min. The measurements were then collapsed into 6min bins. Measurements were made in plasma with a Pyrochrome Chromogenic Limulus Amebocyte Lysate (endpoint method with diazo-coupling).
Results: Prolonged partial sleep deprivation alone lead to elevated LPS-BP in the 4hr-group over the 8hr-group ($p<0.05$). Endotoxin levels increased within the first 30min post-injection and were higher in the endotoxin group compared to the placebo group at 20min post-injection ($p<0.10$). Endotoxin clearance was not significantly different for the 4hr- and 8hr-groups in this preliminary data set, but analyses of the remaining subjects is underway.
Conclusion: Our data suggests that sleep loss itself increases the level of circulating LPS-BP, but that endotoxin clearance is not affected by this degree of accumulated sleep deficit.
Support (optional): National Institutes of Health (R01 MH60641, and GCRC grant RR01032)

0434

DRIVING SIMULATOR TESTING WITH A RURAL DRIVE SCENARIO SHOWS GREATER SENSITIVITY TO SLEEP LOSS THAN OTHER OBJECTIVE MEASURES IN HEALTHY PARTICIPANTS

Ware J,[1] May J,[2] Rosenthal T,[3] Park G,[4] Guibert M,[4] Allen R[3]
(1) Eastern Virginia Medical School, Norfolk, VA, USA, (2) Eastern Virginia Medical School, VA, USA, (3) Systems Technology, Inc., Hawthorne, CA, USA, (4) Systems Technology, Inc, Hawthorne, CA, USA

Introduction: This study compared driving simulator (DS) performance in healthy participants to other performance measures after sleep loss.
Methods: After IRB approval, 14 healthy participants (19-57 years, 7 females) completed 3 separate 24-hour counterbalanced visits sleeping for either 8, 4, or 0 hr. Participants completed the study in pairs and interacted to keep each other awake. Technicians helped to ensure wakefulness.
In the morning, participants completed a 60-minute DS task involving a rural drive (Risser et al 2000), the Critical Tracking Task (CTT) (Allen *et al.*, 1999), the Psychomotor Vigilance Task (PVT), the Epworth Sleepiness Scale (ESS), Visual Analogue Scale (VAS), the Stanford Sleepiness Scale (SSS), and a one-nap sleep latency trial.
Results: The DS measure of average lateral lane deviations best discriminated between the sleep deprivation conditions with statistically significant differences among all conditions (8, 4, and 0 hours); 8hr ($M = 1.15$, $SD = .145$); 4hr ($M = 1.64$, $SD = .309$); 0hr ($M = 2.33$, $SD = .490$). Significant differences between the 4 and 0 hr SD nights occurred only when utilizing the full 60 minutes of data. The PVT measures of reaction time were only sensitive between the 8 and 0 hr SD conditions. The sleep questionnaires VAS and SSS showed good discrimination between all three SD conditions. The ESS like the CTT did not discriminate between the 8 and 4 hr sleep conditions. One-nap sleep latencies were similar to that of the PVT results with sensitivity only between the 8 and 0 hr SD conditions.
Conclusion: The DS was the most sensitive to sleep deprivation with lane deviations doubling in size under the no sleep condition. Although the DS task was most sensitive particularly at discriminating between normal and less severe sleep loss (8 to 4 hrs), it required the most time to complete.
Support (optional): National Center for Injury Prevention and Control Funding No. 1 R43 CE000491-01A1

0435

BIOMATHEMATICAL FATIGUE MODELING: INDIVIDUALIZED PREDICTION OF COGNITIVE PERFORMANCE

Van Dongen H,[1] Mott C,[2] Huang J,[3] Mollicone D,[4] McKenzie F,[3] Dinges D[5]
(1) Washington State University, Spokane, WA, USA, (2) Pulsar Informatics Inc., Vancouver, British Columbia, Canada, (3) Old Dominion University, Norfolk, VA, USA, (4) University of Pennsylvania, Philadelphia, PA, USA, (5) University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: Current biomathematical fatigue models do not accurately predict cognitive performance in the face of trait individual differences in vulnerability to sleep loss, especially when initial conditions are also uncertain; and they do not yield valid estimates of prediction accuracy. To overcome these limitations, we implemented for the two-process model a novel prediction approach based on Bayesian forecasting.
Methods: Bayesian forecasting was implemented for three trait parameters (homeostatic buildup rate, circadian amplitude and basal performance level) and two initial condition parameters (homeostatic state and circadian phase angle). Bayesian priors for the trait parameters were derived from a sample of 10 healthy males (ages 21–50y) who participated in a laboratory experiment with 88h total sleep deprivation. Psychomotor vigilance test (PVT) performance lapses (RT≥500ms) measured every 2h were analyzed with mixed-model regression to estimate parameter means and variances over subjects. The PVT data of three additional subjects were set aside for use in prospective simulations. For these subjects, every time after performance was measured, their model parameters were updated through Bayesian forecasting, and then performance was predicted 24h ahead.
Results: Comparison of 24h-ahead predictions to the actual observations revealed that as more data became available for the three individuals, their performance predictions became increasingly more accurate and exhibited progressively smaller 95% confidence intervals, as the model parameters converged efficiently to those that best characterized each individual. Within 16h awake, this constituted an average reduction in prediction error variance of 63.9% relative to what would have been achieved by the non-individualized two-process model ($F_{39,39}=2.77$, $P<0.001$).
Conclusion: Our Bayesian forecasting approach resulted in increasingly accurate individualized performance predictions in the face of unknown subject-specific traits and uncertain initial conditions, and also provided 95% confidence intervals. This yielded the first solution to some of the most critical challenges in biomathematical modeling of cognitive performance.
Support (optional): AFOSR grants FA9550-05-1-0086 and F49620-95-1-0388 and USAMRMC grant W81XWH-04-1-0923.

0436

INCREASE IN HUNGER IN A STATE OF SLEEP DEBT: IMPACT OF AGE

Van Cauter E, Penev P, Whitmore H, Buxton O, Pannain S, Leproult R, Nedeltcheva A
University of Chicago, Chicago, IL, USA

Introduction: We have previously shown that restricting sleep for 2 nights without change in caloric intake and physical activity results in increased hunger in young adults. The present study examines the impact of 5 days of sleep restriction and extension on hunger in young and middle-age adults.
Methods: Fourteen healthy lean adults (young: n=5, 25 ± 1 yr; older: n=9, 45 ± 8 yr) spent 16 days in the laboratory: 3 days with 8-h bedtimes, 6 days with 4-h bedtimes, and 7 days with 12-h bedtime. The subjects were on a weight-maintenance diet for the entire study and had only sedentary activities. Hunger ratings were obtained on a 10-cm visual analog scale at 2-h intervals during the last baseline day and the last days of sleep restriction and extension.
Results: There were large individual differences in hunger ratings at baseline (0.8 – 9.2 cm) and after sleep extension (0.9 – 7.2 cm). Sleep duration had a marked impact on the mean daily hunger rating (mean ± SD; 8h: 4.47 ± 2.16 cm; 4h: 5.54 ± 2.22 cm; 12h: 3.42 ± 2.01 cm; $p=0.0003$; $p<0.05$ for all contrasts). When relative changes were calculated for each individual, hunger ratings were, on average, more than twofold higher at the end of sleep restriction than at the end of sleep extension. The increase in hunger with sleep restriction was significant in both age groups ($p<0.002$) and its magnitude was inversely correlated with age ($r= -0.66$, $p<0.02$). Indeed, during sleep restriction as compared to extension, the increase in hunger ratings was three fold larger in young subjects than in middle-aged adults (3.66 ± 1.13 cm versus 1.13 ± 0.83 cm; $p=0.0001$).
Conclusion: These results suggest that sleep restriction may be associated with a risk of overeating, particularly in younger adults.

0437

DECREASED CEREBRAL ACTIVATION DURING VERBAL LEARNING IN OLDER ADULTS FOLLOWING 36-HRS TOTAL SLEEP DEPRIVATION

Orff H,[1] McKenna B,[1] Meloy M,[2] Eyler L,[3] Salamat J,[4] Drummond S[2]
(1) SDSU/UCSD Joint Doctoral Program in Clinical Psychology, Research Services, VA San Diego HCS, San Diego, CA, USA, (2) UCSD Department of Psychiatry, Research Service, VA San Diego HCS, San Diego, CA, USA, (3) UCSD Department of Psychiatry, CA, USA, (4) Research Service, VA San Diego HCS, CA, USA

Introduction: Research has shown that older adults experience increased activation in both task-specific and non-specific regions relative to young adults when performing encoding tasks. It is assumed that increased activation aids in maintaining performance, however it may be that increased activation reflects a disinhibitory process that impairs performance. In this study we hypothesized that sleep deprivation would lead to increased activation and that increased activation would predict poorer performance on a verbal learning task (i.e., a disinhibition hypothesis).
Methods: 12 subjects (10F, mean age=68yrs) performed a verbal learning task twice: well-rested and following 36-hrs TSD. FMRI analyses focused on task-specific regions of interest and examined BOLD activation for memorization of hard and easy words. Number of words recognized was used as the behavioral measure of learning. Performance data were also regressed onto activation data to identify areas in which performance was related to magnitude of post-TSD activation.
Results: Subjects showed decreased activation after TSD in right inferior parietal lobe (BA40), amygdala, and bilateral hippocampi during memorization of easy words. For hard words, decreased activation was observed in the left parahippocampus. Behaviorally, subjects showed worse recognition memory ($p=.038$) after TSD. Regression analyses showed that increased activation in bilateral inferior parietal lobes (BA40) and right inferior frontal lobe (BA44) and less activation in the left angular/supramarginal gyri (BA30/40) were associated with better performance.
Conclusion: Contrary to our hypothesis, activation in task-related areas decreased after TSD, as did recognition memory performance. However,

when activation was regressed with performance, it appeared that those subjects who were able to recruit additional resources better maintained their performance. Overall, these results are consistent with data on younger adults in that activation level was directionally associated with performance. The results also suggest that some older adults may be resilient to the effects of TSD when performing complex encoding tasks.
Support (optional): R01AG24506
F31 MH077411-01A1
UCSD GCRC M01 RR00827

0438

MILD SLEEP RESTRICTION ON THE COW (CONVEYOR-OVER-WATER) INCREASES FOOD CONSUMPTION IN RATS

Paletz E, Obermeyer W, Baldo B, Kelley A, Benca R
University of Wisconsin-Madison, Madison, WI, USA

Introduction: Recently, it has been suggested that shortened sleep may be one factor contributing to the rise in incidence of obesity. This type of sleep loss is generally milder than what has been traditionally studied in animals, however. We have begun to assess how chronic restriction of sleep, comparable to that typically experienced by humans, affects feeding patterns in rats. In the present pilot study, we sought to determine if increases in feeding seen in investigations of severe sleep deprivation could be replicated under much milder conditions of sleep restriction (SR).
Methods: Male, Sprague-Dawley rats were housed on a conveyor-over-water (COW) apparatus. During baseline, the rats were permitted to sleep. Enhanced video motion detection software was used to detect and record behavioral sleep state (awake or asleep). Following baseline, the rats were restricted to 80% of their baseline sleep by using a "sleep-walk contingency" (when the rat remained motionless for > 4 seconds, the belt would turn toward a water bath). After SR, the rats were permitted to recover on the COW. Rats were provided with ad libitum access to chow and water. Grams of food consumed and body weight were recorded daily.
Results: During SR, rats increased their amounts of food consumption over baseline. However, unlike with studies involving severe sleep deprivation, the rats did not decrease their body weights.
Conclusion: Even mild sleep restriction (~ 80% of baseline) leads to increased food consumption in rats. This change suggests that neurobiological mechanisms which regulate feeding are affected by SR, a finding that may have negative health implications for humans with established patterns of shortened sleep duration.
Support (optional): This work was supported by NIH/NHBLI.

0439

FACTORS AFFECTING ETHNIC DIFFERENCES IN SLEEP DURATION

Ibrahim S, Thornton D, Auckley D
Case Western Reserve University, Cleveland, OH, USA

Introduction: Recent studies have demonstrated an association between insufficient sleep and ethnicity. However, the factors behind this association have not been described. We examined the effect of patients´ behaviors on the relationship between race and self-reported sleep duration.
Methods: A prospective study of consecutive adults undergoing polysomnogram (PSG) at an urban academic sleep center between February and August of 2006 was performed. All patients completed questionnaires regarding sleep duration and behaviors surrounding bedtime. Sleep duration was self-reported as < 4 hours, 4-6 hours, 6-8 hours, 8-10 hours, and > 10 hours. Data was collected regarding demographics, insurance status, 15 co-morbidities, bedtime behaviors and PSG results. Data were analyzed using multiple regression.
Results: 1155 patients were enrolled. Demographics: average age 49 ± 13 years, 63% female, ethnicity - 50% Caucasian, 41% African American, 8% Latino. The average body mass index (BMI) was 40 ± 15 kg/m2 and 81% were diagnosed with obstructive sleep apnea (mean apnea-hypopnea index (AHI) = 33 ± 35). African Americans and Latinos reported 0.4 hours less sleep, on average, than Caucasians ($p<0.001$ and $p<0.01$ respectively). These differences persisted despite adjusting for age, gender, insurance status, BMI, AHI, and co-morbidities, including depression and bipolar disorder. Further adjustment for bedtime behaviors (pre-bedtime caffeine intake, smoking and alcohol consumption; place of sleep; bed cohabitation; and bedroom environmental noise) had no effect on racial differences in sleep duration. Of bedtime behaviors, only pre-bedtime smoking was independently associated with decreased average sleep duration (-0.26 hours, $p = 0.001$).
Conclusion: In this cohort of patients referred for PSG, we found a strong and persistent relationship between decreased self-reported sleep duration and African American race or Latino ethnicity. This could not be attributed to differences in common sleep behaviors. Further work is needed to understand factors associated with diminished sleep among people of color.

0440

AGE DIFFERENCES IN THE ASSOCIATION BETWEEN SLEEP DURATION AND MORTALITY IN A LARGE U.S. SAMPLE

Gangwisch J
Columbia University, New York, NY, USA

Introduction: A u-shaped relationship between sleep duration and mortality has been called one of the most replicated findings in epidemiology. These results are not surprising for short sleep duration since it is associated with obesity, diabetes, and hypertension, but there is little evidence that long sleep duration has adverse effects. Despite this, the findings for long sleep duration have been used to justify recommending sleep restriction to decrease mortality risk. No epidemiological studies have published analyses stratified by age, even though average life expectancy is over 77 years and therefore the majority of those who died were elderly. The relationships between sleep duration and obesity and sleep duration and hypertension have been shown to differ between middle-aged and elderly subjects.
Methods: Multivariate longitudinal (1982-1992) analyses stratefied by age of the NHANES I (n=9,601) using Cox Proportional Hazards models to see whether the relationship between sleep duration and mortality differs between middle-aged and elderly subjects.
Results: No relationship between sleep duration and mortality was found in subjects between the ages of 32 and 59 (p=.53). A U-shaped relationship was found only in elderly subjects between the ages of 60 and 86, with both short sleep durations of <= 5 hours (HR=1.32, 95% CI 1.08–1.60) and long sleep durations of => 9 hours (HR=1.37, 1.15–1.63) having significantly higher hazard ratios.
Conclusion: When those who died over the follow-up period were asked the sleep duration question, they were likely to have suffered from chronic diseases that eventually contributed toward their deaths. Levels of pro-inflammatory cytokines, which contribute toward sleepiness and fatigue, have been found to be elevated in conditions in which the primary pathogenic mechanism is insulin resistance. Long sleep duration is therefore unlikely to have contributed toward mortality, but rather is judged to have been a consequence of conditions associated with chronic inflammation.

0441

EVENING AND MORNING EEG TOPOGRAPHY AFTER ONE NIGHT OF SLEEP DEPRIVATION IN YOUNG ADULTS

Forest G,[1] Lambert A,[2] Godbout R[3]
(1) University of Quebec in Outaoauais, Gatineau, Quebec, Canada, (2) University of Quebec in Outaouais, Quebec, Canada, (3) University of Montreal, Quebec, Canada

Introduction: Quantified analysis of morning EEG activity has been used to characterize the restorative value of the previous night. We used a full EEG montage to better characterize the respective sensitivity of cortical regions to sleep loss.
Methods: Thirty healthy young adults were recorded for two consecutive nights. On the second night, 18 were allowed to sleep while the 12 others were totally sleep deprived (TSD). EEG recordings with eyes closed were obtained for 5 minutes in the evening and in the morning. Spectral analysis was performed on 12 to 15 four-seconds epochs and four frequency bands were generated: Delta (0.75-3.75 Hz), Theta (4.0-7.75 Hz), Alpha (8.0-12.75 Hz), and Beta (13.00-30Hz). Data was grouped into two regions for statistical analysis: fronto-temporal (FT) = (Fz+Fp1+Fp2+F7+F8+T3+T4) and parieto-occipital (PO) = (P3+P4+O1+O2). For each participant, FT and PO morning values were expressed as percentage of evening values. This percentage was tested against the null hypothesis (no change from evening to morning) separately in each group, using single sample t-tests. Groups were then compared using T-tests on each frequency band for both cortical regions.
Results: TSD participants showed little significant differences between recordings, except for *increased* morning Theta activity at FT and PO relative to evening. In control participants, morning activity in FT region was *decreased* in Delta and Beta while in PO only Beta decreased. When groups were compared, we found in the FT region that percentage of change was greater in control participants for Delta and Beta and greater in Theta for the TSD group. For the PO region, control participants showed a greater change compared to TSD for Delta and Beta.
Conclusion: These results suggests that decreased morning Delta and Beta activity could reflect a normal restorative value of sleep while increased Theta could reflect an impaired restorative value of sleep.

0442

INCREASED PAIN RESPONSE DURING PROLONGED TOTAL SLEEP DEPRIVATION (TSD) IS INDEPENDENT OF FATIGUE OR DISSATISFACTION WITH THE EXPERIMENTAL IN-HOSPITAL ENVIRONMENT

Haack M,[1] Toth M,[2] Cohen D,[2] Mullington J[2]
(1) Harvard Medical School, Boston, MA, USA, (2) Beth Israel Deaconess Medical Center, MA, USA

Introduction: The development and augmentation of pain under conditions of insufficient sleep duration and quality is increasingly recognized, but it is still an open question as to whether or not this is just due to a general dysphoric state, characterized by fatigue or dissatisfaction with the experimental environment of the in-hospital setting. It is well known that the experience of pain is comprised of not only sensory, but also emotional and cognitive components. Here, we investigate whether pain develops independent of general dysphoria in response to prolonged TSD.
Methods: Twenty-six healthy participants were randomly assigned to either 88 hours of TSD (N=20) or three nights of 8h-control sleep (23-07h; N=6) after two baseline nights with an 8h-sleep opportunity. Starting on the 2nd baseline day, participants were equipped with intensive recording devices to monitor blood pressure, temperature, EEG, and to collect blood. Computerized visual analog scales (VAS) were presented every 2 hours to assess regional (e.g. headache, backpain) and generalized physical symptoms (e.g. body pain, physical discomfort), as well as general dysphoria by asking participants about their levels of fatigue and satisfaction with the GCRC environment, research staff, study schedule, and food quality. Single self-rated pain items and satisfaction items were compiled to a global pain and satisfaction variable, respectively.
Results: Pain increased throughout three days of TSD by 8 ± 2%, compared to an increase of 3 ± 3% in the 8h-sleep condition ($p<0.05$ for interaction effect). In addition, the first two days in the GCRC introduced an additional pain increase of 5 ± 1% in both conditions, likely due to the environmental change and procedures ($p<0.05$ for time effect). Satisfaction with the study (N=11) was higher during TSD than the control sleep condition ($p<0.05$ for condition effect), thus opposing the pattern seen for pain. After controlling for fatigue, a trend towards increased pain in response to TSD still remained ($p=0.1$).
Conclusion: The development of painful physical symptoms in response to TSD might not be simply attributed to fatigue and dissatisfaction with the experimental environment and procedures.
Support (optional): National Institutes of Health (HL075501, GCRC grant RR01032).

0443

THE EFFECT OF EXTRA SLEEP ON MOOD AND ATHLETIC PERFORMANCE AMONGST COLLEGIATE ATHLETES

Mah C,[1] Mah K,[1] Dement W[2]
(1) Stanford University, Stanford, CA, USA, (2) Stanford University, Palo Alto, CA, USA

Introduction: Although much research has established the detrimental effects of sleep deprivation on cognitive function, mood, and performance, relatively little research has investigated the effects of extra sleep over multiple nights on these variables, and even less on the specific relationship between extra sleep and athletic performance. The results we report herein are directed at illuminating this latter relationship.
Methods: In the first trials of this ongoing study, six healthy students (age 18 – 21) on the Stanford men´s basketball team maintained their typical sleep/wake patterns for a two week baseline followed by an extended sleep period in which they obtained as much extra sleep as possible. Sleep/wake activity was monitored by actigraphy and sleep logs. To assess improvements in athletic performance, indicators including sprint time, shooting percentages, and various rating scales were measured following every practice. Profile of Mood States (POMS) ratings were recorded weekly and the Epworth Sleepiness Scale was administered during baseline and at the end of sleep extension to monitor mood and daytime sleepiness.
Results: Significant improvements in athletic performance were observed including faster sprint time (16.3 ± 0.69 seconds at baseline, 15.3 ± 0.44 seconds at end sleep extension, $p<0.05$) and increased free-throws (7.9 ± 0.47 at baseline, 8.8 ± 0.46 at end sleep extension, $p<0.05$). Athletes also reported increased energy and improved mood during practices and games as indicated by increased POMS vigor ratings (45.5 ± 7.5 at baseline, 56.9 ± 8.5 at end sleep extension, $p<0.05$) and decreased POMS fatigue scores (44.1 ± 6.7 at baseline, 32.3 ± 7.9 at end sleep extension, $p<0.05$). Epworth scores decreased from 9.2 ± 4.0 at baseline to 2.8 ± 1.5, $p<0.05$ at end sleep extension.
Conclusion: Obtaining extra sleep was associated with improvements in indicators of athletic performance and mood among members of the men´s basketball team.

0444

THE EFFECTS OF OSA ON SERUM LEVELS OF BRAIN NATRIURETIC PEPTIDES

Chalhoub M,[1] Maroun R,[2] Harris K,[3] Milhauser R,[2] Chisholm J,[2] Waked A,[2] Azzi J,[2] Diab W[2]
(1) Staten Island University Hospital, Staten Island, NY, USA, (2) SIUH, Staten Island, NY, USA, (3) Staten Island University Hospital, NY, USA

Introduction: Obstructive sleep apnea syndrome (OSA) is a common condition that is characterized by recurrent upper airway obstruction during sleep. Hypoxic stress during apneic events can lead to ventricular stress and stretch. The purpose of this study is to evaluate the effects of OSA on serum levels of BNP.
Methods: Subjects referred for the evaluation of OSA were evaluated. Subjects with history of systolic or diastolic ventricular dysfunction, renal insufficiency, or pulmonary hypertension were excluded. Subjects older than 40 years of age with history of smoking, coronary artery disease (CAD), hypertension (HTN), or diabetes mellitus (DM) underwent a 2-D echocardiogram. Those found to have left ventricular hypertrophy, or systolic or diastolic dysfunction were also excluded. Enrolled patients underwent nocturnal polysomnography (NPSG). Two sets of blood were drawn on the night of the NPSG; One for night BNP (NBNP) and one for morning BNP (MBNP) levels. OSA was defined as Apnea/Hypopnea Index (AHI)>10. Cardiac risk factors were defined as active smoking, and history of DM, HTN, or CAD.
Results: 59 subjects were included. 42 had OSA compared to 17 with no OSA. The N BNP level in subjects with cardiac risk factors and OSA was significantly higher than the N BNP level in subjects with cardiac risk factors but no OSA. (44.1 and 11.1 p=0.02). The M BNP level was significantly higher than the N BNP level in subjects with OSA and cardiac risk factors (55.59 and 44.09 p=0.007) compared to subjects with OSA but no cardiac risk factors (10.70 and 11.11 p=0.69).
Conclusion: In subjects with cardiac risk factors, the presence of OSA raises the level of BNP after sleep. This is probably due to cardiac stress and diastolic dysfunction that develops during sleep. The elevation of BNP level persists throughout the day signaling cardiac stress that might persists during wake.
Support (optional): ECRIP Grant, New York State Department of Health.

0445

INSOMNIA IN OBSTRUCTIVE SLEEP APNEA (OSA) USING THE SLEEPMED INSOMNIA INDEX (SMI)

Turner J, Bogan R
SleepMed, Inc., Columbia, SC, USA

Introduction: Subjects with OSA often report an associated insomnia complaint, especially first night effect, during polysomnography (PSG). The SleepMed Insomnia Index (SMI) is a simple patient self administered tool that has been shown to quantify the severity of insomnia in clinical practice. This study examines co morbid insomnia in subjects with moderate to severe OSA utilizing the SMI to describe their pattern of use of sedative hypnotic agents at PSG, CPAP titration, and office follow-up.
Methods: This is a retrospective review of 50 consecutive subjects who underwent baseline PSG followed by CPAP titration. All underwent pre and post treatment assessment using the SMI to assess the insomnia complaint, especially first night effect, and the Epworth Sleepiness Scale (ESS) to assess daytime sleepiness. The pattern of usage of short acting sedative hypnotics is described to further quantify their insomnia complaint.
Results: Means, standard deviations, and t-tests are reported. SMI scores were 20/40(9) and post therapy SMI scores were 14/40(9) with t-tests significant p=0.003. Less than 10 is considered normal. Pre therapy ESS scores were 13/24(5) and post ESS scores were 9/24(4) with t-test significant p<0.001. The use of a short acting hypnotic agent at baseline PSG was 38%, at CPAP titration was 52% and at follow-up office visit was 23%. Those who stayed on medication at office follow-up, 71% had SMI scores between 20 and 40.
Conclusion: Co morbid insomnia is seen in OSA as well as subjects treated with CPAP. SMI and ESS scores showed improvement with CPAP. Subjects with SMI scores above 20 characteristic of an insomnia complaint were found to have the highest medication usage at follow-up. The SMI can be useful to assist the clinician to quantify insomnia, facilitate management and assess the efficacy of therapy.

0446

PREVALENCE AND FEATURES OF REM SLEEP-RELATED BREATHING DISORDERS

Garewal M,[1] Mettu K,[2] Sarwal A,[2] Sahota P[1]
(1) University of Missouri-Columbia, Columbia, MO, USA, (2) University of Missouri-Columbia, MO, USA

Introduction: To determine the prevalence, clinical features and effect of treatment in patients with REM sleep-related breathing disorders (SRBD).
Methods: Single institution retrospective chart review at an accredited university hospital sleep disorders center. We reviewed all baseline sleep studies conducted over a four month period. REM OSA was defined as an apnea-hypopnea index (AHI) two times the total sleep time (TST) AHI and three times the NREM AHI. REM AHI had to be a minimum of 5. Non-apneic hypoxemia occurring only in REM sleep was defined as REM Hypoxemia.
Results: 256 baseline polysomnograms (PSGs) were performed over a four month time period. 34 patients met criteria (7.5%). Twenty-six patients were female (76%). The average age was 52 (range 25-72). Average BMI was 40 (range 23-56). Snoring (24/34) and excessive daytime fatigue (14/24) were the most common presenting complaints. Mean TST AHI was 8.0 (range 2.1-18.3), REM AHI was 35.0 (range 7.4-77.6) and NREM AHI was 2.7 (range 0.0-9.5). Four patients had REM hypoxemia, three had a combination of REM hypoxemia and REM OSA, and twenty-seven had REM OSA. Three patients with REM hypoxemia were treated with oxygen therapy and the fourth patient received both oxygen and positional therapy. Three patients with REM hypoxemia and REM OSA were treated with oxygen and CPAP therapy. Of the remaining twenty-seven patients with REM OSA seven received positional therapy and twenty received CPAP therapy. Epworth Sleepiness Scores were 10 + 5 before intervention and 6 + 4 afterwards.
Conclusion: Prevalence of REM SRBD was 7.5%. REM SRBD was three times more common in females. Snoring and excessive daytime fatigue were frequent presenting complaints. Higher BMI and age were associated with REM SRBD. Treatment improved daytime symptoms. Therefore, by incorporating the REM AHI and REM-related hypoxemia into the treatment decision tree, patients with REM SRBD can be effectively treated.

0447

EFFECTS OF HYPOXIA AND SLEEP FRAGMENTATION ON EXCESSIVE DAYTIME SLEEPINESS

Ukueberuwa D,[1] Smith S,[2] Oei T[2]
(1) Princeton University, Princeton, NJ, USA, (2) University of Queensland, Brisbane, Queensland, Australia

Introduction: Excessive daytime sleepiness (EDS) is a common symptom of obstructive sleep apnea (OSA). While both nocturnal hypoxia and sleep fragmentation may contribute to the neuropsychological effects of OSA, their relationship to subjective EDS is unclear. The objective of this study was to determine an association between these sleep variables and subjective report of EDS on the Epworth Sleepiness Scale (ESS).
Methods: 562 participants were subdivided into four groups based on high and low hypoxia level measured by percent of sleep time below 90% oxygen saturation (median = 5.5%), and sleep fragmentation level measured by the arousal index (median = 23.5 events/hour). 50 participants with the most extreme scores on each measure were chosen to create a sample of 200 participants (4 groups). Two-way ANOVA tested the main effects and interaction of these two variables on the ESS total score. A chi-square goodness of fit test was used to test differences between the groups for Q8 of the ESS (falling asleep while driving).
Results: There was no significant main effect of arousal or hypoxia level on the ESS score ($p = 0.917$, 0.407 respectively). There was also no interaction between the measures ($p = 0.586$). The chi-square analysis showed no significant difference between the number of participants in each group who indicated a propensity to fall asleep while driving ($p = 0.367$). The only variable significantly correlated with ESS scores was BMI (mean = 33.26, SD = 13.91, $r = 0.27$, $p < 0.01$).
Conclusion: This data suggests that the hypoxia and sleep fragmentation associated with OSA do not directly affect subjective measures of EDS. Furthermore, variation in these sleep variables are not reflected in a patient´s subjective likelihood of falling asleep while driving.
Support (optional): The University of Queensland and the Prince Charles Hospital

0448

PREOPERATIVE SCREENING FOR OBSTRUCTIVE SLEEP APNEA USING THE MODIFIED BERLIN QUESTIONNAIRE AND POST OPERATIVE INTERVENTION WITH AND WITHOUT CPAP. RANDOMIZED CONTROL STUDY OF SAME DAY SURGICAL PATIENTS

Ludwig K,[1] Ross D,[1] Snow G[2]
(1) Intermountain Healthcare, Provo, UT, USA, (2) Intermountain Healthcare, UT, USA

Introduction: Obstructive Sleep Apnea Syndrome (OSAS) affects a large percentage of patients who receive surgical services. Use of the Modified Berlin Questionnaire has assisted in identifying and treating these patients.
Methods: Same day surgical patients age 40 and over were asked to participate in the study. Those who scored greater than 25 on the Modified Berlin Questionnaire, were randomized into the 2 test groups. Group 1 postoperatively, in the Post Anesthesia Recovery Unit (PACU), were place on self-titrating CPAP until they were awake and alert. They were then moved to the post op Same Day Surgical Unit until discharge. Group 2 were taken postoperatively to PACU and given O2 to keep O2 saturations greater than 90%. The final group of patients (control) did not score greater than 25, were also observed. Lengths of stays and other co-morbidities were documented in all three groups.
Results: 482 patients were given the Modified Berlin Questionnaire to complete. 200 patients scored greater than 25, were then randomized into the 2 high-risk groups. Average length of stay were: control group = 203 min, CPAP group = 164 min, non-treatment group = 345 min. Total number of patients who were admitted to the hospital, for greater than 23 hours, n = 8: 1 from the control group, 0 from the CPAP group, 7 from the non-treatment group. There was no statistical significance between the control and CPAP group, but highly significant between the control and non-treatment group.
Conclusion: Preoperative screening for OSAS has shown to be effective in identifying patients at high risk for OSAS. Treatment of those patients postoperatively with CPAP significantly decreases lengths of stay postoperatively. Patients that show high risk for OSAS benefit with the use of CPAP postoperatively.

0449

ROLE OF NASAL OXYGEN IN PATIENTS WHO CAN NOT TOLERATE CPAP FOR THEIR SLEEP APNEA HYPOPNEA SYNDROME

Haddadin F,[1] Lewis K[2]
(1) Carmarthenshire NHS Trust, Llanelli, Wales, United Kingdom, (2) Swansea School of Medicine and Prince Philip Hospital, Llanelli, Wales, United Kingdom

Introduction: Continuous Positive Airways Pressure (CPAP) remains first choice treatment for the Sleep Apnea Hypopnea Syndrome (SAHS). Concordance with CPAP is variable. For those unable to tolerate CPAP, alternative treatments are limited to Mandibular Advancement Devices (MADs) and upper airway surgery. We considered nasal oxygen as an alternative second line treatment for SAHS.
Methods: Type: A prospective, interventional, open labelled, pilot study.
Patients: 8 patients (2 female), mean age 61.4 (13.8) years, mean BMI 34.8 (6.3) kg/m2. All had SAHS with excessive daytime sleepines and an AHI > 10 events / hour. Two were edentulous and 6 were waiting to be fitted with a MAD. These latter 6 patients were considered for interim oxygen because 4 had severe symptoms, 1 was appealing to an urgent Employment Tribunal and 1 had a recent myocardial infarction. All were intolerant of CPAP but none had used it for 3 weeks prior to trying oxygen (unlikely carry-over effect).
Procedure: Epworth Sleepiness Scores (ESS) were recorded at baseline and after 1 month of nasal oxygen, given at 2 litres / minute when asleep. Limited channel sleep studies (Visilab) measured the AHI at baseline and after 1 month of and whilst on 2 liters / minute of nasal oxygen. All episodes of sleep disturbed breathing were manually reviewed and were deemed obstructive rather than central.
Statistics: Wilcoxon rank.
Results: No patient reported discomfort or adverse events with nasal oxygen. All reported 5 or more hours use per night.
The median (range) ESS pre treatment was 13.5 (3-23); the median ESS post- oxygen was 6.5 (3-20); z score -2.2, p=.03.
The median AHI pre treatment was 47.7 (18-112); the median AHI on oxygen was 7 (3-80); z score -2.4, p=.02.
7/8 patients had improvement in AHI with 5/8 now having AHI<10 per hour. 7/8 had lower ESS (1 no change).
Conclusion: Nasal oxygen is well tolerated in those who do not like CPAP. It significantly reduces both ESS and AHIs and could be a useful alternative therapy in SAHS. Possible mechanisms include a direct action on upper airway muscle tone, resetting respiratory drive or by shifting the haemoglobin dissociation curve. A randomized cross-over trial of oxygen vs CPAP would be interesting.

0450

OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME AND SNORING: CEPHALOMETRIC ANALYSIS

Salles C,[1] Carvalho M,[2] PiñOn C,[3] Daltro C,[3] Flores P[3]
(1) Hospital da Bahia, Salvador, BAHIA, Brazil, (2) Hospital da Bahia, Brazil, (3) Hospital da Bahia, BAHIA, Brazil

Introduction: Cephalometric analysis has become an important method in diagnosis reporting specifics craniofacial characteristics such as posterior pharyngeal space, tongue length and hyoid position which may predispose some people to develop obstructive sleep apnea/hypopnea syndrome (OSAHS) and snoring.
OBJECTIVE: The purpose of this study is presenting anatomic topics cephalometric analysis that may have predisposition to the development of upper airway occlusion.
Methods: A retrospective review of 45 Brazilian patients with simple snore and respiratory disturbance index (RDI) > 5 were included. Clinical symptom scores were correlated with the cephalometric measuments. Variables such as RDI and cephalometric analysis data (SNA= sella to A point; SNB=sella to B point angle; PAS ocl=the minimal distance in mm between the velum and nearest point on the posterior pharyngeal wall ;PAS(Ut)=the minimal distance in mm between the most superior point of the tongue and the posterior pharyngeal wall ;PAS(ML)= the minimal distance in mm between the tongue base and nearest point on the posterior pharyngeal wall;PAS(nl)=the distance in mm between the maxilla medial line and the mandibular plane .
Results: Thirty three patients (73,3%) were males. Age varied from 4 to 72 years. All of them were snores and 18,6% had OSAHS, mean RDI= 18,6
(interquartile range 5,8 – 24,4). Below we can see the correlations :

IAH X SNA : r(spearman)= -0,078
p = 0,617
IAH X SNB : r(spearman)= -0,039
p = 0,803
IAH X PAS(Nl) : r(spearman)= -0,291
p = 0,058
IAH X PAS(Nt) : r(spearman)= -0,084
p = 0,593
IAH X PAS(Ml): r(spearman)= -0,193
p = 0,215

Conclusion: Cephalometric analysis show that some anatomical variations on craniofacial and upper airway are likely to contribute to the pathogenesis of OSAHS in Brazilian people.
Support (optional): NO SUPPORT

0451

ADAPTIVE SERVO VENTILATION (ASV) FOR COMPLEX SLEEP RELATED BREATHING DISORDERS (CSRBD)

Sadrnoori, B, Desrosiers, A, Tanguard, D
CARITAS HOLY FAMILY HOSPITAL, Methuen, MA, USA

Introduction: ASV has been used successfully in the treatment of central apnea with CHF with fewer arousals, improvement of the quality of life, and significantly better improvement of the LVEF as compared to other modalities of treatment among others, PAP therapy. We therefore extended our therapy beyond CSA/CHF to other CSRBD.
Methods: We selected 9 patients with a variety of CSRBD, who failed treatment with either CPAP and/or bilevel, either S versus ST mode +/- O2. Out of 9 patients, 2 had CSB/CHF, 1 had S/P CVA, 4 on Mu2 receptor agonist for pain control (methadone, fentanyl, MS), and 2 with complex sleep apnea (central apnea emerging with PAP). All patients had ABG´s on room air prior to ASV application. STD PSG was performed with additional diaphragmatic EMG and RIP, nasal pressure, real time recording of P/F/V and leak among others. ASV was started with EEP of 4 and increased to a maximum of 10, if needed, with the remainder of the setting based on factory default. FFM was used on all patients based on factory recommendations.
Results: In all patients, there was complete improvement of central apnea, improvement of obstructive hypopnea with EEP, desaturation (nadir/mean), sleep architecture, and patient´s perception of quality of sleep.
Conclusion: CSRBD is defined as a combination of OSA + non-obstructive events (central apnea, CSB, PB, etc) in the same PSG. CSRBD could be seen physiologically in high altitude or due to underlying and/or emerging following PAP therapy, and/or underlying TBI, CVA, narcotics use. ASV uses a baseline end expiratory pressure (EEP) of 4-10 and PSV of 4-10 above EEP and tracks the patient´s respiratory effort to maintain the subject´s minute ventilation at 90% of patient´s own long term average ventilation. IN CSR/CHF, the action of ASV is ventilatory resynchronization similar to ventricular resynchronization therapy with cardiac pacing. We conclude that ASV can be successfully used in all types of CSRBD, including patients with S/P CVA, narcotics use, CSB/CHF, and complex sleep apnea (emerging central apnea with positive airway pressure therapy). The original ABG did not affect the success of ASV.

0452

OBSTRUCTIVE SLEEP APNEA SYNDROME: DOES SUBSTANCE USE PREDICT POOR RESPONSE TO CPAP THERAPY?

Jones S,[1] Nijjar V,[2] Chandra A,[3] Zielkiewicz N,[2] Shrivastava D[4]
(1) California pacific medical center, San Francisco, San Francisco, CA, USA, (2) San Joaquin General hospital, French Camp, CA, USA, (3) Parkridge East Hospital, Chattanooga, TN, USA, (4) San Joaquin General hospital/ UCDavis, French Camp, CA, USA

Introduction: Obstructive sleep apnea syndrome (OSAS) results in morbidity and mortality. Substance use is a risk factor for poor sleep quality. While literature is available regarding prevalence of substance use among OSAS patients, no studies are available regarding its influence on CPAP compliance and symptom control. We hypothesize that continued substance use is likely to cause poor compliance and continued symptoms.
Methods: A review of 91 patients with OSAS on CPAP therapy is done. In addition to Epworth sleepiness scale, a screening questionnaire documented their substance use history. Those with a positive history were classified as “high-risk”. On follow-up patients were interviewed

about symptoms and nightly CPAP use.The sample was 58% male, 42% female. The average age was 48 years (16-70) with an average body mass index (BMI) of 42 kg/m2, (21-73). 44% were smokers and 24% drank alcohol, while 13% used recreational drugs. These behaviors were present in 54% of subjects.
Results: There was no difference in screening Epworth scores between patients with and without substance use (13.00 vs. 12.76, p = 0.919). Of the 91 patients, 48 returned for follow-up.There was no statistically significant difference in the follow-up rate (26 versus 22, p = 0.521), nor difference in symptomatic control of the high and the low-risk group noted. 69% of patients with substance use were either non-compliant or poorly controlled on their therapy as compared to 64% of those without substance use (p = 0.458).
Conclusion: The literature indicates that compliance with CPAP dependents on response to treatment. Higher Epworth score correlates with greater compliance. We stratified Epworth scores into patients with and without substance use and found no statistically significant difference. This finding correlated with the statistically indistinguishable rates of compliance and symptom control between the two groups. Studies are needed to assess influence of substance use in the management of OSAS.

0453

ASSOCIATION OF SLEEP-DISORDERED BREATHING WITH POST-OPERATIVE COMPLICATIONS

Shakir N,[1] Limann B,[2] Hwang D,[2] Kalra S,[2] Schulman L,[3] Decourla-Souza A,[2] Greenberg H[4]
(1) Pulmonary, Critical Care and Sleep Medicine, North Shore Long Island Jewish Health System, New Hyde Park, NY, USA, (2) North Shore Long Island Jewish Health System, NY, USA, (3) NY, USA, (4) North Shore Long Island Jewish Health System, New Hyde Park, NY, USA

Introduction: While obstructive sleep apnea (OSA) has been associated with elevated peri-operative risk, the incidence of complications, and the severity of OSA which confers increased perioperative risk, has not been established. We used an OSA symptom questionnaire and home nocturnal oximetry to screen for OSA in patients undergoing elective surgery to evaluate the association of OSA with perioperative complications.
Methods: Patients undergoing preoperative assessment for elective surgery at a tertiary care hospital with symptoms of OSA on a screening questionnaire underwent home nocturnal oximetry. The number of 4% or greater oxygen desaturations per hour was determined (ODI-4%). Review of hospital records was performed to compare age, sex, comorbidities, postoperative complications and hospital length of stay between the OSA group (n=100; 46F, 54M), ODI-4% >5/hr and controls (n=53; 36F, 17M), ODI-4% <5/hr.
Results: A significantly greater percentage of OSA patients experienced post-operative complications (15%; 15 complications) than control patients (3.8%;2 complication), p < 0.05. Categories of surgery(#pts) were gastroinestinal(66), genitourinary(50), cardiovascular(7), thoracic(5), orthopedic(17), neurosurgical(3), ENT(4), ophthalmologic(1). Types of complications were respiratory-9, cardiovascular-5, gastrointestinaI-1, post-operative bleeding-2. There were no significant differences in body mass index (37.6 vs. 35.6 kg/m2), number of comorbidities (2 vs. 1.83), years of smoking (11.9 vs. 10.4), and inpatient days (3.7 vs. 3.25) between groups. Post-anesthesia care unit hours was greater in the OSA group (10.9 vs. 7.1, p < 0.01) which was due to closer monitoring of patients with presumed OSA.
Conclusion: OSA as assessed by ODI-4% > 5/hr during nocturnal oximetry is associated with an increased risk of postoperative surgical complications.
Support (optional): Division of Pulmonary, Critical Care and Sleep Medicine, NSLIJ

0454

CPAP ADHERENCE IN VETERANS WITH PSYCHIATRIC DISORDERS – PRELIMINARY FINDINGS

Means M, Edinger J
VA and Duke University Medical Centers, Durham, NC, USA

Introduction: Despite an increased prevalence of psychiatric disorders such as depression and PTSD in individuals with sleep apnea, little is known about whether such conditions affect adherence to CPAP treatment. The present study examined rates of CPAP adherence in veterans with and without co-morbid psychiatric diagnoses (PD).
Methods: Data were obtained from the Respironics Encore Pro® database of veterans receiving CPAP treatment for sleep apnea between 2002-2006. Investigation of VA medical records was used to determine presence or absence of PD. Patients with PD other than PTSD or mood disorders were excluded.
Results: The first 100 qualifying patients in the database were analyzed (98 males; mean age = 55.9 years, SD = 11.1, mean RDI = 42.8, SD = 29.7). Sixty-five (65%) patients had co-morbid PD. At one month post-CPAP, those with PD used CPAP an average of 4.35 hrs/night on 66% of nights, whereas those with no psychiatric disorders used CPAP 4.72 hrs/night on 74% of nights. This difference in adherence was not significant. Veterans were classified into "good" and "poor" adherence based on whether they used CPAP > 4 hrs/night and > 70% of nights. Although a higher percentage of "good" adherers did not have PD (57% vs. 48%), chi-square analysis was not significant.
Conclusion: In this preliminary investigation, we found that veterans with PTSD and/or mood disorders used CPAP at a slightly (but non-significantly) lower rate compared to those without psychiatric disorders. The presence of co-morbid psychiatric disorders in veterans does not seem to significantly impact adherence to CPAP treatment.

0455

COMPARISON OF SLEEP AND RESPIRATORY PARAMETERS BETWEEN A PORTABLE DEVICE (WATCH-PAT 100),AND A FULL PSG STUDY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME

Inoue A
Center for Sleep Respiratory Disorder at Fukuoka, Fukuoka, Japan

Introduction: Watch-PAT100 (Itamar Medical; Caesarea,Israel)(WP100) is a 4 channel unattended ambulatory device with the peripheral arterial tone (PAT) signal, heart rate, pulse oximetry and actigraphy. To evaluate the accuracy of WP100 we analyzed the sleep architecture and respiratory parameter of WP100 in comparison with those obtained by the conventional PSG study in patients with obstructive sleep apnea hypopnea syndrome(OSAHS).
Methods: 16 subjects including 12 patients with OSAHS and 4 normal subjects were underwent full PSG study simultaneously with a WP100 recording. We compared AHI,%REM sleep and sleep efficiency(SE) studied with between a PSG and a WP100.
Results: 1. The number of OSAHS patients performed with PSG study was as follows; the number of OSAHS patients with AHI less than 30 was 7, that of OSAHS patients with AHI more than 30 was 7 and that of patients with study failure was 2.
2. The correlation of AHI obtained from between PSG and PAT100 study in overall patients was 0.98. The correlation of AHI in patients

with between AHI less than 30 and AHI more than 30 was 0.95 and 0.94 respectively.
3. The correlation of %REM sleep between PSG and PAT100 study in overall patients was 0.34. The correlation of %REM sleep in patients with between AHI less than 30 and AHI more than 30 was 0.64 and 0.08 respectively.
Conclusion: AHI was highly correlated in both PSG and PAT100 study. The percentage of REM sleep was relatively correlated in patients with AHI less than 30 , but not in patients with AHI more than 30. Few correlation of %REM sleep between PSG and PAT100 study in severe OSAHS patients in supposed that many arousals or wakes produced in severe OSAHS patients were regarded activities of sympathetic nervous system as REM sleep in a PAT100 device.

0456

EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY ON HIGH DENSITY LIPOPROTEIN CHOLESTEROL (HDLC) IN COMPLIANT AND NONCOMPLIANT PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

Arfoosh R,[1] Hosni A,[2] Adra F,[2] Cohen M,[3] Fulambarker A[3]
(1) Chicago Medical School at Rosalind Franklin University of Medicine and Science, Des Plaines, IL, USA, (2) Chicago Medical School at Rosalind Franklin University of medicine and Science, IL, USA, (3) Chicago Medical School at Rosalind Franklin University of Medicine and Science, IL, USA

Introduction: Obstructive Sleep Apnea (OSA) is highly prevalent in the population and is an independent risk factor for metabolic syndrome causing low HDLc. Increasing HDLc by 1 mg/dl may reduce the risk of cardiovascular disease by 2% to 3%. Current literature on effect of continuous positive airway pressure therapy (CPAP or BiPAP) on HDLc levels yields inconsistent results. Furthermore, the impact of compliance with therapy on HDLc has not been examined.
Methods: This is a retrospective study to determine the effect of continuous positive airway pressure therapy on HDLc in compliant and noncompliant patients with OSA. All reported polysomnograms done at the VA North Chicago Medical Center between January 2003 and December 2005 were reviewed. This study included all patients diagnosed with OSA, started on CPAP or BiPAP therapy and had HDLc<40 mg/dl. Patients on Niacin, Fibric acid compounds, or with >=10% weight loss were excluded. The most recent HDLc level prior to starting therapy was compared to that measured at least 6 months later. Changes in HDLc were compared in two groups defined by their compliance with OSA therapy; compliance was evaluated either by review of electronic compliance cards, when available, or review of follow-up encounters.
Results: Compliant subjects (N=15) exhibited a significant change in HDLc values over time (Mean Pre HDLc+/-SD=32.87+/-4.55, Mean Post HDLc+/-SD=35.47+/-5.82; P=0.031, paired t-test), while non-compliant subjects (N=17) did not (Mean Pre HDLc+/-SD=32.00+/-3.89, Mean post HDLc+/-SD=31.35+/-5.85; P=0.589, paired t-test). The statistical significance of the difference between compliant and noncompliant subjects, in mean Post HDLc, was determined using analysis of covariance (ANCOVA) with Pre HDLc as the covariate. There was a statistically significant effect of compliance on Post HDLc level (F=4.42, df=1/29, P=0.044).
Conclusion: Continuous positive airway pressure therapy improves HDLc in compliant patients with OSA.

0457

INSPIRATORY FLOW VOLUME LOOP PLATEAUING AS A PREDICTOR OF APNEIC AND HYPOPNEIC EVENTS

Verma A,[1] Anand V,[2] Verma N[3]
(1) University of Missouri-Kansas City, Kansas city, MO, USA, (2) All India Institute of Medical Sciences, Warren, MI, USA, (3) B.G. Tricounty Neurology and Sleep Clinic, Warren, MI, USA

Introduction: Since upper airway obstruction is a common denominator in obstructive sleep apnea as well as plateauing in the inspiratory limb of the flow volume loop, we tested the following hypothesis: apnea-hypopnea index will be higher in those with plateauing in the inspiratory portion of the flow volume loop as compared to those without such plateauing.
Methods: 26 patients with significant plateauing in the inspiratory limb of flow volume loop (Group I, age 26- 63 years, 15 smokers/ex-smokers and 11 non-smokers, BMI 21.5-64.3 Kg/m2 ; 3 with history of tonsillectomy) were compared with 22 patients without such plateauing (Group II, age 21-59 years, 13 smokers/ex-smokers and 9 non-smokers, BMI 21.5-64.3 Kg/m2; 2 with history of tonsillectomy) . Both groups had presented for evaluation for possible sleep apnea and had history of snoring and excessive daytime sleepiness. Both groups were matched for age, BMI, smoking and tonsillectomy history. Overnight standard polysomnography was performed. Statistical analyses were performed using the 2 tailed Fischer´s t test.
Results: AHI in group I (mean per hr 5.15, SD 6.37) did not differ significantly (p=0.903) from group II (mean per hr 4.81, SD 12.34). Likewise the SaO2 nadir (group I: mean 87.96%, SD 4.52; group II: mean 83.18, SD 14.49) did not differ significantly either (p=0.118). Eight of 26 patients in group I had AHI >5/hr as opposed to 4 of 22 in group II (p=0.504).
Conclusion: These preliminary data do not support our hypothesis and suggested the lack of predictive value of inspiratory limb plateauing in flow-volume loop in regard to the apneic and hypopneic events. Possible explanations include: 1. The lack of supine measurement of the flow-volume curve, and 2. the test measures static upper airway obstruction during wakefulness whereas apneic events reflect dynamic upper airway obstruction in sleep .

0458

SLEEP STAGE TRANSITIONS, AROUSAL FREQUENCY, AND SELF-REPORTED SLEEP QUALITY

Laffan A, Caffo B, Swihart B, Punjabi N
Johns Hopkins University, Baltimore, MD, USA

Introduction: Disruption of sleep continuity is a common finding in sleep disorders and is associated with adverse health outcomes. However, assessment of sleep disruption with classical methods such as the arousal frequency is fraught with misclassification given the high inter and intra-scorer variability. Thus, a measure based on sleep-stage transitions was developed and its association with self-rated sleep quality assessed.
Methods: Sleep Heart Health Study participants with complete polysomnography and questionnaire data were examined (N=5,614). Conventional sleep stages were used to create a transition index defined as the number of sleep stage transitions per hour of sleep between Wake, NREM sleep, and REM sleep. Logistic regression was used to model the odds of poor self-reported sleep (defined as light or restless sleep) as a function of the transition index and the arousal index.
Results: The median number of transitions for the study sample was 10.05 per hour of sleep (range: 1.82 to 86.72). Approximately 70% of all transitions occurred between NREM sleep and wake. The least

common sleep-stage transition was Wake to REM sleep. Arousals per hour of sleep ranged from 2.06 to 110.39 (median: 16.61). Adjusting for age and gender, the odds ratios of restless sleep for quartiles of the transition index were 1.00, 1.41, 1.75, and 2.31, respectively. The odds ratios of light sleep for quartiles of transition index were 1.00, 1.35, 1.80, and 2.50. In models controlling for arousal index, the transition index remained a significant predictor of restless and light sleep.
Conclusion: The number of transitions per hour of sleep predicts likelihood of self-reported restless and light sleep independent of the classical arousal frequency. Sleep stage transitions should be further explored as another indicator of sleep disruption in future research linking sleep quality to cardiovascular and non-cardiovascular outcomes.
Support (optional): National Institutes of Health Grants HL07578 and AG025553

0459

VARIABILITY AND POSITION IN SLEEP DISORDERED BREATHING DURING LIMITED HOME AND LAB STUDIES.

Seelall V,[1] Ayappa I,[1] Robert N,[2] Burschtin O,[1] Rapoport D[1]
(1) New York University, New York, NY, USA, (2) New York University, NY, USA

Introduction: In at least one large study, night-night variability of home AHI (not measured directly from airflow) was shown to be low. The ARES Unicorder (Advanced Brain Monitoring, Carlsbad, CA) is a self-applied portable monitor with a validated measure of airflow (nasal cannula), previously reported to have good agreement with lab PSG (Sleep 2006). The present study examines SDB variability across 3 nights using this device.
Methods: 17 asymptomatic volunteers and 52 patients with symptoms of EDS and/or snoring had recordings on 2 nights at home and one night in the laboratory and showed 2-7 hours valid data/night. The Unicorder records nasal airflow, forehead oximetry, position, body movement and snoring. Studies were autoscored with technician review to calculate AHI-4% and RDI (AHI-0%).
Results: For AHI-home the absolute value of the difference (ABSDiff) from night to night was 4.2±6.4/hr; bias was 0.2±7.7/hr and intraclass correlation coefficient (ICC) was 0.9. For Supine AHI-home; ABSDiff was 7.5±8.8/hr; bias was -0.3±11.6/hr; ICC was 0.88. Agreement on presence of SDB by AHI≥5 was 93% and by RDI≥15 was 90%. For AHI-lab compared to AHI-home (nights combined) ABSDiff was 7.1±11.4/hr; bias was 3.0±13.1/hr and ICC was 0.8. %Supine time in the lab was greater than in the home (55% vs 44%). For Supine AHI Lab-Home; ABSDiff was 9.1±12.0/hr; bias was 1.5±15.0; ICC was 0.82 respectively. Agreement on presence of SDB by AHI≥5 was 83% and by RDI≥15 was 90%.
Conclusion: This study confirms that limited monitoring in the home using the ARES Unicorder (including nasal cannula) to measure SDB produces results which are consistent from night to night but which differ slightly from laboratory ARES Unicorder recordings. Despite greater time in the supine position in the lab, analysis of the data only in the supine position does not reduce night-night variability across studies whether in the home or the lab.
Support (optional): NCRR M01RR00096, Advanced Brain Monitoring, Foundation for Research in Sleep Disorders

0460

OSA SYMPTOMS ARE MORE COMMON AMONG AFRICAN-AMERICAN THAN CAUCASIAN WOMEN

Beothy E,[1] Sammel M,[2] Freeman E,[2] Lin H,[2] Pien G[1]
(1) University of Pennsylvania, Philadelphia, PA, USA, (2) University of Pennsylvania, PA, USA

Introduction: Recent studies suggest that African-Americans are at greater risk for obstructive sleep apnea (OSA) than Caucasians. In addition, postmenopausal women have an increased risk of OSA compared to premenopausal women. We examined the relationship between race, menopausal status and OSA symptoms in a large group of African-American and Caucasian women using the Multivariable Apnea Prediction (MAP) Index, which asks about OSA symptoms and is helpful in determining the likelihood of having OSA.
Methods: The Penn Ovarian Aging Study (POAS) is a longitudinal cohort study of African-American and Caucasian women going through the menopausal transition. We administered the MAP questionnaire to 269 POAS participants 8 years after study inception. Linear regression analyses were performed to examine relationships between race, menopausal status, BMI and change in BMI (baseline to time of questionnaire administration) and the MAP apnea subscale score.
Results: Mean subject age was 48 (SD 3.5) years. 49.4% of subjects were African-American. Women were classified as premenopausal, early transition, late transition or postmenopausal as defined by bleeding patterns. Using these criteria (PENN-5), 37.5% of women were premenopausal, 43.0% in the menopausal transition and 19.5% were postmenopausal. In unadjusted analyses, the mean apnea score among African-American women was nearly double that of Caucasian women (0.79 (SE 0.08) v. 0.39 (0.08), p=0.0009). Menopausal status was not a significant predictor of OSA symptoms. Race remained a significant predictor of OSA symptoms (p=0.04) after adjustment for current BMI, BMI change over time, and menopausal status.
Conclusion: Middle-aged African-American women are more likely to experience symptoms of OSA than their Caucasian counterparts. Although menopausal status did not predict OSA symptoms, OSA symptoms in our cohort of menopausal women increased with higher BMI and larger BMI increases over time. Studies to document whether OSA is more common among African-American than Caucasian women should be performed to further investigate these findings.
Support (optional): Supported by grants from the National Institutes of Health (K23-HD-41465, RO1-AG-12745).

0461

SLEEP DISORDERED BREATHING AND CEREBRAL VASOREACTIVITY TO CO2

Reichmuth K,[1] Austin D,[2] Peppard P,[2] Nieto J,[1] Young T,[3] Barczi S,[1] Skatrud J,[2] Morgan B[2]
(1) University of Wisconsin School of Medicine and Public Health, madison, WI, USA, (2) University of Wisconsin-Madison, Madison, WI, USA, (3) Madison, WI, USA

Introduction: Sleep disordered breathing (SDB) is associated with impaired forearm vasodilation, a marker for endothelial dysfunction. We determined whether cerebrovascular function is similarly affected by assessing responsiveness to hypercapnia (PETCO2=+10 mmHg).
Methods: We measured cerebral blood flow velocity (CBF; transcranial Doppler) and mean arterial pressure (MAP; photoplethysmography) during a daytime rebreathing test in 79 women and 127 men from the Wisconsin Sleep Cohort (age 59±7 years; range 44-76). Cerebral blood flow (CBF), cerebrovascular resistance (CVR), and MAP reactivities were calculated as the slopes of the linear relationships between these

variables and PETCO2. Apnea-hypopnea index (AHI) was evaluated by polysomnography. General linear models were used to calculate least squares means of CBF, CVR, and MAP reactivities for three categories of SDB: AHI < 5, AHI > 5, and current CPAP users. Adjusted models included potential confounders (age, sex, BMI, current smoking, hypertension, history of vascular disease, medications, and, for CBF only, blood pressure response to hypercapnia).
Results: CBF reactivity was reduced in AHI > 5 vs. < 5 [(2.0 (1.8 – 2.3) vs 2.3 (2.2 – 2.5) p<0.05] and there were trends toward reduced CVR reactivity (-0.042 vs -0.051) and increased MAP (1.22 vs 1.06) in this group. In CPAP users, CBF reactivity was more similar to individuals with AHI < 5 than AHI > 5 (2.4) ; however, there were no clear trends for CVR and MAP.
Conclusion: These findings provide evidence for impaired cerebrovascular function in individuals with SDB and could explain, at least in part, the recently demonstrated association between SDB and stroke.
Support (optional): National Institutes of Health R01 HL62252 Medical Research Service Department of Veterans Affairs

0462

CLINICAL DIAGNOSIS OF SLEEP APNEA BASED ON SINGLE NIGHT OF POLYSOMNOGRAPHY VS. TWO NIGHTS OF POLYSOMNOGRAPHY

Ahmadi N,[1] Shapiro G,[2] Chung S,[1] Shapiro C[2]
(1) University Health Network, Toronto, Ontario, Canada, (2) University Health Network, Ontario, Canada

Introduction: Despite a large nightly variability in polysomnographic (PSG) respiratory variables, diagnoses are generally made from one PSG study night. Aim: To investigate respiratory disturbance index (RDI) across two PSGs to examine RDI variability and impact on clinical diagnosis
Methods: Two-night PSGs of 193 sleep clinic patients were reviewed. Anonymized records from 5 patients with significant night-to-night RDI variability were used in this study: two-night PSGs from 2 patients were represented as 4 individual PSGs; the two-night PSG for 2 others were represented as being obtained from two different sleep clinics; the last patient´s PSG was shown as a two-night study. Twenty-two sleep experts attending the APSS meeting were recruited to make diagnoses based on the PSGs. They were told that the PSGs were from 7 patients: 4 with single-night PSG; 2 with two PSGs each one from a different clinic; and 1 patient with a two-night PSG.
Results: 21% of the 193 sleep clinic patients had a nightly PSG RDI variability > 5. Using an RDI>15 diagnostic criteria, sleep apnea would have been undetected in 20% (n=39) of patients due to low RDI on one night. For the 7 cases, 27- 36% of sleep experts failed to identify sleep apnea especially when presented with the PSG containing the lower RDI. Incidences of missed sleep apnea diagnoses were reduced to 15-18% when information from two PSGs was presented to the sleep experts.
Conclusion: Utilizing a large patient population, this study supports the significant night-to-night variability in PSG respiratory variables. This variability has direct impact on sleep apnea diagnosis as identification of sleep apnea is greatly reduced when sleep experts are provided with only one PSG recording. The clinical implication is that when the first night recording in a patient suspected of having sleep apnea is negative, a second study should be conducted.

0463

COMPARISON OF FEATURES OF CENTRAL SLEEP APNEA AND OBSTRUCTIVE SLEEP APNEA

Budhiraja R,[1] Zeater M,[1] Parthasarathy S,[2] Quan S[1]
(1) University of Arizona, Tucson, AZ, USA, (2) United States Department of Veterans Affairs, Tucson, AZ, USA

Introduction: Central sleep apnea (CSA) and Obstructive sleep apnea (OSA) may have distinct etio-pathogenesis. We aimed to determine whether the demographics, presence of comorbidities or other clinical features can help differentiate CSA from OSA, as well as whether there is a perceived difference in benefit from the positive airway pressure (PAP) treatment during the titration night between the two groups.
Methods: We performed a retrospective chart review of 15 consecutive patients with CSA and 15 random patients with OSA diagnosed during the same time period.
Results: Patients with OSA and CSA were similar in age (63 vs. 61 years, P=0.68), BMI (36 vs. 39, P=0.41), Epworth sleepiness score (11 vs. 12, P=0.54), nasal symptoms score (8 vs. 11, P=0.23), prevalence of witnessed apneas (36 vs. 39, P=0.41), daytime fatigue (67% vs. 73%, P=0.95), waking up gasping (20% vs. 20%, P=1.0) or hypertension (68% vs. 80%, P=0.34). The OSA group reported a higher prevalence of snoring (100% vs. 67%, P=0.04) and the CSA group had a higher prevalence of congestive heart failure (27% vs. 0%, P=0.05). The severity of sleep apnea (apnea-hypopnea index, 34 vs. 49, P=0.11), baseline oxygen saturation (93 vs. 94, P=0.38) and baseline heart rate (71 vs. 71, P=0.99) were also similar in the OSA and the CSA groups. A slightly higher percentage of OSA patients reported improvement in sleep from the PAP treatment during titration night than the CSA patients, but the results were not statistically significant (93% vs. 67%, P=0.16).
Conclusion: OSA is more frequently associated with snoring and CSA with congestive heart failure. Other clinical symptoms, demographics or sleep laboratory parameters fail to differentiate between CSA and OSA. A slightly, but not significantly, greater percentage of OSA patients perceive benefit from the PAP treatment during the titration night when compared to CSA patients.

0464

TREATMENT OF CENTRAL SLEEP APNEA: COMPARISON OF CPAP\BILEVEL WITH ADAPTIVE SERVO VENTILATION

Mclain W,[1] Mahaffey D,[1] Turner J[2]
(1) SleepMed, Columbia, SC, USA, (2) SleepMed, Inc., Columbia, SC, USA

Introduction: Patients with predominantly central sleep apnea account for 5%-10% of the apnea patients seen in most sleep labs. Yet 40% to 50% of congestive heart failure patients have primarily central sleep apnea and its been estimated 15% of titrated obstructive sleep apnea patients will have the newly termed “complex sleep apnea”(CompSAS). There has not been to date a predictably good treatment for these. Adaptive Servo Ventilation (ASV) is reported to be an effective treatment for central sleep apnea.
Methods: Thirty subjects with central sleep apnea of various types (idiopathic, Cheyne-Stokes, CompSAS, narcotic induced) received an ASV study in our lab. Twenty four of them received a baseline study and twenty four received CPAP\Bilevel titration. Fourteen were split-night. A retrospective chart audit was performed to assess treatments with mean scores, standard deviations, and t-tests.
Results: All subjects were males. Results for the group of 24 studied at baseline were RDI 49(20), AHI 46(19), central events 39(73), total sleep time (minutes) 226(122), sleep efficiency percent 73(15), REM sleep

percent 9(7), and minimum oxygen saturation 81(7). Results for the group of 24 who underwent CPAP/Bilevel trial were RDI 46(28), AHI 42(27), central events 40(66), total sleep time (minutes) 116(109), sleep efficiency percent 69(25), REM sleep percent 12(15), and minimum oxygen saturation percent 87(5). Results for the group of 30 studied with ASV were RDI 11(15), AHI 7(11), central events 2(4), total sleep time (minutes) 213(145), sleep efficiency percent 75(19), REM sleep percent 19(22), and minimum oxygen saturation percent 88(3). T-tests comparing RDI baseline with CPAP/Bilevel and with ASV were significant p<0.001. T-tests comparing central events baseline with CPAP/ Bilevel and with ASV were significant p<0.003.
Conclusion: ASV is an effective treatment for central sleep apnea of various types.

0465

AMBULATORY MONITORING AND AUTO-TITRATION VERSUS POLYSOMNOGRAPHY FOR DIAGNOSIS AND TREATMENT OF SLEEP APNEA

Berry R,[1] Hill G,[2] Kakkar R[3]
(1) Malcom Randall VAMC/University of Florida, Gainesville, FL, USA, (2) Malcom Randall VAMC, Gainesville, FL, USA, (3) Malcom Randall VAMC/Univ of Florida, gainesville, FL, USA

Introduction: The utility of unattended ambulatory monitoring (AM) as an alternative to polysomnography (PSG) for the diagnosis of obstructive sleep apnea (OSA) is diminished if a subsequent positive airway pressure titration PSG is needed in a large percentage of the cases. We hypothesized that an AM study followed by unattended auto-titration might offer an effective alternative to PSG.
Methods: Patients with suspected OSA were randomized to one of two arms. The AM-APAP arm included diagnosis using the Watch_PAT 100 (peripheral arterial tonometry, oximetry, heart rate, and actigraphy) followed by unattended auto-titration (ResMed S8 Vantage) for 1-3 nights if appropriate. The PSG Arm included diagnostic and PAP titration PSG (on 1 or 2 nights as appropriate). CPAP was initiated at a class with education and CPAP instruction using a Respironics RemStar Pro. The endpoints determined in clinic after 6 weeks of treatment were the change in the Epworth Sleepiness Scale (ESS) and objective CPAP adherence (average daily use).
Results: The first 12 subjects in each study arm to complete the interventions were compared (mean ± SEM). The diagnostic AHI was 37.4 ± 6 /hour (AM-APAP) and 45.5 ± 9 /hour (PSG), p=NS. The mean treatment pressures for the two groups were 11.5.± 0.4 (AM-APAP) and 12.1 ± 0.8 cm H2O (PSG), p=NS. The average change in the ESS for AM-APAP (- 6.8 ± 1.4) and PSG (-6.7 ± 1.2) did not differ and both showed improvement in sleepiness. The average nightly objective CPAP use (all days) for AM-APAP arm was 5.3 ± 0.8 hours/night and for PSG arm was 4.9 ± 0.6 hours/night (p=NS).
Conclusion: Preliminary results suggest that the combination of AM and unattended auto-titration can provide comparable results to the pathway using PSG.
Support (optional): Itamar Medical

0466

GENDER AND ETHNICITY DO NOT PREDICT EFFECTIVE CONTINUOUS POSITIVE AIRWAY PRESSURE IN SEVERE OBSTRUCTIVE SLEEP APNEA

Won C, Guilleminault C
Stanford University, Stanford, CA, USA

Introduction: The apnea-hypopnea index (AHI) and body mass index (BMI) have been shown to predict effective continuous positive airway pressure (Peff) in adults with obstructive sleep apnea (OSA). We explored additional clinical and polysomnographic parameters including gender, ethnicity, age, the presence of heart or lung disease, and REM versus NREM disease predominance, in a prediction model for Peff for severe OSA.
Methods: Our study included 478 patients (age>18 years) who underwent a first-time CPAP titration study for OSA at the Stanford Sleep Disorders Center. Studies were conducted using the same instruments, and scored by the same sleep-boarded physician.
Results: There were 114 women and 364 men in the study. At baseline, women were significantly older (54±14 vs 51±13 years), but had less severe disease (AHI 49±34 vs 58±33). Our sample had greater Black (6.5 vs 3.9%) and less Hispanic (3.3 vs 7.0%) women than men, while the proportion of Asian (4%) and White (70%) patients were similar. In addition, while the AHI during REM sleep was similar in men and women, women had significantly less AHI during NREM sleep. More women than men had lung disease (33 vs 15%), but heart disease was equally prevalent (15%). Multiple linear regression confirmed AHI (parameter estimate â=0.02, p<0.001) and BMI (â =0.10, p<0.001) as important predictors of Peff in both men and women. The AHI in NREM sleep was also a significant predictor (â=0.02, p<0.001), unlike the AHI in REM sleep (p=0.91). Gender, ethnicity, age, heart disease, and lung disease were not significant predictors of Peff.
Conclusion: BMI and AHI were significant predictors of Peff, with the AHI during NREM sleep being more significant than events during REM sleep. Gender, ethnicity, age, and the presence of heart or lung disease did not predict Peff.

0467

GENDER DIFFERENCES IN TREATMENT RESPONSE TO CONTINUOUS POSITIVE AIRWAY PRESSURE IN OBSTRUCTIVE SLEEP APNEA

Ye L,[1] Weaver T,[1] Pack A,[2] Dinges D,[1] Group M[3]
(1) University of Pennsylvania, Philadelphia, PA, USA, (2) Philadelphia, PA, USA, (3) AA

Introduction: Understanding gender differences in illness and response to treatment has been a critical area of exploration. However, the majority of obstructive sleep apnea (OSA) studies have been predominantly conducted in male samples, and also have failed to provide gender-specific results. Moreover, little is known about how genders differentially respond to treatment, specifically continuous positive airway pressure (CPAP).
Methods: To examine gender differences in functional status, daytime sleepiness, and mood disturbances at baseline and following CPAP treatment, we conducted an analysis of data on 176 patients (152 men and 24 women) with severe OSA who participated in a multicenter study of CPAP treatment. Functional status was measured with the Functional Outcomes of Sleep Questionnaire (FOSQ), daytime sleepiness with the Epworth Sleepiness Scale (ESS), and mood state with the Total Mood Disturbance (TMD) score from the Profile of Mood States.
Results: The FOSQ total score at baseline was significantly lower in women (F: 12.8±3.7, M: 15.0±2.9; p<0.01), indicating poorer overall functional status, despite similar age, obesity, and OSA severity. After 3 months CPAP treatment, women showed greater improvement in functional status (ΔF: 3.8±3.5, ΔM: 2.9±2.9; p<0.01), controlling for pre-treatment FOSQ total score. Similarly, women showed greater improvement in daytime sleepiness (ΔF: 8.2±7.0, ΔM: 6.5±5.9; p<0.01) and mood states (ΔF: 21.3±19.4, ΔM: 14.0±22.6; p<0.01) after 3 months CPAP treatment than men, controlling for pre-treatment symptom scores. No significant gender difference was observed in CPAP

adherence.
Conclusion: The results of this study support the idea that gender differences exist in CPAP treatment response. Despite the poorer ability to conduct daily behaviors at baseline, women might show greater improvement in functional status, daytime sleepiness, and mood states following CPAP treatment. Further study in larger clinical samples is warranted to clarify our findings.
Support (optional): Funded By: NIH HL53991, HL60287; Respironics, Inc., Nellcor Puritan Bennett Inc., DeVilbiss HealthCare, Inc.

0468

IMPACT OF OBSTRUCTIVE SLEEP APNEA ON POST-OPERATIVE MORBIDITY AND MORTALITY IN PATIENTS UNDERGOING ELECTIVE GENERAL SURGICAL AND ORTHOPEDIC PROCEDURES

Raj R, Corona R, Phy M, Nugent K
Texas Tech University Health Sciences Center, Lubbock, TX, USA

Introduction: Untreated obstructive sleep apnea (OSA) in the general population translates into increased morbidity and mortality but the impact of OSA on postoperative morbidity and mortality after general surgical and orthopedic procedures is not clear. Data from the only two large studies examining postoperative outcomes in patients undergoing general surgical and orthopedic procedures are conflicting (Sabers *et al.* Ambulatory Anesthesia 2003: OSA not related to any adverse outcomes) (Gupta *et al.* Mayo Clin Proceedings 2001, OSA related to increased ICU admissions). This concern has important clinical implications, and the current study was undertaken to help clarify the impact of OSA on postoperative morbidity and mortality in patients undergoing elective general surgical and orthopedic procedures.
Methods: A total of 87 (23 prospective and 64 retrospective) consecutive patients were selected from a general medicine clinic where they are referred for preoperative evaluation and clearance before orthopedic and general surgical procedures. Relevant data were abstracted from patient records.
Results: Overall prevalence of OSA was 10% in this population. None of these patients were on any treatment for the OSA. ASA score for this population ranged from 1-4 (Mean 2.8, SD 0.7). The prospective and retrospective group were similar in all aspects. There were no postoperative deaths in this group. Patients with OSA did not differ from those without OSA in length of hospital stay (6.75 OSA vs. 6.5 others), postoperative hypoxemia (2.3%), respiratory failure needing invasive ventilation (2.3%), postoperative myocardial infarction (2.3%), postoperative renal failure (2.3%), need for ICU admission postoperatively (6.9%) and need for postoperative admission for rehabilitation (10.3%).
Conclusion: Untreated OSA does not have any significant impact on postoperative morbidity and mortality in patients undergoing elective general surgical and orthopedic procedures. Therefore, we do not recommend routinely delaying outpatient general surgical and orthopedic procedures while awaiting formal evaluation and treatment of patients suspected to have OSA preoperatively.
Support (optional): Texas Tech University Health Sciences Center Internal Medicine departmental seed grant 2006-2007

0469

OPIOID USE AND SLEEP DISORDERED BREATHING: A CASE CONTROL STUDY

Talcott B, Morgenthaler T, Silber M
Mayo Foundation for Medical Education and Research, Rochester, MN, USA

Introduction: Opioids, increasingly prescribed for chronic pain, can cause hypoventilation and may worsen sleep apnea. An important question is whether sleep apnea patients using opioids differ clinically from those not using opioids and if opioid use results in differences in the characteristics of sleep apnea.
Methods: We identified all sleep apnea patients using opioids diagnosed in our sleep center in January 2004 and between January-March 2005 (45 patients). Control patients were all those with sleep apnea not on opioids diagnosed in January 2004 (169). The two groups were compared using appropriate statistical methodology.
Results: 58% of opioid users were women compared to 32% of controls. There were no differences in age, BMI and ESS values. The mean daily dose was 95 mg oral morphine equivalents. Sleep efficiency was higher in the opioid group (77 versus 71%). Total AHI did not differ between groups (31.3 and 28.2/hr) but the central AHI was higher in the opioid group (3.1 versus 0.4/hr). Minimum SpO2 during NREM sleep was lower in the opioid group (81 versus 84%). During the CPAP trial, more central apneas occurred in the opioid group (central AHI 12.4 versus 3.5/hr) and minimum SpO2 was lower in the opioid group (87 versus 90%) ($p<0.05$ for all comparisons noted).
Conclusion: We found significant differences between sleep apnea patients taking opioids and controls. More women were in the opioid group, probably because women more frequently use opioids for chronic pain. Opioid users have higher sleep efficiency but lower SpO2 and increased frequency of central apneas, especially during CPAP titration, possibly due to opioid induced dysregulation of brainstem respiratory centers. Physicians should be aware that sleepiness in opioid users may be due to sleep apnea and is not necessarily caused by drug-induced sedation. Central apneas may develop with CPAP use, making treatment more complex.
Support (optional): Piscopo funds of Mayo Foundation

0470

NOCTURNAL GASTROESOPHAGEAL REFLUX AND SLEEP-DISORDERED BREATHING AFTER LUNG TRANSPLANT

Shepherd K,[1] Chambers D,[2] Gabbay E,[2] Hillman D,[3] Eastwood P[1]
(1) Sir Charles Gairdner Hospital, Perth, Western Australia, Australia, (2) Royal Perth Hospital, Western Australia, Australia, (3) Sir Charles Gairdner Hospital, Western Australia, Australia

Introduction: Gastroesophageal reflux has been implicated in the pathogenesis of bronchiolitis obliterans syndrome (BOS), the major contributor to chronic allograft rejection in lung transplant, perhaps due to aspiration of refluxed acid into the lungs. Risk of aspiration of gastric contents is increased during sleep and may be increased further by the presence of sleep-disordered breathing (SDB).
Methods: Eight lung transplant patients (6 male) underwent overnight polysomnography with simultaneous dual esophageal pH monitoring (electrodes 5 and 20cm above the lower esophageal sphincter).
Results: Subjects were 59 (7) years of age (mean (SD)), 3.7 (4.6) years from transplant, with an average FEV_1 of 79 (0.2)% predicted. Four subjects had undergone bilateral lung transplantation, three single lung transplantation and one heart-lung transplantation. Three subjects showed no evidence of BOS with five subjects in various stages of BOS. The average time spent below a pH 4.0 for the group was 1.6 (3.5)%.

An abnormally high occurrence of reflux was evident in 1/8 subjects with a time spent below pH 4.0 of 10%. Notably, all subjects had sleep apnea (apnea-hypopnea index, AHI > 10 events/hour), the average AHI for the group being 35 (26) events/hour. Obstructive apneas were uncommon however, with the majority of respiratory events being hypopneas (average hypopnea index of 24 (16) events/hour). There was no relationship between either AHI or BOS status and reflux parameters.
Conclusion: SDB was common in this group of transplant patients but its severity was not related to nocturnal reflux or BOS status. While significant nocturnal gastroesophageal reflux was noted in one subject this does not appear to be a consistent problem in this group or to be correlated with BOS status.

0471

CPAP CLINIC: A NOVEL STRATEGY DESIGNED TO IMPROVE CPAP COMPLIANCE

Zimmerman M, Goldman S, Sumpter T, Phifer M, Malow B
Vanderbilt University, Nashville, TN, USA

Introduction: Continuous positive airway pressure (CPAP) is the most common, and effective, method for treating obstructive sleep apnea (OSA) in adults and in some children. Although the equipment and masks have improved and are more user friendly, compliance with CPAP treatment remains low. The Vanderbilt CPAP clinic was established in March 2006 with the goals of improving CPAP tolerance during CPAP titration, and long term CPAP compliance at home.
Methods: We reviewed our experience in the Vanderbilt CPAP Clinic since its origination. Adult and pediatric patients are referred to the clinic by their sleep specialist. At the clinic, patients are evaluated by nurse practitioners specializing in sleep medicine and family practice, and a sleep technologist specializing in mask and equipment related issues. The clinic operates ancillary to the general sleep clinic, three afternoons per week. Our goal is to be able to accommodate all patients prior to their sleep titration and for follow-up after titrations as soon after referral as possible.
Results: In the first seven months, 248 individuals have been seen in the CPAP clinic. Reasons for referral include: known or suspected claustrophobia, anxiety or hesitancy over CPAP use, poor mask tolerance, or CPAP intolerance or failure during a titration in the sleep center. The practitioners work with the patients on a one on one basis providing education, mask fitting, and review of sleep studies and compliance data. The clinic has been well received by both patients and sleep specialists with the majority of patients tolerating subsequent CPAP titration in the sleep center, or improving CPAP compliance at home.
Conclusion: Our experience suggests a dedicated CPAP troubleshooting and education clinic may improve long term CPAP acceptance and compliance. We are currently evaluating long term compliance in the patients seen.

0472

THE EFFECT OF CPAP THERAPY ON BLOOD PRESSURE UPON AWAKENING IN PATIENTS WITH SEVERE SLEEP APNEA

Szakacs Z,[1] Bernath I,[2] Vida Z,[2] Horvath A,[2] Szternak N[2]
(1) Central Hospital of the Hungarian Home Defence Force, Budapest, Hungary, (2) Central Hospital of the Hungarian Home Defence Force, Hungary

Introduction: Well-adjusted CPAP therapy eliminates pathological respiratory events and thereby substantially reduces symptomatic activity in severe obstructive sleep apnea. The authors studied the effects of chronic CPAP therapy on blood pressure.
Methods: Two hundred patients with severe obstructive sleep apnea were enrolled. All patients have been receiving treatment for hypertension. Half of the study population was treated with CPAP, whereas the other half rejected this treatment. No changes to the antihypertensive regimen was allowed during the one-year study period – any modification entailed exclusion from the trial. At the end of the one-year period, the CPAP group comprised 62 patients (56 males and 6 females), whereas the control group consisted of 54 subjects (48 males and 6 females).
Results: Baseline parameters of CPAP and control patients were as follows: mean age 54.1±11.9 years vs. 50.7±13.0 years; BMI 32.0±4.9 kg/m^2 vs. 31.8±4.5 kg/m^2; Epworth score 13.8±3.7 vs. 13.4±6.8, respectively. Pre-treatment AHI was 61.1±11.2/hours vs. 64.6±16.1/hour; arousal index was 61.2±17.9/hour vs. 60.1±17.9 hour; mean SaO2 was 90.9±2.9% vs. 90.3±2.9%. Morning systolic and diastolic blood pressure values were 137.7±12.8 mmHg vs. 136.8±10.6 mmHg, and 81.4±9.1 vs. 80.9±7.3 mmHg. By the end of one-year CPAP treatment, AHI decreased to 4.0±1.9/hour, arousal index to 23.9±7.5/hour, and mean SaO2 increased to 94.9±1.4%. Morning systolic blood pressure decreased to 123.4±12.3 mmHg, and diastolic BP to 73.0±6.3 mmHg. In the control group, by contrast, AHI was 65.7±15.2/hour; arousal index was 63.8±20.1/hour, mean SaO2 was 89.4±1.4%, morning systolic BP was 137.3±9.4 mmHg and morning diastolic BP was 81.9±6.2 mmHg. Analyzing the results of the two groups with the two-tailed t-test revealed a statistically significant ($p<0.01$) reduction of morning systolic and diastolic blood pressure in patients treated with CPAP.
Conclusion: CPAP therapy significantly reduced blood pressure upon awakening.

0473

THE IMPACT OF ANDROID OBESITY ON RESPIRATORY DYNAMICS IN SEVERE OBSTRUCTIVE SLEEP APNEA

Gyorfi M,[1] Szakacs Z,[1] Horvath R,[2] Sandra S[3]
(1) Central Hospital of the Hungarian Home Defence Force, Budapest, Hungary, (2) Central Hospital of the Hungarian Home Defence Force, Hungary, (3) Central Hospital of the Hungarian Home Defence Force, AE (Europe)

Introduction: Male-pattern obesity is associated with enhanced health risk. This study investigated the influence of abdominal fat quantity on the severity of obstructive sleep apnea and of restrictive respiratory disorder.
Methods: The study population comprised 58 consecutive male patients referred to the sleep ambulance for suspected OSAS. Cardiorespiratory polygraphy was performed during sleep to determine AHI, as well as minimum and mean oxygen saturation. Regional fat distribution was evaluated with DEXA – total body fat mass, trunk fat and abdominal (L2-4 depicted) fat mass were measured. Additionally, vital capacity, FEV1 and FEF25-75 were determined by respiratory function testing.
Results: Mean age of subjects was 51.1±12.3 years. In addition to evident correlations (between body weight, BMI, total body fat mass, abdominal fat, as well as vital capacity, FEV1, and FEF25-75), multiple correlation analysis demonstrated a significant relationship between the following: AHI and minimum SaO2 (R= -0.68); AHI and total body fat mass (R= 0.72); AHI and abdominal fat (R=0.63), as well as abdominal fat and vital capacity (R= -0.68).
Conclusion: Both increased total body fat mass and abdominal fat are correlated with the severity of OSAS. Excessive abdominal fat leads to diminished vital capacity and predisposes to restrictive pulmonary disease.

0474

DOES CPAP/BPAP TREATMENT INFLUENCE RESPIRATORY FUNCTION IN SEVERE SLEEP APNEA?

Horvath R, Szakacs Z
Central Hospital of the Hungarian Home Defence Force, Budapest, Hungary

Introduction: During normal respiration, intrathoracic pressure fluctuates between -8 and 0 mbar; air flow within the airways is driven by pressure difference. CPAP/BPAP treatment, by contrast, continuously maintains positive airway pressure often exceeding 10 mbar. This has an uninterrupted dilatory effect on small airways for the duration of nocturnal CPAP/BPAP respiratory support.
Methods: The effects of 2- to 6-month CPAP/BPAP treatment on the respiratory function of patients with severe sleep apnea (n=68) were studied. Mean age of subjects was 54.2 years (range: 28 to 72 years); mean BMI was 34.0 (range: 22.7-46.2). The proportion of active smokers was 23.5%; 44.1% of patients have quitted smoking, whereas 26.5% have never smoked.
Results: Twelve patients (17.6%) had COPD established in conformity with GOLD criteria (disesase severity was mild in 5.9%, moderately severe in 10.3%, and severe in 1.5%). All patients were subjected to polysomnography (Alice4) or polygraphy (Stardust). Eight patients (11.8%) required BPAP for severe sleep-related respiratory disorder; the remaining subjects received CPAP. After CPAP/BPAP treatment for 2 to 6 months, 86.8% of patients reported subjective improvement. The change in FVC and FEV1 was +1.0% and -1.4%, respectively (N.S.); however, baseline FVC and FEV1 values had largely determined subsequent volume changes. Accordingly, a predictive FVC%/FEV1% above 80 per cent was associated with 4.9%/-6% decrease in these parameters. In the range between 70 to 79 per cent, however, FVC increased by +10.1% and FEV1% decreased by -1.4%. Similarly, a +24.5% increase of FVC% and a +7.6% increase of FEV% was seen in the range between 60 to 69 per cent, whereas increases of +13.7% and +13.2%, respectively, were observed below 60 per-cent.
Conclusion: Although short-term CPAP/BPAP treatment (for 2 to 6 months) causes mild respiratory decline in patients with FVC/FEV1 values above 80%, it accomplishes significant improvement in patients with impaired respiratory function.

0475

ASSESSMENT OF PATIENT COMPLIANCE DURING INITIAL AS WELL AS LATER STAGES OF CPAP AND BIPAP THERAPY FOR OSAS

Horvath A,[1] Szakacs Z[2]
(1) Central Hospital of the Hungarian HomeDefence Force, Budapest, Hungary, (2) Central Hospital of the Hungarian Home Defence Force, Budapest, Hungary

Introduction: The efficacy of CPAP and BIPAP for OSAS is directly proportional to the duration of use. Although it approaches 100%, patient compliance – the determinant of long-term efficacy – is 60 to 70 per cent only. Factors reducing compliance include dryness of the nasal and oral mucosa, as well as high airway pressure, which interferes with expiration. This study compared patient compliance during fixed or variable-pressure (c-flex, bi-flex) CPAP and BIPAP techniques during treatment for 1 vs. 12 months with lower vs. higher effective pressure.
Methods: Compliance with fixed low- or high-pressure (<8 cmH2O vs. >8 cmH2O) Remstar plus CPAP (n=110) or c-flex CPAP (n=90), as well as with low- or high-pressure (<14/10 cmH2O vs. >14/10 cmH2O) Remstar BIPAP pro (n=60) or BIPAP bi-flex (n=40) therapy for one or 12 months was compared in parallel groups of patients with severe OSAS (RDI: 45±8/hour, mean oxygen saturation: 80±12%; Epworth score: 18±3). Male to female ratio was 3:1; mean age of subjects was 53±12 years. Patient compliance was assessed by determining mean duration of respiratory support use in hours. Therapeutic efficacy was appraised by monitoring RDI, arousal index and the Epworth score at control visits. All patients used heated humidifiers and all had normal, mild respiratory dysfunction. Patients with heart failure or advanced respiratory disease were excluded.
Results: After one month, mean daily duration of low-pressure respiratory support was as follows: Remstar plus CPAP 4.8±1.4 hours vs. c-flex CPAP 5.15±1.8 hours; BIPAP pro 5±0.8 hours vs. BIPAP bi-flex 5.76±2.15 hours. As regards high-pressure treatment, the corresponding values were: 4,25±1,27 hours vs. 5,23±1,68 hours and 4,87±1,85 hours vs. 6,71±2,02 hours, respectively. After 12 months, the following mean daily durations of low-pressure treatment were recorded: Remstar plus CPAP 5,76±1,95 hours, c-flex CPAP 6,43±2,11 hours, BIPAP pro 6,36±1,93 hours vs. BIPAP bi-flex 6,72±2,14 hours. The corresponding 12-month values for high-pressure therapy were: 6,2±1,7 hours vs. 6,8±0,95 hours, and 6,45±2,28 hours vs. 6,8±1,93 hours, respectively.
Conclusion: The use of c-flex and bi-flex techniques significantly improved patient compliance with high-pressure treatment. This applies also to low-pressure respiratory support, as well as to long-term (12-month) treatment. In the latter cases, however, improvement was not statistically significant.

0476

ALTERED CEREBRAL ACTIVATION DURING A RESPONSE INHIBITION TASK IN SLEEP APNEA PATIENTS

Ayalon L,[1] Ancoli-Israel S,[2] McKenna B,[3] Drummond S[4]
(1) University of California, San Diego, Department of Psychiatry and Research Services VA San Diego Healthcare System, San Diego, CA, USA, (2) University of California, San Diego, Department of Psychiatry and VA San Diego Healthcare System, San Diego, CA, USA, (3) SDSU/UCSD and Research Services VA San Diego Healthcare System, San Diego, CA, USA, (4) University of California, San Diego, Department of Psychiatry and Psychology Services VA San Diego Healthcare System, San Diego, CA, USA

Introduction: Patients with obstructive sleep apnea syndrome (OSA) present with impairments in various cognitive domains. Despite the considerable data about the behavioral correlates of OSA, much less is known about changes in the brain substrates underlying the behavioral deficits. Here, we assessed performance and cerebral response to a response inhibition task in OSA patients.
Methods: Fourteen OSA patients and 14 age and BMI matched controls (1 woman in each group; age: mean=44.6 years, SD=10; BMI: mean=29.6, SD=4.7) were studied with functional magnetic resonance imaging (FMRI). As part of the FMRI session, subjects performed the Go-NoGo task. T-tests were used to examine group differences (OSA vs. Control) in performance and in cerebral responses for the NoGo trials.
Results: OSA patients showed an increase in false alarm rates during the NoGo trials (Control: 6±3%; OSA: 11±12%) and decreased brain activation in several brain regions compared to Controls. These regions included left postcentral gyrus (PCG), cingulate gyrus, and inferior parietal lobe (IPL), as well as right insula and putamen ($p<0.05$).
Conclusion: These findings suggest that response inhibition may be impaired in OSA and that this impairment is associated with decreased activation in task-related brain regions. In particular, regions involved with conflict monitoring (cingulate), attention (IPL), motor function

(PCG, putamen) and decision making (insula) showed diminished responses in OSA patients. These data, and those of other FMRI studies in OSA using different tasks, suggest that individuals with OSA show impaired cerebral responses during tasks traditionally thought to rely on executive function, but compensatory responses on encoding tasks. Future work should examine a wider range of cognitive tasks and measures of brain function to fully characterize brain dysfunction in OSA.
Support (optional): NIH M01 RR00827, NIMH 5 T32 MH18399, NIA AG08415

0477

QUALITY OF LIFE OF OSA SUBJECTS DIAGNOSED AND TREATED AT HOME

Skomro R,[1] Cotton D,[2] Reid J,[3] Gjevre J,[3] McNab B,[4] Ward H,[3] Stiles M,[1] Jokic R,[5] Grover V[1]
(1) University of Saskatchewan, Saskatoon, Saskatchewan, Canada, (2) University of Saskatchewan, Canada, (3) University of Saskatchewan, Saskatchewan, Canada, (4) University of Alberta, Alberta, Canada, (5) Queen's University at Kingston, Ontario, Canada

Introduction: Current guidelines recommend an overnight polysomnography (PSG) in cases of suspected OSA but access to PSG is limited. Home diagnosis and treatment of OSA may provide an alternative to in-lab PSG. The purpose of this study was to compare quality of life after CPAP therapy in OSA subjects diagnosed on the basis on level III testing (Embletta) at home with those diagnosed and treated in the sleep lab.
Methods: One hundred adults referred for suspected OSA were randomised to either: 1. In-Lab testing with PSG and CPAP titration and four weeks of fixed pressure CPAP therapy, or 2. Home investigations (HI) with level III testing followed by one week of AutoCPAP and three weeks of fixed pressure CPAP (derived from 95% AutoCPAP pressure). Subjects with cardiac, respiratory failure, previous upper airway surgery, suspicion of another sleep disorder or in safety-sensitive positions were excluded. The primary outcome was HRQOL evaluated by the SF-36 and Calgary Sleep Apnea Quality of Life instruments. Subjects completed questionnaires prior to testing and after four weeks of CPAP.
Results: Thirty subjects (18 males, age: 49.5 +/- 11.8, AHI: 23.3+/- 21.9, ESS: 12.8+/- 3.5) in the HI arm and 34 (21 males) in the PSG arm completed the study. The groups were similar in age, sex, AHI, ESS and baseline SF-36 and SAQLI scores. Both groups had significant and similar improvement in SAQLI scores and in SF-36 Vitality, Social Functioning, Role Emotional, Mental Health subscales and the composite MCS score. The magnitude of the improvement in all subscales of SF-36 was similar between the groups.
Conclusion: Diagnosis and treatment of OSA at home using level III testing and AutoCPAP followed by fixed pressure CPAP therapy results in significant improvement in HRQOL. These improvements are similar to those observed after in lab diagnosis and treatment of OSA.
Support (optional): Lung Association of Saskatchewan. Saskatoon Health Region. Kelsey Trail Health Region.

0478

OCCURENCE OF GASTROESOPHAGEAL REFLUX SYMPTOMS IN A SLEEP CLINIC POPULATION

Shepherd K, Hillman D, Eastwood P
Sir Charles Gairdner Hospital, Perth, Western Australia, Australia

Introduction: Studies have shown that individuals with sleep-disordered breathing have a higher incidence of reflux during sleep than the general population. However, the frequency of nocturnal symptoms in them is unknown as is the nature of reflux symptoms: distal (heartburn) or proximal (acid regurgitation).
Methods: 1329 consecutive patients undergoing overnight polysomnography completed a validated gastroesophageal reflux symptom questionnaire. These were compared to normative data for the general population (n=1511)(Locke G *et al.* Gastroenterology 1997; 112:1448-1456) (Chi-square test; $p<0.05$).
Results: Compared to the general population sample, a greater proportion of the sleep clinic population reported: heartburn in the previous year (42% vs 49%, $p<0.05$); nocturnal heartburn in the previous year (15% vs 25%, $p<0.05$); acid regurgitation in the previous year (45% vs 49%, $p<0.05$); acid regurgitation more than once a week (6% vs 13%, $p<0.05$); nocturnal acid regurgitation in the previous year (15% vs 24%, $p<0.05$); heartburn or acid regurgitation in the previous year (59% vs 63%, $p<0.05$); heartburn or acid regurgitation more than once a week (20% vs 25%, $p<0.05$); and the use of prescribed reflux medications (9% vs 20%, $p<0.05$).
Conclusion: Symptoms of distal and proximal reflux during the day and overnight are common in patients being investigated for sleep-disordered breathing, substantially exceeding that of the general population.

0479

COMPARING CPAP COMPLIANCE BETWEEN SPLIT-NIGHT STUDIES AND FULL-NIGHT STUDIES FOR PATIENTS WITH SLEEP APNEA/HYPOPNEA SYNDROME

Botros W, Rowlands S, Armstrong M
Sleep Clinic London, London, Ontario, Canada

Introduction: Continuous Positive Airway Pressure (CPAP) compliance between split-night studies and full-night studies for patients with sleep apnea/hypopnea syndrome was examined. Protocol for split-night studies involve standard polysomnographic collection for a minimum of 2 hours and maximum of 3 hours, in which subjects exhibit symptoms that are perceived as severe sleep apnea (desaturations in oxygen of less than 75% a minimum of 3 times) proceeded by CPAP titration for the remainder of the 7 hour study. In contrast, for a full-night study, subjects attend a standard 7 hour polysomnograph test and a 7 hour CPAP titration.
Methods: A stratified sample of 22 CPAP studies from the clinic patient database was drawn from the period of 2005 -2006, and each subject was asked to complete a short questionnaire regarding their CPAP device compliance. Of the 22 subjects, 11 were full-night studies and 11 were split-night studies. The full-night subjects were classified as having a severe Apnea Hypopnea Index (AHI), defined as a minimum of 50 breathing events per hour.Compliance was measured in terms of nights per week and percentage of hours per night the CPAP device was used.
Results: Comparison of number of nights CPAP device was used showed no significant difference ($n = 11$, mean usage = 6.45 nights/week, $p = 0.50$) between the two groups. Furthermore, comparison of proportion of nightly use of CPAP device showed no significant difference ($n = 11$, $p = 0.2855$).
Conclusion: Therefore, on either measure of compliance, there was no significant difference between split-night and full-night studies.

0480

DOSE EFFECT OF ACETAZOLAMIDE ON POST-HYPOXIC UNSTABLE BREATHING IN THE C57BL/6J MOUSE

Yamauchi M,[1] Dostal J,[2] Strohl K[1]
(1) Division of Pulmonary, Critical Care and Sleep Medicine, Case Western Reserve University, Cleveland, OH, USA, (2) Louis Stokes Department of Veterans Affairs Medical Center, Cleveland, OH, USA

Introduction: Acetazolamide (ACZ), a carbonic anhydrase inhibitor, will reduce clinically important periodic breathing at altitude and with heart failure, and is believed to work by increasing respiratory drive. We examined whether ACZ would alter post-hypoxic ventilatory behavior in a dose-dependent manner in the C57BL/6J (B6) model of recurrent central apnea.
Methods: Experiments were performed with unanaesthetized, awake adult male B6 mice (n=15), ventilatory behavior was measured using flow through whole body plethysmography. Mice were given an intraperitoneal injection of either vehicle or ACZ (high dose; 40mg/kg, n=9), and one hour later exposed to 1-min of 8% O_2 -balance N_2 (Poikilocapnic hypoxia) or 12% O_2, 3% CO_2-balance N_2 (Non-poikilocapnic hypoxia) followed by rapid reoxygenation (100% O_2). The low dose (4mg/kg) effect of ACZ was examined in another 6 mice.
Results: With high dose ACZ, ventilation including respiratory frequency, tidal volume, and minute ventilation in room air were significantly higher and hypercapnic ventilatory responsiveness was significantly lower compared to vehicle. In contrast, low dose ACZ resulted in no statistical difference in ventilation in room air or hypercapnic ventilatory responsiveness compared to vehicle. Poikilocapnic and non-poikilocapnic hypoxic ventilatory responsiveness was similar among treatments. One minute after reoxygenation, animals given high dose ACZ exhibited post-hypoxic frequency decline, a lower coefficient of variability for frequency, and no tendency towards periodic breathing, as compared to vehicle or to low dose treatment.
Conclusion: High dose ACZ improves unstable breathing in the B6 model of periodic breathing, without altering hypoxic response or producing short-term potentiation, but with a blunting of hypercapnic responsiveness.
Support (optional): NIH (NS052452), VA Research Service, and Fuji Respironics Co. Ltd.

0481

EXCESSIVE SLEEPINESS IN DIVISION I-A COLLEGE FOOTBALL PLAYERS: A PILOT STUDY

Winter W, Hammond W, Green N
Martha Jefferson Hospital, Charlottesville, VA, USA

Introduction: Studies suggest professional football players, particularly linemen, are at an increased risk for obstructive sleep apnea syndrome (OSAS). In this pilot study, we gathered player data from 8 Atlantic Coast Conference (ACC) football teams and evaluated their degree of sleepiness through Epworth Sleepiness Scale (ESS) data. We also collected information about player size, position, medical history and sleep history.
Methods: All 12 ACC college football programs were invited to participate. All players surveyed were active team members during the 2006-2007 football season. Age, height, weight, BMI, neck circumference, position (e.g. quarterback), bed time, wake time, sleep quality, presence of snoring, presence of tonsils, nap tendencies and duration, caffeine intake, hypnotic/stimulant use and ESS score were recorded.
Results: 560 players (ages 17-24, X=20.0 ± 1.3; 560 male) consented to the survey. These individuals had elevated BMI (30.3 ± 5.6) and large neck sizes (44.8 ± 3.8 cm) comparable to professional football players. Despite weighing slightly less than the average professional player (106.3 ± 22.2 kg vs. 112 ± 20.5 kg), the average college player scored higher on the ESS (9.0 ± 4.0 vs. 7.3 ± 4.0) with 252 of 557 players (45.2%) scoring 10 or above, indicating pathological sleepiness. 286 of 560 (51.1%) report snoring and 253 of 533 players (47.5%) admit to at least 1 caffeinated beverage per day. 277 of 558 players (49.6%) reported napping with an average nap duration of 1.3 ± 0.6 h daily.
Conclusion: These results demonstrate that when compared to professional football players, college football players may be sleepier. Professional football players have been shown to have a higher incidence of sleep-disordered breathing. We strongly suspect this trend may be present in college football players. Further studies will be done to evaluate individual `high-risk´ players (e.g. lineman) identified in this pilot study for sleep disturbances including OSAS.

0482

INCREASED ERYTHROCYTES ADHESIVENESS AND AGGREGATION IN OBSTRUCTIVE SLEEP APNEA SYNDROME

Peled N,[1] Kassirer M,[2] Rogowski O,[3] Shlomi D,[4] Fox B,[4] Berliner A,[3] Shitrit D,[4] Kramer M[4]
(1) Rabin Medical Center, Israel, Petach Tiqwa, Israel, (2) Tel Aviv Sourasky Medical Center, Israel, (3) Tel Aviv Souraski Medical Center, Israel, (4) Rabin Medical Center, Israel

Introduction: Obstructive sleep apnea (OSA) is associated with increased incidence of strokes and myocardial infarctions as well as with increased pro-thrombotic and inflammatory processes. Erythrocyte adhesiveness/aggregation (EAA) is also increased in cardiovascular diseases and has never been evaluated in OSA. Therefore the aim of this study was to examine the possible association of sleep apnea with erythrocyte adhesiveness.
Methods: Patients: Seventy nine patients (mean age 57.1±12.9 years) with a diagnosis of OSA (Apnea hypopnea index 41.2±25.9) and 1079 sex-, age- and body mass index (BMI) matched controls free of clinical symptoms of OSA participated in the study in our Sleep laboratory of tertiary university center..
Interventions: Overnight polysomnography and blood sampling for erythrocyte sedimentation rate (ESR), Fibrinogen, high-sensitivity C-reactive protein (hs-CRP), serum amyloid A (S-AA) and erythrocyte adhesiveness/aggregation (EAA) test. EAA was determined by erythrocyte percentage (EP), which represents the probability to have aggregation on specific pixel on smear and vacuum range (VR) that represents the distance (microns) between aggregation cells.
Results: ESR, fibrinogen and hs- CRP were significantly elevated in OSA vs. control (24.7±19.6 mm/h vs. 13.4±9.1 $p<0.001$; 408.5±82.7 mg% vs. 299.0±57.2 $p<0.001$; 4.73±4.41 mg% vs. 2.30±2.70 $p=0.037$ respectively). EAA was stonger significantly in OSA vs. control (EP 84.05±15.97% vs. 90.79±11.23 $p<0.001$ and VR 8.22±7.98 microns vs. 4.63±4.05 $p<0.001$). Both EP and VR significantly correlated with inflammation markers (EP&ESR $r=-0.630$ $p=0.005$; VR&ESR $r=0.494$ $p=0.001$).
Conclusion: OSA is associates with increased EAA activity and with inflammation. The increased EAA is correlated with inflammation activity. These findings might be associated with the increased cardiovascular morbidity in OSA.

0483

THE EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON CHRONIC PAIN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

Gentry S,[1] Ware J[2]
(1) Eastern Virginia Medical School, Hampton, VA, USA, (2) Eastern Virginia Medical School, Norfolk, VA, USA

Introduction: The initiation of continuous positive airway pressure therapy (CPAP) in patients with obstructive sleep apnea (OSAS) improves quality of life. The purpose of this study was to determine whether patients with chronic pain who are newly diagnosed with OSA experience improvement in their pain severity following institution of CPAP.
Methods: Per hospital policy, outpatients attending certain clinics are asked about the severity, duration, and location of any pain they are experiencing. Severity of pain is recorded on a 0-10 analog scale. Records of patients initiating CPAP for OSA or upper airway resistance syndrome (UARS) over the previous three years were reviewed. Patients were identified with pain lasting more than six months, and the highest pain ratings in the six months before and after initiating CPAP were compared. Demographic data, diagnoses, and pre-CPAP apnea-hypopnea index (AHI) also were recorded.
Results: Forty-three patients were identified with reported chronic pain and sufficient data for analysis. The average age was 48 years, and 84% were male. The most common locations reported for chronic pain were back (44%) and legs (26%). Concomitant diagnoses included hypertension (51%), hyperlipidemia (47%), osteoarthritis (40%), and diabetes (33%). Most patients (56%) had a diagnosis of depression and/or post traumatic stress disorder. Pre-CPAP AHI ranged from 4 to 99, with a median of 17. The pre-CPAP pain assessment ranged from 2 to 10, with a mean of 6.7, while post-CPAP pain assessment ranged from 0 to 10, with a mean of 5.2. Twenty-seven patients (63%) had a fall in their maximum recorded pain scale. Over all patients, the average change in maximum pain assessment pre- and post-CPAP was a fall of 1.6 points (P=.0001).
Conclusion: We conclude that patients with chronic pain and newly diagnosed OSAS or UARS report improvement in their pain assessment following the institution of CPAP.

0484

THE DIAGNOSIS AND SEVERITY OF OBSTRUCTIVE SLEEP APNEA (OSA): A COMPREHENSIVE ANALYSIS OF DIFFERENT PREDICTIVE MODELS

Ioachimescu O,[1] Bedford T,[1] Stephenson L,[2] Foldvary-Schaefer N,[1] Golish J[2]
(1) Cleveland Clinic Foundation, Cleveland, OH, USA, (2) Cleveland Clinic, Cleveland, OH, USA

Introduction: Several anatomic, functional and polysomnographic characteristics have been shown to be independent determinants in different predictive models for the diagnosis and severity evaluation of OSA. At least 9 distinct models have been published before, including our own models, and derived on different series of patients. Our aim was to include these 9 models in a comprehensive performance analysis and identify the best simple model which can be used clinically.
Methods: 319 consecutive patients underwent split-night studies or CPAP titration studies after baseline polysomnogram (PSG) at the Cleveland Clinic Sleep Disorders Center were analyzed. The specific information considered useful clinically and for the construction of the predictive models was collected. The two types of prediction models included linear and logistic regression analysis, calculating the optimal CPAP setting and the OSA likelihood, respectively. Comparison with the prescribed CPAP setting and the ground truth for presence of moderate/severe OSA has been made. JMP 5.0.1 software (SAS Institute, Cary, NC) was used for the statistical analysis.
Results: The area under the receiver operating characteristic curve (AUROC) for different models was between 0.69 and 0.90. Although reasonable predictions can be made with respect to the optimal CPAP setting, in our hands most of the models explored tend to underestimate the optimal pressure. The main parameters found to be useful clinically were: body mass index, neck circumference, age, gender; a history of habitual snoring, witnessed apneas or snorting/choking/gasping for air, hypertension as comorbidity; and polysomnographic data such as apnea-hypopnea index and (separately) apnea index.
Conclusion: This is a comprehensive analysis of different predictive models of OSA, which points out the clinical utility, pitfalls and their inherent limitations. This study shows that these models need to be validated in a particular patient population or sleep laboratory and used clinically in concordance with their performance parameters.
Support (optional): None.

0485

HIGHER RATE OF DROPOUT FROM CPAP IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA WITHOUT EXCESSIVE DAYTIME SLEEPINESS

Kawai M,[1] Yamamoto K,[2] Koike S[2]
(1) Toyota Memorial Hospital, Toyota, Aichi, Japan, (2) Sleep Disorders Center, Toyohashi Mates Clinic, Toyohashi, Aichi, Japan

Introduction: Excessive daytime sleepiness (EDS) is a significant symptom of obstructive sleep apnea (OSA). EDS is one of the most frequent symptoms of OSA and makes physicians order overnight polysomnogram for the diagnosis. Occasionally, polysomnogram is performed in patients without EDS because of witnessed apnea, loud snoring or uncontrolled hypertension. Though continuous positive airway pressure (CPAP) has been proven to be effective for the treatment of OSA, often times the compliance and dropouts make treatment plan complicated. It is still not clear whether patients with severe OSA without EDS have higher risk of dropout or not.
Methods: We performed retrospective review of medical charts of all patients who underwent polysomnogram in Toyohashi Mates clinic, Toyohashi, Japan from 2001 to 2006. Those patients with severe OSA (apnea-hypopnea index (AHI) greater than 30) who attempted CPAP treatment were included.
Results: We identified total of 2399 patients who underwent overnight polysomnogram. 1191 patients were diagnosed as severe obstructive sleep apnea. Out of 1191 patients, CPAP treatment was attempted for 1070 patients. In these patients, dropouts were observed in 132 out of 885 patients (14.9%) with ESS greater than 5, 40 out of 175 patients (22.9%) with ESS equal or less than 5. The patients with ESS equal or less than 5 had higher rate of dropout from CPAP with statistical significance (p=0.0068).
Conclusion: In our patients with severe OSA, ESS score equal or less than 5 seems to be related to higher rate of dropout from CPAP treatment. These patients with OSA without EDS may require special support for continuing CPAP treatment.
Support (optional): None

0486

PREVALENCE OF THE UPPER AIRWAY TUMOR AND CYST AMONG PATIENTS WHO SNORE

Hanako S,[1] Suzuki M,[2] Chiba S,[3] Yaguchi Y,[4] Hoshino T,[5] Okamoto M[6]
(1) Teikyo University, Tokyo, Japan, (2) Teikyo University, Japan, (3) Ota General Hospital, Japan, (4) Jikei University School of Medicine, Japan, (5) Hoshino ENT clinic, Japan, (6) Kitasato University School of Medicine, Japan

Introduction: Sleep doctors usually do not pay much attention to the upper airway in patients with snore because they can make the diagnosis of sleep disordered breathing (SDB) without nasopharyngeal endoscopic examination if they have the scores of patients´ Epworth Sleepiness Scale and results of polysomnography. The purpose of this study is to determine the prevalence of benign, malignant tumor and cyst in the upper airway in patients who snore.
Methods: Retrospective multicenter trial in four sleep laboratories affiliated with university teaching hospitals or a general hospital. New adult male and female patients whose chief complaint was witnessed snore were enrolled in this study. Patients with excessive daytime sleepiness or unfreshing sleep were also involved. Patients were evaluated by nasopharyngeal endoscopy to detect organic diseases in the upper airway.
Results: Among 3023 patients, 2 patients had malignant tumors, 5 had benign tumors and 2 had cysts in the upper airway. The prevalence of upper airway benign, malignant tumor and cyst in adult male and female patients was 0.24 %.
Conclusion: Routine evaluation of the upper airway of patients who snore is very important; however, it is as yet not established in sleep laboratories. Routine detailed endoscopic evaluation should be adopted by every institution so as not to overlook tumor or cyst in the upper airway among patients who snore.
Support (optional): This work was supported by Research Grant No. 17591802 to M. S. from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

0487

FACTORS DETERMINING ADHERENCE TO CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) THERAPY IN VETERANS WITH OBSTRUCTIVE SLEEP APNEA (OSA)

Budhiraja R,[1] Zeater M,[2] Parthasarathy S,[3] Quan S[4]
(1) Southern Arizona VA Healthcare System, Tucson, AZ, USA, (2) AZ, USA, (3) United States Department of Veterans Affairs, Tucson, AZ, USA, (4) University of Arizona, Tucson, AZ, USA

Introduction: Sleep during the titration night has been suggested to determine adherence to CPAP therapy in patients with obstructive sleep apnea (OSA) in one study. We aimed to determine whether the sleep efficiency during the diagnostic or therapeutic portion of a split-night study correlates with future CPAP adherence in veterans with OSA. We also aimed to assess the relation between demographics and clinical features of OSA and adherence to CPAP therapy.
Methods: We performed a retrospective chart review of 15 consecutive patients with OSA newly diagnosed by a split-night study at a Veterans Affairs hospital. The night prior to the split-night polysomnographic study, all veterans completed a questionnaire comprising questions regarding the symptoms of OSA. The hours on the CPAP machine were evaluated 28 days after such therapy was dispensed to assess nightly adherence. Usage index was calculated as the number of days CPAP was used for over 4 hours divided by the total days studied.
Results: The subjects were 63 ± 11 years old (mean ± s.d.) with a BMI of 36 ± 8. There was no significant correlation between the symptoms of OSA including snoring, witnessed apneas, daytime fatigue, or Epworth sleepiness scale score; and adherence to CPAP therapy. The BMI correlated with AHI (R=0.59, P=0.02), average nightly CPAP use (R=0.78, P=0.02) and the usage index (R=0.75, P=0.03). There was significant inverse correlation between the sleep efficiency during the diagnostic part of the study and the average nightly CPAP use (R=-0.79, P=0.02) and the usage index (R=-0.73, P=0.04).
Conclusion: The preliminary results from this ongoing study suggest that a higher BMI is associated not only with a higher severity of sleep apnea, but also with greater adherence to CPAP therapy. Furthermore, lower sleep efficiency during the diagnostic portion of the split-night study, suggesting worse baseline sleep quality, is associated with a higher adherence to CPAP therapy.

0488

SLEEP PROFILE OF APNEA AND INSOMNIA CO-MORBIDITY

Hofman W,[1] Kumar A[2]
(1) Psychonomics/Psychology, University of Amsterdam, Amsterdam, Netherlands, (2) Personal Health Institute International, Amsterdam, Netherlands

Introduction: 19935 individuals completed a 15 items symptoms checklist covering major sleep disorder symptoms, gender and age category. 5594 of these individuals also completed a questionnaire about their sleep and wake times (sleep profile).
This paper reports the comparison of the sleep profile of patients with apnea symptoms, insomnia symptoms and with symptoms of apnea/insomnia co-morbidity.
Methods: 4.35% of the respondents reported both symptoms of sleep apnea (snoring, gasping for breath), 13.9% reported all symptoms of insomnia, 3.2% reported symptoms of narcolepsy and 1.65% reported symptoms of limb movement disorder.
The sleep profile of respondents with all apnea symptoms were compared with an age and gender matched group of respondents with all insomnia symptoms (N=119). A group of 84 subjects with apnea/insomnia co-morbidity was analyzed separately.
Results: More females (10.8%) than males (4.4%) reported breathing difficulty, whereas more males (7.6%) than females (5.9%) reported both snoring and breathing difficulty. Although the main population was above 35 years, 8.5% of the respondents younger than 18 years reported apnea symptoms.
In comparison with an age and gender matched group with insomnia symptoms, the apnea group showed: statistically significant later bedtimes and times of waking up, shorter sleep latencies and less minutes awake after sleep onset, less early morning awakenings and less time awake in bed before getting up.
As expected the apnea group showed more daytime sleepiness and more napping.
The sleep profile of the group with apnea/insomnia co-morbidity resembled that of the matched control insomnia group.
Conclusion: The apnea symptoms group showed a less disturbed sleep pattern than the insomnia symptoms group. However, 40% of the apnea symptoms group had insomnia co-morbidity and this group had a similar pattern and intensity of sleep disturbance as insomniacs. This indicates that insomnia should be part of the treatment strategy of apnea patients.

0489

PREDICTING THE FAILURE OF POSITIVE AIRWAY PRESSURE TITRATION USING ECG-DERIVED CARDIOPULMONARY COUPLING SPECTROGRAMS

Weiss M,[1] Thomas R,[1] Mietus J,[1] Peng C,[1] Gilmartin G,[1] Daly R,[2] Goldberger A,[1] Gottlieb D[3]
(1) Beth Israel Deaconess Medical Center, Boston, MA, USA, (2) The Periodic Breathing Foundation, Wellesley Hills, MA, USA, (3) Boston University, Chestnut Hill, MA, USA

Introduction: Complex sleep apnea is a newly recognized subset of sleep apnea (SA), characterized by induction of central apneas and periodic breathing in patients appearing to have obstructive SA on the diagnostic polysomnogram. We assessed the utility of a previously

described ECG-based cardiopulmonary coupling assay, the sleep spectrogram, in predicting positive (PAP) titration outcomes.
Methods: ECG's extracted from seventy-seven archived polysomnographic data files were used. Standard scoring and sleep spectrograms were analyzed. The latter provided measures of stable and unstable sleep, as well as identification and quantification of high (HFC) and low frequency cardiopulmonary coupling (LFC). A subset of LFC, narrow-band elevated (NB-eLFC), is associated with central-like physiology on polysomnograms (unpublished data), and its predictive value for PAP failure (vs. central apnea index, desaturation severity) was assessed. Acute PAP titration success or failure (induction or amplification of central apneas and periodic breathing) was assessed by independent review of the raw polysomnogram.
Results: NB-eLFC was the best predictor of PAP titration failure (induction of complex sleep apnea). Twenty-nine of the 32 with the presence of any (17 minutes of central-like physiology) NB-eLFC failed CPAP titration, while 5/45 of those without NB-ELFC failed titration. This ECG-based biomarker had the following characteristics: sensitivity: 95.24%, specificity: 85.7%, positive predictive value: 88.89%, negative predictive value: 93.7% correctly classified: 90.8%. The odds ratio of titration success in the presence of narrow band NB-ELFC was 0.01 (Confidence Intervals: 0.01-0.05; Chi Square = 50.5, p: < 0.001). These associations remained significant after adjustments for age, body mass index, apnea hypopnea index, central apneas, and minimal nocturnal desaturation. Severe sleep fragmentation and respiratory abnormalities persisted despite use of PAP in those with complex SA.
Conclusion: In severe SA, ECG-based spectral analysis allows automated, operator-independent risk stratification for acute failure of PAP titration.
Support (optional): Grants from the National Institutes of Health Heart Lung and Blood Institute (R21HL079248) and National Center for Research Resources (P41RR013622), the James S. McDonnell Foundation, the G. Harold and Leila Y. Mathers Foundation, the Defense Advanced Research Projects Agency, and an unrestricted grant from the Periodic Breathing Foundation.

0490

USE OF ADAPTIVE SERVO VENTILATOR FOR TREATMENT OF CENTRAL AND COMPLEX SLEEP APNEA SYNDROMES: A REVIEW OF 100 CASES

Allam J,[1] Gay P,[2] Morgenthaler T,[2] Olson E[1]
(1) Mayo Foundation for Medical Education and Research, Rochester, MN, USA, (2) Mayo Clinic, Rochester, MN, USA

Introduction: Complex sleep apnea syndrome (CompSAS) is recognized by either mixed or obstructive events that convert to largely central apneic events upon exposure to CPAP. Treatment of CompSAS or central sleep apnea (CSA) with an Adaptive Servo Ventilator (ASV) is now an option but no large series exist describing the application of ASV, or the factors that predict response to treatment.
Methods: We studied the first 100 patients with CompSAS or CSA who underwent a polysomnogram (PSG) using ASV at our institution. We extracted data from patient charts and PSG reports.
Results: The main indications for an ASV titration were CompSAS or central sleep apnea/Cheyne Stokes breathing pattern. The median age was 72 years (range 18-88), with 87% males. The mean diagnostic sleep apnea hypopnea index (AHI) was 46±3 events/hr and was unchanged with CPAP (AHI=45±3, p=0.7791). With spontaneous bilevel PAP (10% of patients) AHI worsened to a mean of 60. Bilevel PAP with a backup rate improved the AHI to 31 (26% of patients). Use of the ASV resulted in a dramatic improvement of the AHI to a mean of 8±3 vs baseline as well as CPAP (p<0.0001), a significant increase in REM sleep (18±1 % vs 10±1 %; p<0.0001), and improvement in minimal oxygen saturation during REM (83±4 % vs 60±4 %; p<0.0001). Both central and obstructive events were significantly reduced. Overall, 73% of patients responded to the ASV treatment with a mean AHI <10. The presence of atrial fibrillation and congestive heart failure significantly reduced the likelihood of response to ASV with an odds ratio of 0.28 (95% CI=0.11-0.70) and 0.32 (0.13-0.80) respectively.
Conclusion: The ASV device appears to be a more effective treatment of both CompSAS and Central Sleep apnea syndromes compared to CPAP and bilevel PAP with back-up rate.

0491

INTERMITTENT HYPOXIA AND SLEEP RESTRICTION: MOTOR, COGNITION AND NEUROCHEMICAL ALTERATIONS IN RATS

Perry J,[1] D´Almeida V,[2] Lima M,[3] Godoi F,[4] Vital M,[5] Oliveira M,[6] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil, (3) Universidade Federal de Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (4) Sao Paulo, Brazil, (5) Univ Fed Paraná, Curitiba, PR, Brazil, (6) Univ Fed Sao Paulo, SP

Introduction: The present study was designed to evaluate the effects of subchronic (4 days) and chronic (21 days) sleep restriction (SR) and intermittent hypoxia (IH) on motor and cognitive function in rats. Moreover, we evaluated the effects of catecholamine concentrations and tyrosine hydroxylase protein expression in forebrain regions.
Methods: Wistar-Hannover rats were submitted to IH exposure (2 min room air - 2 min 10% O2 for 1000-1600h) followed by a SR period of 18h (1600-1000h). Rats were randomly assigned to four treatment groups: 1) control 2) SR 3) IH and 4) SR-IH. In the inhibitory avoidance task, an additional group of rats was submitted to paradoxical sleep deprivation (PSD) for 96 consecutive hours.
Results: Results showed that subchronic and chronic SR induced an increase in motor activity without modifying neurotransmission in the frontal cortex and striatum. Neither SR periods induced cognitive deficits. However, 96h of PSD led rats to display impairment in acquisition/retention in the inhibitory avoidance task. Exposure to IH did not affect motor and cognitive function but IH associated to SR increased motor activity. In the chronic IH and SR-IH groups norepinephrine concentration in the striatum was reduced although neither chronic SR nor IH affected tyrosine hydroxylase protein expression.
Conclusion: These results suggest that SR induced motor alterations were not related to the synthesis of catecholamine. However, chronic IH increases striatal norepinephrine concentrations without modifying behavior. Thus, the present results confirm the deleterious effects of sleep loss on inhibitory avoidance learning, but suggest that such deficits have different temporal characteristics.
Support (optional): AFIP, FAPESP, CEPID, CNPq

0492

INFLAMMATORY AND METABOLIC DISTURBANCE IN OSA PATIENTS. IMPACT OF LONG-TERM CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY

Sales L,[1] Bittencourt L,[2] Garbuio S,[2] Trukisinas V,[2] D´Almeida V,[2] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil

Introduction: Obstructive Sleep Apnea Syndrome has many consequences such as metabolic and inflammatory alterations that increase cardiac morbidity. This study evaluates metabolic and

inflammatory markers in OSA patients prior and subsequent to six months of CPAP treatment.
Methods: Thirteen middle age male subjects, without relevant underlying cardiologic or morbid obesity, with clinical and polissonographyc criteria for OSA were recruited from the Sleep Institute in 2003. The laboratorial analyses were performed in the morning after a 12-hour fast and included: Homocysteine, vitamins B11 and B12, cholesterol, triglycerides, fasting glucose, insulin, creatinin, TGO, TGP, T3, T4, TSH. All patients had made use of the CPAP (Mallinckrodt) for six months and were examined monthly by trained professionals. We also analyzed 13 volunteers matched for sex, age and body mass index (BMI) with the same protocol. After CPAP treatment patients were their own controls.
Results: Regarding laboratorial evaluation patients presented increased values of homocysteine, triglycerides, LDL, VLDL, insulin, and decreased values of vitamin B11 and HDL when compared to control group. They also showed normal values of total cholesterol, fasting glucose and vitamin. Considering BMI (mean (SD)) there was no significant difference between controls and patients (26.3,,b3.9 vs 29,,b3.5, Kg/m2, NS). Mean CPAP use was 5,,b1 hrs/night and the pressure was 9,,b1.7 cmH2O. The BMI was kept constant with no meaningful statistical difference prior and subsequent to CPAP use (BMI: 29 ,,bn3.5 vs 28.8 ,,bn2.9 Kg/m2,NS). After treatment the AIH returned to normality values. We also observed a decrease in homocysteine and an increase in Vitamin B11 concentrations that returned to normality values but insulin, HDL, LDL and triglycerides had no significant reduction.
Conclusion: There was inflammatory and metabolic alteration in middle age OSA patients in our group of OSA patients without important obesity or cardiovascular morbidity. There was partial response of these changes to long-term use of CPAP.
Support (optional): FAPESP, CEPID, AFIP and CNPq

0493

NIGHT SWEATS: PREVALENCE AND RELATED SYMPTOMS IN A CLINICAL SAMPLE

Goodrich S,[1] Mold J,[2] Orr W[3]
(1) Lynn Health Science Institute, Oklahoma City, OK, USA, (2) University of Oklahoma, Oklahoma City, OK, USA, (3) Oklahoma City, OK, USA

Introduction: Sweating at night is a common patient complaint, yet very little is known about the pathogenesis of this complaint. It has been suggested that night sweats could be caused by obstructive sleep apnea (OSA) and putative sympathetic activation. It has also been found to be associated with leg jerking during sleep, awakenings with pain during the night, and daytime fatigue.
Methods: Data from 282 patient charts were analyzed on objective and subjective polysomnographic (PSG) variables. Objective sleep variables included sleep efficiency, sleep onset latency (SOL), apnea hypopnea index (AHI) and periodic limb movement (PLM) index. Subjective variables included a question related to the frequency of night sweats. Patients were divided into those who complained of night sweats and those who did not. Data were analyzed via t tests and chi square tests.
Results: 28% of the sample reported night sweats (i.e., night sweating occurred often, frequently, or always). There were no demographic differences between those with or without night sweats. There was no significant difference on the AHI or other objective sleep measures. The night sweats group had significantly greater subjective reports of leg kicking during sleep, restless legs symptoms, difficulty breathing at night, and morning headaches (all $p < .01$). Patients with night sweats also had a significantly higher Epworth score ($p < .001$).
Conclusion: 1) These data do not support the notion that OSA is linked to complaints of night sweats. 2) Though patients complaining of night sweats are also more likely to report other sleep-related symptoms, they appear to be no more likely to have objective evidence of disordered sleep or sleep related breathing disorders by polysomnography.

0494

DOES CPAP LEAD TO CHANGE IN BMI?

Redenius R,[1] Murphy C,[2] O'Neill E,[1] Al-Hamwi M,[3] Zallek S[3]
(1) OSF Saint Francis Sleep Disorders Center at the Illinois Neurological Institute, Peoria, IL, USA, (2) OSF St. Francis Medical Center, Peoria, IL, USA, (3) University of Illinois at Peoria, Peoria, IL, USA

Introduction: Obstructive sleep apnea syndrome (OSAS) is the repeated cessation of breathing in sleep due to upper airway obstruction. Obesity is the most common cause of OSAS in adults. Daytime sleepiness due to OSAS can lead to decreased physical activity and increased weight. Patients with OSAS have been found to have "leptin resistance," which limits response to this satiety hormone and can make weight management difficult. CPAP (continuous positive airway pressure) is the most effective treatment for OSAS. We hypothesize (1) subjects with OSAS lose weight after 1 year of CPAP and (2) these subjects lose more weight or gain less weight than untreated control subjects.
Methods: 228 subjects (64% men) with OSAS (AHI ≥ 5) were identified retrospectively from the patient database at OSF Saint Francis Sleep Disorders Center. Treatment subjects used CPAP ≥ 4 hours a night and ≥ 70% of nights for 1 year. Controls used no applied treatment (CPAP, oral appliances, or surgery) for OSAS or used CPAP < 4 hours a night or < 70% of nights for 1 year.
Results: Body mass index (BMI) did not change in treated subjects ("subjects") (0.11kg/m2, n=183) vs. controls (-0.22kg/m2, n=45, P=0.3157). BMI of non-obese subjects increased (27.08kg/m2 to 27.53kg/m2, n=46, P=0.0443). BMI did not increase in obese subjects, obese or non-obese controls. BMI increased in treated women compared to both prior BMI (38.60kg/m2 to 39.63kg/m2, n=64, P=0.0319) and treated men (women: 0.55kg/m2; men: -0.12kg/m2, n=119, P=0.0228).
Conclusion: BMI increased with 1 year of CPAP use in women but not men and in non-obese CPAP users. Interestingly, BMI did not decrease in any group. This differs from expectations that effective CPAP use leads to increased physical activity and responsiveness to leptin, which could lead to weight loss. A larger, prospective study may help clarify these findings.

0495

CPAP COMPLIANCE IS HIGHER WITH COLLABORATION BETWEEN THE CLINICAL SLEEP CENTER AND PAP DISPENSING HOME CARE COMPANY

Plotkin K,[1] Blodgett S,[1] Woolrich E,[2] Timothy B[3]
(1) Sleep Insights Medical Services, Rochester, NY, USA, (2) Associated Healthcare, NY, USA, (3) Sleep Insights Medical Services, NY, USA

Introduction: The data acquired to track CPAP compliance for insurance purposes can also provide clinicians and PAP providers with feedback regarding ways to improve patient care. Clinical sleep centers are ideally positioned to initiate PAP treatment quickly after a titration PSG, and CPAP compliance appears to be better when patients obtain on-site CPAP titration versus automated home CPAP titration1. Most

centers defer PAP set-up and compliance tracking to home care companies. Utilizing a collaborative approach to establish PAP treatment of OSA leads to higher overall compliance versus the traditional home-care set-up approach. By using a collaborative method, patients benefit from the shared expertise and continuing care of both the sleep laboratory staff and the home care company.
Methods: This study utilized measured compliance data generated by patient surveys and data card downloads obtained from PAP devices. The collaborative data (sleep center plus home care company, Associated Healthcare, n = 99) for PAP compliance in 2006 was obtained by a Registered Respiratory Therapist through patient follow-up phone calls and data downloads at one week, one month, and three months. The 2006 data for the home care company alone ("traditional approach", n = 6597) was obtained from routine calls by representatives of Associated Healthcare, a full service respiratory home care company in New York State. Their data was tabulated as cumulative compliance for PAP use for all of their patients in 2006. These statistics were compared to data for the national average regarding PAP compliance2.
Results: With the collaborative approach to initiation of PAP, patient compliance was 85% after one week of use, 89% after one month of use, and 83% after three months of use. After the three month milestone, the collaborative approach yielded an overall 84% overall compliance rating as compared to 81% for the traditional method, and as compared to 50% for the national average for PAP compliance.
Conclusion: The overall results of the collaborative approach to initiating PAP therapy yielded higher compliance when compared to the traditional approach in which PAP therapy is initiated and tracked by the respiratory home care company alone. PAP compliance was also higher than the national average when therapy was initiated and closely tracked by way of regular phone calls by the DME provider (Associated Healthcare). The results of this collaborative approach are similar to those obtained by a comprehensive sleep center-based DME program3. A collaborative approach can provide sleep centers and home care companies with better ongoing information regarding PAP equipment changes and problems during ongoing therapy, while providing patients with unified clinical care.

0496

HYPERVISCOSITY INDUCED BAEP CHANGES AS A MARKER OF INCREASED STROKE RISK IN OBSTRUCTIVE SLEEP APNEA PATIENTS

Bernath I,[1] Koves P,[2] Szakacs Z,[1] Horvath A[2]
(1) Central Hospital of the Hungarian Home Defence Force, Budapest, Hungary, (2) Central Hospital of the Hungarian Home Defence Force, Hungary

Introduction: Based on our previous findings, that OSA induced hyperviscosity can give rise to brainstem acoustic evoked potential (BAEP) changes we put the question whether pathological BAEP findings reveal a higher risk for cerebrovascular events.
Methods: 280 patients newly diagnosed with severe OSA (apnea/hypopnea index >35/h) by a polisomnographic study, and reluctant to accept adequate CPAP therapy underwent hemorheological and BAEP evaluations. All patients were male, aged 30-55 years, with unremarkable cardiological findings and negative results on transcranial and neck Doppler sonography or MRI angiography. Follow up: repeated polisomnography, BAEP and rheological investigation was performed once pro year. Endpoints were either 3 year follow up ending with a control MRI, or symptomatic cerebrovascular events.Appearance of a new MRI lesion compatible with single or multiple lacune,territorial or borderzone densitiy changes was considered as MRI progression.
Results: 212 patients had hyperviscosity and 68 had normal rheological findings. Evoked potential changes – 70 sensorineuronal (total lack of any waveforms) and 108 brainstem type (significant prolongation of wave III latencies) – appeared only in the hyperviscosity positive subgroup. 34 patients had hyperviscosity without the evidence of BAEP changes. Patients with hyperviscosity and sensorineuronal BAEP alteration had a higher incidence of MRI progression or symptomatic stroke (24/70person) than did patients with hyperviscosity and brainstem type of BAEP lesion (7/108), or those with hyperviscoity but no BAEP changes (6/34) and those with normoviscosity and normal BAEP findings (8/68). Logistic regression analysis was carried out to confirm subgroup homogenity regarding BMI, and age. Cox's proportional hazards regression model – adjusted for potential confounding factors as hypertension,diabetes,elevated serum cholesterol and trigliceride level, drinking and smoking habit – showed that the presence of hyperviscosity induced sensorineuronal BAEP changes significantly increased the risk of MRI progression (OR:3,91) compared with participants without OSA related hemorheological disorder. Brainstem type BAEP changes (OR:1,94), or hyperviscosity without BAEP changes (OR:1,29) showed lower risk.
Conclusion: Our findings indicate that sensorineuronal BAEP changes in untreated OSA patients with concomitant hyperviscosity syndrome can be an early marker of an increased risk of primary or recurrent stroke.

0497

SCREENING FOR SLEEP APNEA IN CANDIDATES FOR BARIATRIC SURGERY: ANALYSIS OF THE BERLIN QUESTIONNAIRE

Steinel J,[1] Shaman Z,[2] Auckley D[1]
(1) Case Western Reserve University, Cleveland, OH, USA, (2) Case Western Reserve University, OH, USA

Introduction: The prevalence of obstructive sleep apnea (OSA) in candidates for bariatric surgery is high (55-98%). OSA is associated with increased complications following bariatric surgery. Preoperative polysomnography (PSG) may not be required in all patients as a screening tool. We hypothesized that an OSA screening questionnaire could determine which patients need preoperative PSG evaluation.
Methods: Consecutive bariatric surgery candidates at our institution completed the Berlin Questionnaire (BQ), Epworth Sleepiness Scale (ESS) and PSG preoperatively. Data were collected and analyzed in SPSS.
Results: Seventy Five subjects completed the protocol. Demographic data: age 40.5 +/- 10.6 years, 84% female, ethnicity – 48% Caucasian, 41% African American, 11% Hispanic. The mean BMI was 51.3 kg/m2 (range 35.7 to 78.2) and the mean ESS was 12. Sixty two patients (83%) were identified as high risk for OSA by the BQ. By PSG, the mean apnea-hypopnea index (AHI) was 39.0 (range 0.3 to 152). When OSA was defined as AHI > 5, it´s prevalence was 93% and the BQ had a sensitivity of 0.83, specificity of 0.20, PPV of 0.93 and negative predictive value (NPV) of 0.08. Using an AHI > 15 to define OSA, the prevalence was 68% and the BQ had a sensitivity of 0.86, specificity of 0.22, PPV of 0.70 and NPV 0.42. Comparing groups by BQ categorization (low vs. high risk), there were no significant differences in age, gender, ethnicity or AHI (36.0 vs. 39.7), though differences were seen in BMI (47.7 vs. 52.0 kg/m2) and ESS (9 vs. 13). In the low risk group, 5 patients (38%) had an AHI > 30.
Conclusion: While the BQ has a high PPV for OSA in the bariatric population, the NPV is quite low, limiting its discriminative value. With the high prevalence of OSA in our population, preoperative PSG seems warranted in all patients.
Support (optional): None

0498

HIGH FREQUENCY OF OBSTRUCTIVE SLEEP APNEA IN PRIMARY CARE PATIENTS WITH DIFFICULT TO CONTROL BLOOD PRESSURE

Zoller R,[1] Chung S,[1] Novak M,[2] Fargher T,[3] Shapiro C[2]
(1) University Health Network, Toronto, Ontario, Canada, (2) University Health Network, Ontario, Canada, (3) West Parry Sound Health Centre, Ontario, Canada

Introduction: Two to four percent of the general population has obstructive sleep apnea (OSA) but a high prevalence (60-86%) of OSA has been reported in treatment resistant tertiary care hypertensive patients. Aim: to determine the frequency of OSA in primary care patients with difficult to control hypertension.
Methods: Patients with difficult to control blood pressure (taking >3 antihypertensive medications with clinical blood pressure >140/90 mmHg) were selected from 10 rural primary care practices. After informed consent was obtained, an overnight sleep study was conducted and 24-hour blood pressure, weight, height, neck circumference and patient health-related demographics data were collected.
Results: Thirty-eight (62%) of 61 eligible patients participated in the study, 23 (61%) were female. The average age, BMI, neck size and 24-hour blood pressure in males and females were: 68 and 69 years, 31.8 and 33.7 kg/m2, 42 and 36.9 cm and 141/78 and 143/71 mmHg respectively. Twenty-four (63%) patients were found to have OSA: 13/15 men and 11/23 women. The frequencies of OSA and AHI were higher in men compared to women, $p<0.05$. Patients with OSA had a higher 24-hour blood pressure than those without OSA (144/77 vs. 138/68 mmHg, $p<0.05$). There was no significant difference in age (69.4 vs. 68.2 years), BMI (33.4 vs. 32.7 kg/m2) or neck size (39.0 vs. 38.7 cm) in patients with OSA versus non-OSA.
Conclusion: OSA frequency is high (63%) in primary care patients with difficult to control hypertension. The frequency and severity of OSA is significantly greater in male hypertensive patients. Although a study with a larger population and a control group is required, our findings support the need to screen for OSA in difficult to control hypertensive patients in primary care.

0499

SLEEP RELATED BREATHING DISORDER IN HEART FAILURE PATIENTS: A RETROSPECTIVE STUDY OF SIXTY PATIENTS

Linarez E,[1] Budur K,[1] Stephenson L,[2] Ioachimescu O,[1] Foldvary-Schaefer N[3]
(1) Cleveland Clinic Foundation, Cleveland, OH, USA, (2) Cleveland Clinic, Cleveland, OH, USA, (3) Cleveland Clinic Foundation, OH, USA

Introduction: Congestive heart failure (CHF) is a common disorder with significant morbidity and mortality. Prior work suggests that sleep related breathing occurs in 30-50% of patients. Our objective was to describe the clinical and polysomnographic features of patients with CHF referred for polysomnography (PSG).
Methods: This is a retrospective review of 60 patients with CHF who underwent PSG for suspected sleep apnea. Information on various demographic and functional variables, the Epworth Sleepiness Scale (ESS) and PSG parameters were reviewed.
Results: There were 42 males and 18 females with a mean age of 60.4 + 13 years (mean+1SD) and mean BMI of 35.4 + 9. Mean BMI was higher in females than males (41.5 vs. 32.9; p=0.05). By history, 32.2% had self-reported excessive daytime sleepiness (EDS), 94% had habitual snoring and 33.3% had both. The mean ESS for the group overall was 11.2 +6. The mean ESS was higher for those with self-reported EDS than those without EDS (13 vs. 7.2; p=0.01). 84% had obstructive, 6.8% had central, 5.1% had mixed sleep apnea and 3.4% had primary snoring. The overall mean AHI was 39.8 + 29 and was significantly higher for males (46.5 vs. 24.5; p=0.006).
Conclusion: Subjects with CHF and obstructive sleep apnea commonly report habitual snoring, but only 1/3 report EDS. Women with sleep apnea and CHF were more obese yet had lower AHI´s compared with men. In contrast to prior studies in which ESS scores have been low, a positive association was found between self-reported EDS and ESS suggesting it may be a useful tool in the CHF population. Given the high prevalence of sleep apnea in patients with CHF population, further research is needed to identify reliable clinical predictors.
Support (optional): None.

0500

THE EFFECTS OF HYPOXIA ON SCALENE VERSUS GENIOGLOSSUS REFLEX RESPONSES TO BRIEF PULSES OF NEGATIVE AIRWAY PRESSURE

Eckert D,[1] Catcheside P,[2] George K,[3] Thompson K,[3] McEvoy D[2]
(1) Adelaide Institute for Sleep Health, Repatriation General Hospital and School of Molecular and Biomedical Science, Discipline of Physiology, Adelaide University, Australia, Boston, MA, USA, (2) Adelaide Institute for Sleep Health, Repatriation General Hospital, South Australia, Australia, (3) Adelaide Institue for Sleep Health, Repatriation General Hospital, South Australia, Australia

Introduction: The respiratory pump muscles respond to brief respiratory loading via reflex inhibition followed by excitation. Respiratory muscle inhibition (eg scalene, sc) is enhanced in OSA patients and may help alleviate upper airway (UA) collapsing forces. In an UA dilator muscle (genioglossus, gg), we recently observed short-latency reflex activation followed by inhibition with a similar inhibition onset-latency to that reported in respiratory pump muscles. However, UA and respiratory pump muscle reflex responses have not been directly compared. Hypoxia has depressant effects on ventilation, respiratory load sensation and the cough reflex. In sleep-disordered breathing, increased respiratory load and hypoxia frequently coexist. Our aims were therefore to 1) compare sc and gg reflex responses and 2) examine the effect of hypoxia on these reflexes.
Methods: On two nights, healthy subjects were instrumented with intramuscular gg and surface sc electrodes. In random order, subjects received normoxia or isocapnic hypoxia (SaO2~85%). To elicit EMG reflexes, brief pulses (250ms) of negative UA pressure were delivered during early inspiration in stable sleep and wakefulness.
Results: Ensemble-averaged, rectified EMGgg and EMGsc revealed clearly defined reflex responses in 11 and 10 subjects respectively during wakefulness and sleep under both gas conditions. The EMGgg reflex consisted of short-latency activation followed by inhibition (latencies ~24ms and ~38ms respectively), which was not different between normoxia and hypoxia. Conversely, the predominant EMGsc response was inhibition followed by activation (~36ms and ~87ms), with more pronounced inhibition during hypoxia compared to normoxia (eg wakefulness inhibition-duration; 63±9ms vs. 36±8ms, $p<0.01$).
Conclusion: These data indicate that the EMGgg reflex response to negative UA pressure is maintained during mild hypoxia while reflex inhibition of EMGsc is more pronounced. The net effect would likely serve to protect the UA against collapse. Comparable reflex inhibition-onset latencies between EMGgg and EMGsc suggest involvement of similar pathways in these reflex components.
Support (optional): NHMRC, Australia

0501

MODAFINIL IMPROVES PATIENTS´ ABILITY TO SUSTAIN WAKEFULNESS IN EVERYDAY SITUATIONS: AN ANALYSIS OF RESPONSES TO THE INDIVIDUAL QUESTIONS OF THE EPWORTH SLEEPINESS SCALE

Harsh J,[1] Bogan R,[2] Roth T[3]
(1) University of Southern Mississippi, Hattiesburg, MS, USA, (2) SleepMed, Inc., Columbia, SC, USA, (3) Henry Ford Hospital, Sleep Disorders and Research Center, Detroit, MI, USA

Introduction: Excessive sleepiness (ES) affects patients´ ability to engage in everyday situations. The effect of modafinil, a wake-promoting agent, on patients´ functional status was evaluated by determining patient responses to individual questions of the Epworth Sleepiness Scale (ESS).
Methods: This retrospective analysis pooled results from 4 studies of patients with ES associated with nCPAP-treated obstructive sleep apnea (OSA; N=466) or narcolepsy (N=558). Patients were randomized to receive modafinil (200–400 mg/day) or placebo for up to 12 weeks. The ESS assessed the likelihood of falling asleep during 8 everyday activities, using a scale of 0 (would never doze) to 3 (high chance of dozing). A clinically meaningful response for total score was defined as a change of ≥4 points from baseline; response to any of 8 individual questions was defined as an improvement of ≥1 point from baseline.
Results: Of patients with OSA, 55.6% of patients receiving modafinil showed improvement based on total ESS score vs 27.2% of patients receiving placebo (P<.0001). Of patients with narcolepsy, 52.7% of patients receiving modafinil showed improvement based on total ESS score vs 26.1% of patients receiving placebo (P<.0001). Response to modafinil was significantly greater for all ESS questions vs placebo for both populations (P<.01), except for "sitting in a car while stopped in traffic" for patients with OSA (32.3% vs 26.1%; P=.16). For both populations, response to modafinil vs placebo was greatest for "sitting and reading" (OSA, 60.9% vs 35.6%; narcolepsy, 57.0% vs 31.1%; P<.0001 for both) and "watching television" (OSA, 59.8% vs 31.1%; narcolepsy, 55.6% vs 28.3%; P<.0001 for both).
Conclusion: In patients with ES associated with OSA or narcolepsy, modafinil significantly improves patients´ ability to remain awake in everyday situations.
Support (optional): Cephalon, Inc.

0502

THE RELATION BETWEEN SLEEP-DISORDERED BREATHING AND SLEEP DISRUPTION IN HEALTHY MIDDLE AGED AND OLDER ADULTS

Laffan A, Caffo B, Swihart B, Punjabi N
Johns Hopkins University, Baltimore, MD, USA

Introduction: Sleep disordered breathing (SDB) is a chronic disorder associated with hypertension and cardiovascular disease. Defining whether SDB-related disruption is an important mediator of health outcomes is vital to better characterize the intermediates in the causal pathway. Currently, the independent contribution of SDB to sleep disruption in the absence of other medical morbidities is not known.
Methods: Sleep Heart Health Study participants free of all medical conditions except SDB were examined (N=1,861). Sleep-stage data was used to define the hazard of transitioning between wake, NREM sleep, and REM sleep. SDB severity was defined using respiratory disturbance index (RDI) as follows: none (<5 apnea or hypopnea events per hour of sleep), mild (5 -15), moderate (15–30), and severe (>30). Multi-state survival analysis was used to model the effects of SDB severity on the hazard of sleep stage transitions.
Results: Multivariable models that included age, gender, body mass index, and race showed that the hazard ratio of transitioning from NREM-to-wake for the four SDB groups were 1.00, 1.13, 1.24 and 1.34, respectively. The hazard ratios for REM-to-wake transition for the four SDB groups were 1.00, 1.32, 1.30, and 1.34. Tendency to transition from NREM-to-REM sleep decreased as severity of SDB increased. No significant associations were observed between the hazard of other sleep-stage transitions (Wake-to-NREM, REM-to-NREM, and Wake-to-REM) and SDB severity.
Conclusion: Among this group of healthy middle-aged and older adults free of medical conditions, SDB was associated with increases in the hazard of waking and a decrease in hazard of moving to deeper stages of sleep. The changes observed increased as SDB severity increased and were largest among those with severe SDB. Further work should focus on defining the contribution of medical morbidities to sleep disruption and possible interactions with SDB in mediating adverse health outcomes.
Support (optional): National Institutes of Health Grants HL07578 and AG025553

0503

DOES THE TYPE OF STUDY INFLUENCE CONTINUOUS POSITIVE AIRWAY PRESSURE COMPLIANCE?

Mcleland J,[1] Doerr C,[2] Kampelman J,[1] Boero J,[2] Duntley S[2]
(1) Washington University in St. Louis, St. Louis, MO, USA, (2) Washington University in St. Louis, Saint Louis, MO, USA

Introduction: There is an increasing demand for patients with obstructive sleep apnea (OSA) to be diagnosed and treated with continuous positive airway pressure (CPAP) therapy during the initial polysomnogram (PSG). This can be due to the demanding schedules of patients, insurance reimbursement, and sleep center waiting lists. A retrospective chart review was performed to determine if patients are more compliant when a split night protocol is implemented versus a second night CPAP titration.
Methods: We studied 32 patients (19 males) with moderate to severe OSA (baseline AHI 44.0±25.2). The patients were divided into two groups based on the study procedure performed. Group 1 (n=24) age 52.4±12.2 yrs underwent a split night study and were treated on CPAP during the initial PSG. Group 2 (n=8) age 49.5±9.7 yrs underwent a diagnostic PSG and returned to the sleep center for a full night CPAP titration. Smart Card data was downloaded and CPAP compliance was defined as >4 hours of usage on >70% of nights.
Results: Group 1 and 2 had similar findings pertaining to BMI (37.5±7.3 vs. 37.15±5.7), complaint of excessive daytime sleepiness (1.3±0.4 vs. 1.3±0.5), baseline Epworth Sleepiness Scores (10.2±4.6 vs. 11.0±6.8), lowest oxygen desaturation during the baseline (80.0%±8.1 vs. 81.6%±5.4), optimal CPAP pressure (9.8±2.9 vs. 8.8±1.8), highest attempted CPAP pressure during titration (10.3±3.0 vs. 9.3±2.1), residual AHI at optimal CPAP pressure (1.5±1.9 vs. 1.6±1.8). Group 1 and 2 had dissimilar reports of AHI (51.1±24.9 vs. 22.8±9.1) and neck circumference (15.9±1.8 vs. 14.9±0.8). There was a slight variation between groups in mallempati scores (3.2±1.0 vs. 3.4 ±7.9) and tonsil classifications (1.3±1.5 vs. 2.0±0.8). CPAP compliance was moderately higher in Group 1 (71.0%) vs. Group 2 (62.5%).
Conclusion: These results suggest an improvement in CPAP compliance when a split night protocol is implemented. A larger sample size could influence the results by correcting for the higher AHI in Group 1.

0504

PRELIMINARY VALIDATION OF A COMPREHENSIVE SLEEP APNEA DISEASE-SEVERITY INDEX

Balakrishnan K,[1] James K,[2] Weaver E[1]
(1) University of Washington, Seattle, WA, USA, (2) University of Washington & Harborview Medical Center, Seattle, WA, USA

Introduction: Apnea-hypopnea index (AHI) is the generally accepted metric of sleep apnea severity. However, AHI correlates poorly with important subjective aspects of the disorder. Previously, Piccirillo and colleagues proposed an alternate severity index combining anatomic (pharyngeal morphology), anthropomorphic (obesity), subjective (daytime sleepiness), and physiologic (AHI, lowest oxyhemoglobin saturation) aspects of sleep apnea. Scores ranged I-III (III most severe) and demonstrated a significant relationship with general health status, possibly reflecting aspects of sleep apnea beyond those for which AHI is a physiologic surrogate.
Methods: We hypothesized that index score was better associated than AHI with important patient-centered variables including sleep apnea-specific quality of life and sleep quality, as well as physiologic (intermittent hypoxia) and cardiovascular risk (arterial blood pressure, serum C-reactive protein) markers. We present here an independent cross-sectional validation of this index in new adult sleep apnea patients in the Seattle Sleep Cohort. We also present a modified system, replacing pharyngeal morphology with the more clearly defined tonsil size. Subjective, physical exam, and serum C-reactive protein data were collected at initial diagnostic polysomnography. Blood pressures and PSG variables were extracted from patient charts. Bootstrapping generated mean correlation coefficients for comparing associations, and multivariable ordinal logistic regression was used to control for potential confounders.
Results: In our first 49 subjects, severity index scores are evenly distributed (I=16, II=18, III=15). Index score correlates better than AHI with key variables, namely sleep apnea-specific quality of life and sleep quality. The "modified" index, using tonsil size, is similarly better associated with quality of life and sleep quality.
Conclusion: AHI and other individual PSG indices, quality of life, and patient experience are internally valid measures of sleep apnea, but they address different aspects of the disease. Based on our results, we suggest that the more comprehensive Sleep Apnea Severity Index may be a viable alternative measure of disease burden.
Support (optional): 1) American Academy of Otolaryngology - Head & Neck Surgery Health Services Research Grant. 2) NIH K23 - HL068849.

0505

FUNCTIONAL EFFECTS OF MANDIBULAR ADVANCEMENT ORAL APPLIANCES ON AWAKE UPPER AIRWAY PATENCY IN OBSTRUCTIVE SLEEP APNEA

Tsuiki S,[1] Ryan F,[2] Alan L,[2] Inoue Y[1]
(1) Japan Somnology Center, Neuropsychiatric Research Institute, Tokyo, Japan, (2) University of British Columbia, British Columbia, Canada

Introduction: In the narrowed upper airway of patients with obstructive sleep apnea (OSA), a neuromuscular compensatory mechanism augments the activity of the upper airway dilator muscles in defense of upper airway patency, particularly during inspiration. We hypothesized that mechanical enlargement of the upper airway by a mandibular advancement oral appliance would permit a reduction in this neuromuscular compensation during wakefulness. To test this hypothesis, we focused on changes in the cross sectional (CS) area of the upper airway before and after emplacement of a ventrally titrated oral appliance in awake OSA patients.
Methods: The CS area at the end of tidal expiration (CS area-EET) and at the nadir of intraluminal pressure during inspiration (CS area-IN) were obtained using videoendoscopy in 12 awake OSA patients.
Results: The median apnea hypopnea index decreased with mandibular advancement. Before mandibular advancement, there was no difference between CS area-EET and CS area-IN in the velopharynx, oropharynx and hypopharynx. This indicates that upper airway dilator muscle activity increased during inspiration to counteract the intraluminal negative pressure of the upper airway. After mandibular advancement, CS area-EET increased in the velopharynx, oropharynx and hypopharynx, but CS area-IN was unchanged at any level and was less than CS area-EET in the velopharynx and oropharynx.
Conclusion: These findings suggest that mandibular advancement enlarges the upper airway, and may reduce upper airway dilator muscle activity during inspiration. We conclude that oral appliances act to return the upper airway towards a normal configuration and pattern of muscle function in OSA patients.
Support (optional): This study was supported by the British Columbia Health Research Foundation and the Canadian Respiratory Health Network of Centres of Excellence (Inspiraplex) and Grants-in-Aid for Scientific Research Projects (18791581) from the Japanese Ministry of Education, Culture, Sports, Science and Technology.

0506

DISCRIMINANT VALIDITY OF SYMPTOM PROFILES FOR SLEEP DISORDER

Bailes S,[1] Baltzan M,[2] Rizzo D,[3] Fichten C,[4] Amsel R,[1] Libman E[3]
(1) McGill University, Montreal, Quebec, Canada, (2) Mount Sinai Hospital, Montreal, Montreal, Quebec, Canada, (3) Sir Mortimer B. Davis - Jewish General Hopital - Montreal, Montreal, Quebec, Canada, (4) Dawson College, Montreal, Quebec, Canada

Introduction: We previously developed a one-page, 21-item screening instrument, the Sleep Study Checklist (SSC) to identify risk for sleep disorders in primary care. The present study evaluates the discriminant validity of its four empirically derived subscales: Insomnia, Sleep Disorder, Daytime Functioning, and Psychological Distress.
Methods: Family Practice Sample: 191 older patients.
Sleep Clinic Sample: 117 consecutive patients.
Test-Retest Sample: 23 non-patient volunteers.
Medical patients were recruited in their respective waiting areas prior to their appointments. Test-retest participants were a convenience sample. Respondents rated the severity of each SSC symptom item from 0 (not at all severe) to 3 (very severe). All participants in the Family Practice Sample were offered an evaluation at a sleep clinic, including polysomnography. Of these, 145 declined further participation (Refusers), 20 began the evaluation but did not do the PSG study (Drop-Outs), and 26 completed all of the sleep clinic evaluation (Completers).
Results: Subscale scores were calculated for the Refusers, Drop-Outs, and Completers (Family Practice Sample), and for the Sleep Clinic and Test-Retest Samples. Completers and Sleep Clinic participants had similar severity ratings on SSC Insomnia, Daytime Distress, and Sleep Disorder subscales, and their scores were significantly higher than those of the Refusers, Dropouts, and Test-Retest groups.
Refusers, Dropouts and Test-Retest participants were not significantly different from each other. Cut-off scores were determined using receiver operating curves (ROC) for Completers and Sleep Clinic participants for each subscale.
Conclusion: Primary care patients who are willing to complete a sleep clinic evaluation have significantly more severe symptoms than those

who decline or drop out. Their Insomnia, Daytime Distress, and Sleep Disorder subscale scores resemble those of physician-referred sleep clinic patients. Subscales of the SSC display good discriminant validity. Cut-off scores may help identify those likely to fit a sleep clinic patient "profile".
Support (optional): Canadian Institutes of Health Research

0507

CHARACTERISTICS OF OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH HEAD AND NECK CANCER: A CASE-CONTROL STUDY

Pusalavidyasagar S, Slocumb N, Morgenthaler T, Tallent P, Silber M
Mayo Foundation for Medical Education and Research, Rochester, MN, USA

Introduction: Quality of life studies indicate that sleep is a problem for patients with head and neck cancer (HNC). Development of OSA in HNC patients could be due to mechanical obstruction of the tumor, and/or the effects of surgery or radiation. We hypothesized that OSA patients with HNC would have higher total AHI and require higher CPAP pressure than OSA patients without HNC.
Methods: We identified all HNC patients at Mayo Clinic who were subsequently diagnosed with OSA from 1980 through November 2006. Controls were all patients without HNC diagnosed with OSA in January 2004. OSA was defined as an AHI>5. Charts were reviewed and data analyzed.
Results: We identified 67 patients (mean age 61±12 years; males 89.6%). 52% received just surgical treatment, 8% radiation alone, and 40% both. We identified 124 controls (mean age 58±12 years; males 66.1 %). Ages were not significantly different but there were more men in the HNC group. HNC patients had a lower BMI compared to the controls (31.2±8.5 vs. 35.5±9.5; p=0.0008). The total AHI was higher in the HNC patients than in the controls (46±29.7 vs. 26±24.8; p<0.0001). This was true for both patients who received radiation alone or combined with surgery (45.4±32.2) and those who had surgery alone (46.6±27.6). Subjective reports of snoring, Epworth Sleepiness Scale scores and optimal CPAP pressures were comparable in both groups.
Conclusion: HNC patients with OSA have higher AHIs than controls, despite having lower BMIs. Both changes in neck anatomy from surgery, and fibrosis or edema from radiation may be responsible. The male predominance in the HNC group is probably due to the gender distribution of these cancers. Contrary to our hypothesis and in spite of their higher AHIs, the HNC patients did not require higher CPAP pressures than controls.

0508

WHAT CHARACTERIZES PATIENTS WHO ARE CPAP ADHERENT?

Sorensen J
PRO2 Respiratory Services, Lexington, KY, USA

Introduction: We assessed the factors associated with CPAP use in a clinical setting.
Methods: We retrospectively reviewed clinical data for patients who had CPAP provided by a single Home Medical Equipment company. Respiratory therapists made phone call follow-ups at 24/48 hours and 7/10 days to address problems. Data was collected from surveys and from computer cards inserted in CPAP machines at 30 days, 60days, and 6 months.
Results: In this unselected group of 109 consecutive patients (57% men, 40% smokers), 64% had verified average use of > 4 hours of use per night and average use was 6 hours at 6 months. The 3 most common benefits reported by patients were improved sleep quality (62 %), fewer trips to the bathroom at night (49 %), and more alert driving (39%). Adherence was no different for those who had in-laboratory titrations (n=23) compared with those who were empirically treated with autotitrating CPAP (n=83). Interventions at follow-up included change in mask type or fit (34%), pressure change (44%), and mode change (10%). Overall, 34, 37 and 29% chose full face, nasal pillows, or nasal masks respectively; at 6 months, use of > 4 hrs/night by mask type was 72%, 43%, and 50% respectively. Twenty one percent (23/109) discontinued CPAP treatment within the first 2 months, including 11 smokers, and 17 with AHI´s < 30/hr. Seven of these patients undertook alternative treatment with surgery (4), oral appliances (1), or weight loss (2); 3 switched to oxygen, bilevel pressue, or autotitrating CPAP. Eleven remain untreated.
Conclusion: CPAP adherence in clinical practice may be better than what is classically reported. Involvement of an RT may improve adherence. Changes in mask type and pressure are frequent. In discussing benefits of CPAP with patients, improved sleep, reduced nocturia and better driving performance should be emphasized.
Support (optional): none

0509

RELATIONSHIP OF SNORING SEVERITY TO APNEA HYPOPNEA INDEX AND EFFECTIVE CONTINUOUS POSITIVE AIRWAY PRESSURE

Chirakalwasan N,[1] Ashizawa S,[2] Hlebowicz V,[2] Appel D[2]
(1) Albert Einstein College of Medicine, Bronx, NY, USA, (2) Albert Einstein College of Medicine, NY, USA

Introduction: While snoring is ubiquitous among those with obstructive sleep apnea syndrome (OSA), Woodson and Han found little correlation between patient reported snoring intensity and OSA severity (1). Most likely, patients exaggerate the loudness of their snoring. Contrarily, we hypothesized that snoring severity, directly observed, may correlate with OSA severity and with effective continuous positive airway pressure (e-CPAP).
Methods: We reviewed 163 charts of patients from our laboratory diagnosed with OSA after they performed overnight polysomnography (NPSG) for diagnosis and NPSG- titrated e-CPAP. Based on what they heard, technicians had rated patients´snoring intensity and then we classed these patients as either mild-moderate snorers (MMS) or severe snorers (SS). We used Student´s t-test to determine significant differences among the two snoring groups for apnea hypopnea index (AHI), hypopnea index (AHI), sleep efficiency, sleep latency, baseline awake oxyhemoglobin saturation (SaO2), nadir saturation and e-CPAP.
Results: We found 72 MMS and 91 SS. Respectively, AHI and e-CPAP were significantly higher among SS (p=0.006; p=0.025). Other cited parameters did not differ significantly among the two groups.
Conclusion: Since AHI and e-CPAP differed significantly according to observed snoring intensity, snoring severity may be useful when treating those with suspected OSA; specifically, when they have long waits for (still) essential diagnostic NPSG and e-CPAP titration NPSG.
References: 1. Woodson BT, Han JK. Relationship of snoring and sleepiness as presenting symptoms in a sleep clinic population. Ann Otol Rhinol Laryngol 2005; 114(10):762-767

0510

CAN SPLIT NIGHT POLYSOMNOGRAMS BE IMPROVED BY USING AN ALGORITHM TO PREDICT THE STARTING CPAP?

McWhirter D, Bae C, Edwards R, Ioachimescu O
Cleveland Clinic Foundation, Cleveland, OH, USA

Introduction: Frequently, an optimal CPAP setting is not identified during a split night polysomnogram because of either insufficient time for the titration or a starting CPAP setting that is too low. The number of split night polysomnogram failures may be reduced if there is a better way of predicting the starting CPAP setting.
Methods: Split night polysomnogram reports between November 2004 through November 2006 at the Cleveland Clinic Sleep Disorders Center were reviewed. Patients who had to return for a full night titration study were considered split night polysomnogram failures. A previously derived and published algorithm using neck circumference, BMI, and baseline AHI predicted a starting CPAP setting. This predicted setting was compared to the starting pressure from the split study and to the prescribed pressure from the full night titration study.
Results: There were 916 split studies. Fifty studies were considered failures and followed by full night PAP titration studies. During these full night studies, 2 patients ended up on adaptive servo ventilation, 27 patients on Bilevel PAP, and 21 patients on CPAP. Of the CPAP patients, there were 18 males and 3 females. Mean age was 56±14 (mean±SD). Mean BMI was 37.9±9. Mean neck circumference was 45.0±4. Median Epworth Score was 11 (7.5-15.5 [25%, 75% quartile]). Mean starting CPAP setting in the split study was 5.0±1 and was 8.0±3 in the full night titration. Mean predicted CPAP setting was 10.1±1 and the mean final prescribed CPAP pressure was 13.2±2, resulting in a mean difference of 3.2±0.4 (R2 = 0.42), p<0.0001. One patient had a final prescribed CPAP pressure lower than the algorithm´s predicted pressure.
Conclusion: This algorithm may be helpful in predicting a starting pressure for the titration portion of split night polysomnograms. Further research with a larger sample size is necessary to validate the algorithm´s utility.
Support (optional): None.

0511

THE ROLE OF ACTIGRAPH FOR CPAP THERAPY FOLLOW-UP IN PATIENTS WITH SLEEP-DISORDERED BREATHING

Ohtake M,[1] Noda A,[2] Kojima J,[2] Nakata S,[3] Hara Y,[3] Adati Y,[2] Miyata S,[3] Koike Y[2]
(1) Nagoya University School of Health Sciences, nagoya, Japan, (2) Nagoya University School of Health Sciences, Japan, (3) Nagoya University Graduate School of Medicine, Japan

Introduction: Actigraph is an apparatus which changes body movement in an electrical signal using an acceleration sensor and record them, and it enable to evaluate the time which subjects do not notice and the wake time during sleep.The rhythm parameters and sleep/wake parameters before and on nasal continuous positive airway pressure (CPAP) therapy using actigraph have not been systematically evaluated. We have examined to determine whether actigraph might be helpful for the follow-up of patients with sleep-disordered breathing (SDB).
Methods: Eight healthy volunteers (54.1±9.9yrs, control group) and 13 SDB patients who were diagnosed SDB by standard polysomnography (51.4±13.7yrs, SDB group) enrolled in this study. Actigraphy and polysomnography were performed in all subjects. Actigraph was worn around the wrist of a non-dominant hand. The rhythm parameters and sleep/wake parameters by actigraphy; total sleep time, percent of time spent asleep (%sleep time), number of wake episodes, and activity per minute (activity score) were calculated.
Results: The number of wake episodes and activity score during sleep were significantly greater in SDB group than in control group (number of wake episodes:6.2±2.8vs14.5±6.2 ,activity score:9.9±3.1 vs 29.5±21.6 counts/min, p<0.05). On CPAP therapy night, %sleep time and total sleep time significantly were increased than on natural sleep (%sleep time:63.7±22.5 vs 76.8±26.8%, total sleep time:250.3±74.1 vs 316.5±103.5min, p<0.05). The number of wake episodes during sleep was significantly lower on CPAP therapy night than on natural sleep (17.2±9.1 vs 9.3±3.9, p<0.05).
Conclusion: The number of wake episodes during sleep and sleep time were improved with CPAP in patients with SDB. Actigraph provides an important information about the efficacy of CPAP therapy.Our findings suggest that actigraphy could be a good tool for CPAP follow-up in such patients.

0512

ASSOCIATIONS OF DIETARY INTAKE AND PHYSICAL ACTIVITY WITH SLEEP DISORDERED BREATHING

Vasquez M,[1] Goodwin J,[1] Drescher A,[2] Smith T,[2] Simon R,[3] Quan S[1]
(1) University of Arizona, Tucson, AZ, USA, (2) University of Arizona, AZ, USA, (3) St Mary Medical Center, Walla Walla, WA, USA

Introduction: Increased physical activity is associated with decreased severity of sleep disordered breathing (SDB). Furthermore, sleep deprivation is associated with alterations in dietary intake. Despite these potentially important observations, relationships among physical activity, nutrient intake, and SDB have not been well explored. Therefore, the purpose of this study is to examine these relationships in individuals with SDB.
Methods: Subjects were 156 adults with SDB (60.9% male) enrolled from the Tucson and Walla Walla sites of APPLES, a randomized, double blind sham controlled trial of the effects of CPAP on neurocognitive function. The Arizona Activity Frequency Questionnaire and a computerized dietary intake survey from the Fred Hutchinson Cancer Center were used as validated instruments to assess activity and diet at study entry.
Results: The mostly Caucasian sample (85.3%) had mean weight of 204.4 pounds and mean age of 55.6 years. 46.8% were obese and had a mean Respiratory Disturbance Index (RDI) of 43.2. Increasing RDI was associated with a progressively higher Body Mass Index (p<0.0001). In comparison to those with less SDB, the most severe subjects (RDI>75, n=28) consumed more fat (107 vs 80g, p=0.0424), total saturated fatty acids (38 vs 27g, p=0.0274), cholesterol (477 vs 288mg, p=0.0076) and protein (96.5 vs. 80.0g, p=0.0332). Furthermore, those with RDI>75 had higher levels of adjusted energy expenditure for all activity, but not for recreational activities. The most severe subjects had lower % energy expenditure for recreational activities (6.7% vs 10.3%, p=0.0376).
Conclusion: In individuals with symptomatic SDB, obesity becomes more severe as a function of increasing RDI. Those with most severe SDB are more likely to consume a diet high in fats, saturated fatty acids, cholesterol, and protein. In addition, they have higher total energy expenditure. However, their recreational activity level was lower than those with less severe SDB.
Support (optional): HL68080

0513

CO-MORBIDITIES AND CARDIAC ARRHYTHMIAS IN REM SLEEP-RELATED BREATHING DISORDERS

Mettu K,[1] Garewal M,[2] Sarwal A,[1] Sivaraman M,[1] Sahota P[2]
(1) University of Missouri-Columbia, MO, USA, (2) University of Missouri-Columbia, Columbia, MO, USA

Introduction: To determine co-morbidities and prevalence of cardiac arrhythmias in patients with REM SRBD.
Methods: Single institution retrospective chart review at an accredited sleep center. We reviewed all baseline sleep studies conducted over four month period. Heart rhythm reviewed on a single lead EKG. Arrhythmias included three or more premature contractions, sinus pauses or irregular rhythm occurring during sleep. Premature contractions included premature atrial, junctional or ventricular. REM OSA was defined as an AHI two times the total sleep time (TST) AHI and three times the NREM AHI.
Results: 256 baseline polysomnograms (PSGs) were performed over a four month time period. 34 patients met criteria (7.5%). Average BMI was 40 (range 23-56). Mean TST AHI was 8.0 (range 2.1-18.3), REM AHI was 35.0 (range 7.4-77.6) and NREM AHI was 2.7 (range 0.0-9.5). The commonest co-morbidities were: hypertension 14/34 (41%), depression 13/34 (38%), diabetes mellitus 10/34 (29%) and hyperlipidemia 10/34 (29%). 32/34 patients had sinus rhythm. 2/34 had paced rhythms. 21/34 (61%) patients had cardiac arrhythmia. 2/34 had intermittent bigeminy occurring in NREM and REM, 1/34 had clusters of sinus pauses of up to two seconds occurring in REM, 1/34 had complex ventricular ectopy in NREM and REM, 2/34 had supraventricular tachycardia in REM, and remaining patients had isolated premature contractions. Pre-existing heart disease was observed in three patients who had premature contractions and in one patient with complex ventricular ectopy.
Conclusion: Most co-morbidities observed in REM SRBD are similar to those observed in patients with non-specific SRBD with the exception of depression. The reason for the higher incidence of depression in REM SRBD compared with non-specific SRBD is uncertain. Cardiac arrhythmias may have a higher prevalence in patients with REM SRBD. Increased age and history of hypertension are associated with arrhythmia in REM SRBD but not severity of the REM AHI.
Support (optional): none

0514

CLINICAL CHARACTERISTICS AND PREVALENCE OF SUPINE-SPECIFIC SLEEP-RELATED BREATHING DISORDERS

Garewal M,[1] Mettu K,[2] Sahota P[1]
(1) University of Missouri-Columbia, Columbia, MO, USA, (2) University of Missouri-Columbia, MO, USA

Introduction: Thirty to sixty percent of patients with sleep-related breathing disorders (SRBD) are reported to have events predominantly in supine position. Patients with supine predominant SRBD have been found to be younger with lower BMI and milder disease compared to patients with position independent SRBD. We sought to determine the prevalence and clinical characteristics of patients with supine SRBD.
Methods: Single institution retrospective chart review at an accredited sleep center. We reviewed all baseline sleep studies conducted over a two-month period. We defined supine SRBD as a supine apnea-hypopnea index (AHI) two times the lateral position AHI. Total AHI was > 5 and nonsupine AHI was < 5 in all selected patients.
Results: 146 baseline polysomnograms (PSGs) were performed over two month period. 82 patients had SRBD. Supine SRBD was seen in 27/146 baseline studies (18%) and in 27/82 patients with SRBD (33%). Sixty-six percent of supine SRBD patients were female. The average age was 50 (range 30-81). Average BMI was 37 (range 23-72). Snoring (24/34) and excessive daytime fatigue (14/24) were the commonest presenting complaints. Mean TST AHI was 11.3 (range 5.3-28.0), supine AHI was 23 (range 8.7-68.7), left side AHI 0.7 (0.6-6.5), right side AHI 1.85 (0.7-4.8). The commonest co-morbidities included hyperlipidemia 11/27 (41%), hypertension 9/27 (33%), diabetes mellitus 8/27 (29%), and depression 7/27 (26%).
Conclusion: The prevalence of supine SRBD was 18% in baseline studies and 33% of all SRBD cases at our institution. There appeared to be a higher incidence in females. Higher BMI and age were associated with supine SRBD. Unlike previous reports co-morbidities present in supine SRBD were similar to those in non-positional SRBD. Patients with supine SRBD had milder disease.
Support (optional): none

0515

FACTORS AFFECTING MOUTH BREATHING DURING SLEEP

Lee W, Jung K, Kim H
Samsung Medical Center, Seoul, South Korea

Introduction: Mouth breathing during sleep can be affected by various factors including anatomical abnormalities, obesity, sleeping position et cetra, but exact cause of mouth breathing has not been identified yet.
Methods: The effects of various factors on the presence of mouth breathing in 48 consecutive patients who were suspected to have sleep disordered breathing (SDB) and had undergone polysomnography from Mar 2005 to Jun 2006 were analyzed retrospectively. Patients were catergorized into two groups, mouth breathing group and non-mouth breathing group according to the presence of mouth breathing in nasal and oral pressure transducer. Included parameters were as follows: age, BMI, neck and waist circumference, presence of retrognathia, nasal cross-sectional area, hypertrophies of tonsils and tongue base, apnea-hypopnea index (AHI), AHI in supine and lateral position, arousal index, lowest O2 desaturation level, sleep position, ratio of REM sleep, Epworth sleepiness scale and apnea level using pressure probe.
Results: Patients´ ages ($p = 0.016$), ratio of duration of sleep in supine position ($p = 0.022$) and lateral AHI ($p = 0.022$) were significantly different between the mouth breathing groups and non-mouth breathing group. No other factor including anatomical variations in upper airway, total AHI, subjective assessment of sleepiness, or obesity could reach the statistical significance.
Conclusion: old age, low lateral AHI, and preference for supine position-sleep had increased propensity for mouth breathing during sleep.

0516

EFFECTS OF WEIGHT REDUCTION PROGRAM ON SLEEP DISORDERED BREATHING IN JAPANESE

Katayose Y, Tanigawa T, Sakurai S, Yasuda K, Satoh M
University of Tsukuba Graduate School, Tsukuba, Ibaraki, Japan

Introduction: Most of the epidemiologic studies suggested that obesity is significantly associated with the onset of sleep disordered breathing (SDB) and the severity of SDB. However, to date, there is little knowledge on the effects of weight reduction program on SDB patients in Japanese.
Methods: Forty-five men (mean age 52.7) and 23 women (mean age 51.9) with mild to severe SDB were recruited among four communities in Fukushima prefecture, Japan. They completed a supervised dietary therapy program for three-months using well-balanced formula foods (Micro-Diet®). They also received one night home sleep monitoring. Respiratory disturbance index (RDI) was estimated by the flow-sensor method consisted of one channel oral and nasal airflow monitoring. The subjects received health check-ups before and after the program.
Results: After three-months intervention, significant differences on body weight, body fat percentage, neck circumference, abdominal

circumference and BMI were observed. RDI was significantly decreased from 29.3 to 18.7 in men, and from 12.0 to 9.8 in women. After intervention, 8% of the women turned to the normal range of RDI (5 or less/h).
Conclusion: Our data indicated that weight reduction program using the well-balanced formula foods (Micro Diet®is effective to weight loss and the improvement of SDB among Japanese community- based subjects.
Support (optional): Sunny Health Corporation

0517

PLASMA CYSTEINE CONCENTRATION INCREASES WITH SLEEP APNEA SEVERITY

Cintra F,[1] Poyares D,[2] D'Almeida V,[3] Calegare B,[2] Roizenblatt S,[2] Rotella L,[4] De Paola A,[2] Carvalho A,[2] Guilleminault C,[5] Tufik S[2]
(1) Univ Fed Sao Paulo, Santana de Parnaiba, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil, (3) Universidade Federal de São Paulo, São Paulo, Brazil, (4) Univ Fed Sao Paulo, Sao Paulo, Brazil, (5) Stanford University, Stanford, CA, USA

Introduction: Plasma cysteine (Cys) levels has been reported to be risk factor for coronary heart disease as homocysteine is. The role of homocysteine and cysteine in the pathophysiology of cardiovascular consequences of Obstructive Sleep Apnea (OSA) is less understood. We sought to evaluate changes in plasma Cys and homocysteine concentration and the related vitamin in patients with stratified OSA severity levels.
Methods: All OSAS patients with AHI > 6 were consecutively recruited from Sleep Disorders Ambulatory of Federal University of Sao Paulo during three-month period.
Patients were divided into three groups: mild OSA (n= 27, mean age 50.9,,b12.5), moderate OSA (n= 37, mean age 57.7,,b9.8), and severe ones (n= 51, mean age 57.7,,b11.5). Patients underwent clinical evaluation, echocardiogram, and 12-lead ECG. Blood sample were obtained in the morning, and Cys, homocysteine, Cholesterol, Uric Acid, vitamins B6, B12, E, C, folato, and many other blood parameters were analyzed. Statistics: One-way ANOVA and Chi-Square test were performed.
Results: Cys level, Vitamin B6, and Uric Acid significantly increased according to OSA severity [495.7,,b20.2; 547.4,,b16.0; 565.3,,b13.4; (p=0.02)]; [32.2,,b2.1, 34.3,,b1.9, 38.7,,b1.5; p=0.03]; [5.6,,b0.3, 5.6,,b0.2, 6.4,,b6.4; (p=0.03)], respectively. Arterial hypertension was significantly more frequent in severe OSAS patients (65.3%, p=0.01). Groups had similar BMI, age, left ventricular ejection fraction, ECG, homocysteine, and other blood parameters.
Conclusion: This is the first study assessing plasma Cys levels in patients with OSA, to our knowledge. OSA severity is associated with Cys, Uric acid, and vitamin B6 increase.
Support (optional): AFIP, FAPESP/CEPID

0518

VALIDATION OF A SELF-EFFICACY SCALE FOR CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY

Taylor Y,[1] Eliasson A,[2] Howard R,[2] Kristo D[2]
(1) Walter Reed Army Medical Center, Washington, DC, USA, (2) Walter Reed Army Medical Center, DC, USA

Introduction: Adhering to continuous positive airway pressure (CPAP) therapy is difficult for many patients. Knowledge of an individual´s level of confidence to implement CPAP (self-efficacy for CPAP therapy) may help predict CPAP adherence and allow extra attention to patients with low predicted adherence. This study aimed to validate a self-efficacy scale to use CPAP (SEC) among individuals beginning therapy for obstructive sleep apnea syndrome (OSAS).
Methods: A five-member panel of experts in sleep medicine, self-efficacy, and the management of chronic health behaviors reached 100% agreement on content validity of a 12-item instrument after two rounds of review. Consecutive patients beginning CPAP therapy completed the questionnaire at enrollment. The reliability of the SEC was estimated by the Cronbach´s coefficient alpha. CPAP adherence was measured by automated internal CPAP devices. SEC and CPAP adherence were compared using Pearson´s correlation.
Results: 114 patients with OSAS showed a high degree of self efficacy for using CPAP (SEC mean = 8.3, +/- 1.52, possible range 1 to 10). Cronbach alpha for SEC was 0.94, (M = 98.8, SD +/- 18.2) confirming internal consistency of the tool. Adherence to CPAP was 4.25 hr, +/- 2.10. There was no correlation between SEC and CPAP adherence (Pearson´s R = 0.76, p = 0.44).
Conclusion: Content validity of this measure of self-efficacy was strong. Reliability of the SEC for internal consistency was very high. However, lack of correlation between SEC and measured CPAP adherence indicates poor predictive value of the tool for adherence to CPAP in this clinical setting. We postulate that the high degree of self-efficacy in our population of military members, active and retired, does not lend itself to prediction of poor adherence. Study of the SEC in other populations may be of value.

0519

DETERMINING THE TYPE OF AIRWAY OBSTRUCTION IN OBSTRUCTIVE SLEEP APNEA WITH SLEEP VIDEOFLUOROSCOPIC IMAGING

Kim J,[1] Lee C,[1] Kong I,[2] Cha W[2]
(1) Seoul National University Bundang Hospital, Seongnam, Kyunggi-do, South Korea, (2) Seoul National University College of Medicine, Seoul, South Korea

Introduction: To determine the site of upper airway obstruction in patients with obstructive sleep apnea (OSA) and their changes during midazolam-induced sedation with sleep videofluoroscopic imaging (SVFI).
Methods: Fourty patients with OSA underwent SVFI. The obstruction site was classified as soft palate (SP), tongue base (TB) and mixed (MX) type. Before and after sedation, the length from the posterior nasal spine (PNS) to the uvula tip (UT) and the angle between nasal floor (a line from anterior nasal spine (ANS) to PNS) and uvula (PNS to UT) were measured during inspiration and expiration.
Results: The number of patients for SP, TB, MX type obstruction were 14, 9, 17, respectively. There was significant elongation of uvula from expiration to inspiration (P=0.009, Kruskal-Wallis test) in SP type obstruction after sedation. The angle difference had no significant difference between obstruction types.
Conclusion: SVFI may be useful to identify obstruction site in OSA patients. The measurement of uvula elongation could be useful in assessing the SP type of obstruction in patients with OSA.

0520

COMPARISON OF BIPOLAR AND UNIPOLAR RADIOFREQUENCY TREATMENT IN PORCRINE'S TONGUE AND PALATE

Chen G,[1] Lu X,[1] Tang Y[2]
(1) Shanghai 9th Hospital, Shanghai, China, (2) shanghai 9th hospital, Shanghai Jiaotong University, Shanghai, China

Introduction: Radiofrequency have been used to treat snoring and mild OSAS since 1997. As a new RF device, Thermocouple Feedback

Radiofrequency generates more energy in local tissue by couple of RF needles, which avoids ambustion. Compared with tranditional monopolar Temperature Controlled Radiofrequency (TCRF) changeing its energy according to temperature in local tissues, bipolar RF device's energy change with reactance in local tissues. Our study try to compare the effect of these two different RF devices acting in Procrine's tongue and palate.
Methods: 1) 6 Swine's tongue in vitro were treated by bipolar RF devices in 1W, 2W, 3W, 5W, 10W, 15W, 20W and in 10W by monopolar RF device. Histological examination and measurement is procedured instantly.
2) 8 porcrines received radiofrequency treatment in tongue and palate in 0J, 300J, 700J, 1400J. The power is set in 3W in biplor device and 10W in monopolar device. After 4 weeks, the tissues were be taken to do histological examinations. The tongue tissue are also made to standard samples to do the elasticity test.
Results: 1) Our research shows in the same power setting, energy generated by bipolar device raised more rapidly, the lesion is deeper but smaller than monopolar device.
2) When the power setted around 1:3~1:4 in bipolar and monopolar devices, they generate similar lesions in tongue in vivro.
3) In this power ratio(1:3~1:4), same energy generated by bipolar and monopolar RF devices made similar lesions in porcrine's palate and tongue in vivo. After 4 weeks, the scars formated in soft palate and tongue tissues, which repair the lesions, is similar in histological examnation. The range of the scar is similar too.
4) The scar in tongue reduce the elasticity of tongue base, which correlate to the energy in 100~700J energy. In power ratio 1:3~1:4, this effect is same in bipor and monopolar RF treatment.
Conclusion: The bipor and monopolar RF devices is different in energy generation and control. But they achieved similar effect in Porcrine's tongue and palate in vivo and vitro, when their power ratio is set in 1:3~1:4. Moreover, scar will formate 4 weeks after RF treatment, which will reduce the elasticity of tongue. This will help to explain mechanism of RF treating snoring and OSAS.

0521

INFLUENCE OF BODY MASS INDEX ON FUNCTIONAL CAPACITY IN OSAS PATIENTS

Cintra F,[1] Poyares D,[2] Rizzo C,[2] Rissi T,[2] Skomro R,[3] Montuori Neto E,[2] Vicente R,[2] De Paola A,[2] Guilleminault C,[4] Tufik S[2]
(1) Univ Fed Sao Paulo, Santana de Parnaiba, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil, (3) University of Saskatchewan, Saskatoon, Saskatchewan, Canada, (4) CA, USA

Introduction: It has been suggested a reduction in cardiopulmonary functional capacity in OSAS patients. Since obesity is a risk factor for OSA, we sought to evaluate the functional capacity of OSAS patients according to BMI.
Methods: OSAS patients with AHI > 6 were pulled from Sleep Institute, (Federal University, Sao Paulo, Brazil) database since 2000. Patients underwent cardiologic evaluation with clinical evaluation, 12-channel ECG, espirometry, and echocardiogram. Patients with pulmonary diseases and morbid obesity (BMI>40) were excluded. Cardiopulmonary test was performed according to a standard ramp protocol. The maximum Oxygen (VO2max) was obtained using analysis of expired gases during effort for each breathing cycle. Patients were then allocated into two groups: G1.BMI>27 (n=47, 30 male) and G2. BMI<27 (n=18, 13 male). Mann Whitney test was performed to analyze data.
Results: Mean age: G1= 56.0 ± 11.3; G2= 48.9 ± 15.0 (ns). There were no differences for the following parameters: AHI, arousal index, % of REM sleep, Epworth Sleepiness Scale score, blood pressure, baseline heart rate, and ejection fraction of left ventricle between groups. G1 showed lowest mean SaO2 during sleep (p = 0.006), and highest percentage of time of SaO2 bellow 90% (p=0.01). There was a significant reduction in VO2máx for group G1 (overweight) when compared to G2 (31 ± 8,5 ml/kg/min; 41 ± 11 ml/kg/min, respectively).
Conclusion: BMI negatively influenced cardiopulmonary capacity in OSAS patients.
Support (optional): AFIP, FAPESP/CEPID

0522

CARDIOVASCULAR RESPONSES TO EFFORT IN OSAS PATIENTS

Cintra F,[1] Poyares D,[2] Pulz C,[2] Rizzo C,[2] Rissi T,[2] Fujita L,[2] Skomro R,[3] Guilleminault C,[4] Vicente R,[2] Tufik S[2]
(1) Univ Fed Sao Paulo, Santana de Parnaiba, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil, (3) University of Saskatchewan, Saskatoon, Saskatchewan, Canada, (4) Stanford University, Stanford, CA, USA

Introduction: There are few studies assessing the cardiovascular responses to effort in OSAS patients.
Methods: Sixty five OSAS patients were evaluated and allocated into two groups: G1.BMI>27 (n=47, 30 male) e G2. BMI<27 (n=18, 13 male). Patients underwent clinical evaluation, espirometry, echocardiogram, espirometry, and cardiopulmonary exercise test (ramp protocol). Heart Rate (HR), Systolic and Diastolic Blood Pressure (BP) were evaluated in six occasions: baseline, maximum effort, and 1st, 2nd, 4th, and 6th minutes of recovery period. Two-way ANOVA was performed.
Results: There were significant differences for factor group for all analyzed occasions for SBP and DBP [F(1,66)=6,4,p=0,01]; [F(1,66)=7,3,p=0,008], respectively. Intercation factor was not significant.
Significant difference was detected for HR behavior between groups during the test. Interaction factor [F(5,325)=4.5, p=0.0005] and group factor [F(1,65)= 3.7, p=0.057].
Conclusion: : Being overweight influenced both, chronotropic and pressoric responses during the exercise test in OSAS patients. Overweight patients (G1) showed higher SBP and DBP before and during the test. Heart Rate did not differentiate both groups. However, overweight subjects were unable to increase their HR in the same proportion as non-overweight did.
Support (optional): AFIP, FAPESP/CEPID

0523

BLOOD GLUCOSE LEVELS AFTER ISCHEMIC STROKE IN PATIENTS WITH AND WITHOUT SLEEP APNEA

Siccoli M,[1] Bassetti C[2]
(1) Department of Neurology, University Hospital of Zurich, Zurich, Switzerland, (2) University Hospital Zürich, Zürich, Switzerland

Introduction: Sleep apnea (SA) is is well recognized as risk factor for cardiovascular morbidity and mortality, and is present in 50-70% of patients with acute ischemic stroke. Elevated blood glucose after stroke is associated with a worse outcome. The aim of our study is to investigate changes in blood glucose in patients with acute ischemic stroke and their relationship to SA severity and type.
Methods: We included 29 consecutive patients with acute ischemic stroke admitted within 96 hours after stroke onset, in which fasting blood glucose level was repeatedly assessed at day 1, 2, 3, 4, 7, and 15 after admission in the same period of time (between 6 and 10 a.m.).

Stroke severity on admission (NIH Stroke Scale, NIHSS) and stroke outcome at discharge (modified Rankin Disability Scale, mRS) were recorded. Respirography was performed in the first night and scored according to standard criteria.
Results: The mean age was 62±12 [25-83], 75 (66%) were male. NIHSS on admission was 7±5 [0-21], mRS at discharge (11±6 days after admission) was 1.7±1.4 [0-5]. Blood glucose on admission was 7.4±2.9 [4.1-19.9], and 6.4±2.0 [4.6-11.1] at day seven. We found a significant correlation between glucose at day seven and apnea-hypopnea-index (p=0.002, r=0.622), central apnea-index (p=0.009, r=0.556), and oxygen desaturation-index (p<0.0001, r=0.751) independent of cardiovascular risk factors, age, and body-mass-index. Glucose at day seven correlated with stroke severity on admission (p=0.004, r=0.607) and with functional disability at discharge (p=0.017, r=0.528).
Conclusion: Glucose level at day seven after ischemic stroke is an independent predictor of stroke severity and outcome, and is associated with severity of SA, central apneas, and oxygen desaturations. Further studies are needed to test the hypothesis that these findings may reflect an increased sympathetic activity possibly related to sleep apnea.

0524

BODY SWAY AND RESPIRATION DURING SLEEP: A PRELIMINARY STUDY

Azevedo E, Moraes W, Poyares D, Tufik S
Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil

Introduction: The respiratory-related movements of the chest wall that can be detected and monitored. Different studies described that a substantial proportion of body sway result from respiratory activity although this phenomenon was not studied during sleep.
Methods: Ten healthy volunteers, 5 males 5 females, age ranging from 20-30yrs, body mass index 20-25, with no sleep complaints were included. Body sway was measured by two load cells (upper and lower) supporting a wooden platform underneath a mattress. Load-cell signals were recorded by a polysomnography system in an extra channel associated to the 16-channel routine recording. Overnight recordings were carried out in all 10 subjects.
Results: Recordings indicated a strong correlation between body sway measured by load cells and respiratory cycle measured by airflow, thoracic and abdominal movements (r=0.87; p<0.01). Load cell recordings varied in opposite phases indicating a shift in gravitational center related to respiration. Body sway amplitude was significantly reduced during slow wave sleep compared to stages 1, 2 and REM (p<0.01).
Conclusion: Body sway associated to respiration was universally present in normal subjects during sleep, seeming to vary according to sleep state. Future research is needed to clarify the utility of the present method.
Support (optional): AFIP, FAPESP/CEPID

0525

AN INTERIM ANALYSIS OF THE IMPACT OF CPAP COMPLIANCE ON ECHOCARDIOGRAPHY AND SERUM MARKERS IN OBSTRUCTIVE SLEEP APNEA SYNDROME

Roy J,[1] Dincer E,[2] Gupta N,[2] Pajewski N,[2] Thielke R,[2] Woods T,[2] Soto F,[2] Franco R[2]
(1) Medical College of Wisconsin, Brookfield, WI, USA, (2) Medical College of Wisconsin, Milwaukee, WI, USA

Introduction: Obstructive Sleep Apnea Syndrome (OSAS) can impair ventricular function and can elevate serum inflammatory markers. Therapy with Continuous Positive Airway Pressure improves cardiopulmonary hemodynamics. Serum markers such as brain natriuretic peptide (BNP) corrected for BMI, highly sensitive C-reactive protein (hCRP), uric acid, and leptin have been shown to be abnormal in OSAS patients and improve with CPAP therapy. At this time, there is no direct correlation of serum markers and echocardiographic improvements with CPAP use.
Methods: 21 men and 13 women aged 58.2 +/- 31.6 years of age, with a body mass index of 36.3 +/- 9.2, and moderate to severe OSAS (AHI 49.9 +/- 11.4) underwent transthoracic echocardiograms (TTE), blood draws, and completed sleep questionnaires prior to and three months after CPAP therapy initiation. Optimal CPAP pressure was considered the pressure at which the residual AHI<10. CPAP compliance was measured by machine download.
Results: 28 patients on CPAP therapy were analyzed. Six patients were unavailable for follow up testing. Epworth Sleepiness Scale (ESS) (score difference: -2.8 +/- 1.0; p<0.05) and intraventricular septal diameter (IVSD) (diameter diff: -0.3 +/- 0.1cm; p<0.05) by TTE improved after 3 months. Average nightly CPAP usage was 5.2 +/- 2.2 hours. 22 patients were compliant with CPAP (>4 hours/night). There was no additional benefit in ESS or IVSD if patients wore CPAP for more than 4 hours/night (p>0.05). There was no significant change in serum levels of BNP, hCRP, uric acid, and leptin, regardless of CPAP compliance (p>0.05). 6 patients non-compliant with CPAP therapy (<4 hours/night) had no significant change in ESS, IVSD, or serum levels (p>0.05).
Conclusion: In patients with moderate to severe OSAS, compliant CPAP use resulted in a statistically significant difference in IVSD and ESS. However, compliant CPAP use did not improve in serum marker levels.

0526

USE OF CPAP EXHALATION COMFORT FEATURES RESULTS IN IMPROVED SLEEP RELATED QUALITY OF LIFE SCORES

Decker M,[1] Stevens R,[2] Messenger R[3]
(1) Emory University, Atlanta, GA, USA, (2) Remedy Sleep Center, Avon Lake, OH, USA, (3) Invacare Corporation, North Ridgeville, OH, USA

Introduction: Continuous positive airway pressure (CPAP) delivered via mask is the primary treatment for sleep disordered breathing. Long term adherence to CPAP is estimated to be less than 70% of all patients prescribed this therapy. Reasons include mask discomfort and an inability to exhale against positive airway pressure. Technology enabling relief in CPAP pressure occurring during the patient´s expiratory phase, commonly known as expiratory unloading, has recently been introduced into CPAP machines. Expiratory unloading putatively facilitates increased nightly use of CPAP. However, it remains unclear whether daytime hypersomnolence and quality of life are improved in those patients using expiratory unloading CPAP devices. Thus, we sought to determine whether CPAP devices utilizing expiratory unloading are associated with improved quality of life.
Methods: Ten consecutive CPAP naive patients requiring pressures of 10 cmH2O or more were followed. Patients completed the SF-36 and Epworth Sleepiness Scale both prior to initiation of CPAP and then again after 30 days of treatment. All unloading therapy was delivered via SoftX technology (PolarisEX CPAP, Invacare, Elyria, OH).
Results: Following 30 days of treatment, SF-36 post treatment scores were significantly improved in the following domains; physical functioning (from 79 to 85, p=0.002), physical role functioning (from 68 to 85, p=0.008), energy/fatigue (from 77 to 90, p=0.052), emotional well-being (from 42 to 62, p <0.001) and social functioning (from 67 to

76, p<0.0001). The mean pre treatment Epworth score of 13 was significantly reduced to a post treatment value of 9 (p=0.004).
Conclusion: In this patient sample, nightly use of CPAP devices employing exhalation unloading was associated with improved quality of life and reduced levels of daytime hypersomnolence. Future studies are now required to determine if these outcomes are comparable to, or exceed, the same quality of life measures obtained from patients receiving CPAP from devices employing fixed pressure.

0527

MODAFINIL IMPROVES BEHAVIORAL ALERTNESS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA WHO REMAIN SLEEPY ON NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE

Dinges D,[1] Hirshkowitz M,[2] Sangal R,[3] Bogan R[4]
(1) University of Pennsylvania School of Medicine, Division of Sleep and Chronobiology, Philadelphia, PA, USA, (2) Baylor College of Medicine, Houston, TX, USA, (3) Beaumont Hospital, Clinical Neurophysiology Services, PC, Troy, MI, USA, (4) SleepMed, Inc., Columbia, SC, USA

Introduction: Modafinil is a wake-promoting agent that significantly improves wakefulness in patients with residual excessive sleepiness (ES) who are otherwise effectively treated with nasal continuous positive airway pressure (nCPAP) for obstructive sleep apnea (OSA). This analysis focuses on the effects of modafinil on behavioral alertness.
Methods: This was a multicenter, double-blind, placebo-controlled, randomized clinical study. Patients with OSA treated with nCPAP therapy who had residual excessive sleepiness were randomized to receive modafinil 200 or 400 mg or placebo once daily for 12 weeks. Four 10-minute Psychomotor Vigilance Test (PVT) sessions were conducted to assess reaction time (RT), the ability to sustain attention (mean number of lapses), and wake state instability (mean standard deviation of corrected RTs). Data were pooled for both doses. Adverse events were monitored.
Results: At final visit, modafinil significantly improved the PVT variables compared with placebo. The mean change from baseline in median reaction time was –14.1 vs +1.3 msec for the modafinil and placebo groups, respectively (P <.0001). Modafinil significantly improved the slowest reaction time, with a mean change from baseline of –246.7 msec vs +294.9 msec for placebo (P<.0001). Change in the mean number of lapses was also significantly improved with modafinil compared with placebo (–1.8 vs 0.2; P<.001). Wake state instability declined –30.4 in the modafinil group compared with an increase of +45.6 in the placebo group (P<.0001). The most common adverse events reported in the modafinil and placebo groups were headache (26% vs 12%), infection (14% vs 21%), and nausea (11% vs 2%).
Conclusion: Modafinil improves behavioral alertness, as evident in sustained attention performance, and it reduced wake state instability in nCPAP-treated patients with OSA and residual ES. Modafinil was well tolerated in these patients.
Support (optional): Cephalon, Inc.

0528

DOES PATIENT´S INITIAL EVALUATION PREDICT A CHANGE IN OPTIMAL PRESSURE ON CPAP RETITRATION?

Anand V,[1] Verma N[2]
(1) All India Institute of Medical Sciences, Warren, MI, USA, (2) B.G. Tricounty Neurology and Sleep Clinic, Warren, MI, USA

Introduction: Only vindication of a nasal CPAP retitration procedure will be an actual change in the optimal CPAP pressure after that test. The purpose of this study was to identify any items in patient characteristics, clinical features and initial CPAP titration as predictors of change in optimal pressure on CPAP retitration.
Methods: 46 patients with OSA were divided in 2 groups: Group I (optimal pressure was changed on CPAP retitration) : N=30, M 22 and F 8, age 31-72 yrs , BMI 26-50 Kg/m 2, neck size 15-20", tonsillectomy in 8 , narrow oropharynx in 15, UP3 in 2, abnormal chin in 3, deviated nasal septum (DNS) and prior nose surgery in 1 each, initial CPAP pressure 6-19 cm, sleep efficiency 65-98%, REM latency 0-304 minutes and residual AHI 0-23/hour . Group II (optimal pressure unchanged after CPAP retitration): N=16, M 11 and 5 F, age 32-69, BMI 23-62 Kg/m2 , neck size 14.5-20 ", tonsillectomy in 6, narrow oropharynx in 5, abnormal chin in 4, corrective nasal surgery in 2, DNS in 1, initial CPAP pressure 8-13 cm of H2 O, sleep efficiency 69-95%, REM latency 0-270 minutes and residual AHI 0-19/ hour. The statistical analyses were performed using the t test.
Results: Patient characteristics (age, gender, neck size, and BMI), clinical features (tonsillar status, oropharyngeal narrowing, chin abnormality, DNS/ nasal surgery or UP3) or initial CPAP titration (sleep efficiency, REM latency, residual AHI and initial CPAP pressure) did not differ significantly between the 2 groups (p=0.22-0.99).
Conclusion: Patient characteristics, clinical features or variables on initial CPAP titration do not predict a change in optimal pressure on CPAP retitration. The results suggest that weight change, patient´s subjective feeling of pressure being too high or insufficient, residual or recurrent daytime sleepiness, post-operative evaluation after palliative UP3, and annual retitrations in high risk occupations (e.g. truck driver or pilot) are the best current clinical guidelines for CPAP retitration.

0529

CORRELATION BETWEEN CPAP PRESSURE AND CEPHALOMETRIC ANALYSIS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME

Takai Y,[1] Yamashiro Y,[2] Sato D,[3] Kusano E,[3] Sugino K,[3] Isobe K,[3] Hamanaka N,[3] Kimura K,[3] Homma S[3]
(1) Toho University School of Medicine, Tokyo, Japan, (2) Ota memorial sleep center, Japan, (3) Toho University School of Medicine, Japan

Introduction: The therapeutic efficacy of continuous positive airway pressure (CPAP) in treating patients with obstructive sleep apnea hypopnea syndrome (OSAHS) has been established. The effective CPAP pressure is usually determined by CPAP titration. However, there is little literature concerning its correlation with the morphology of the face and the jaw. This study was aimed to clarify the correlation between CPAP pressure and the morphology of the face and the jaw by cephalometric analysis to estimate the pressure before treatment.
Methods: Subjects were 50 male patients diagnosed having OSAHS by polysomnography. Mean age was 45.2 years (range, 21-75 years), and mean BMI was 27.6 ± 5.6 kg/m2. Cephalometry was conducted in upright and supine position. As indices of craniofacial skeletal morphology, following values were measured; SNA , SNB, NSBa, and facial axis. In order to examine morphological features of upper airway and to obtain indices characterizing soft tissue morphology, also we measured the followings; MP-H, the length of soft palate, lower pharynx, the length of upper airway, the area of pharyngeal airway, the area of tongue, the area and excessive volume of soft palate.
Results: Correlations were found between CPAP pressure and the area of soft palate, the excessive volume of soft palate, and MP-H in both upright position and supine position. For the prediction of the CPAP pressure, it was the most appropriate to use BMI, MP-H, and the excessive volume of soft palate in supine position, and to use AHI, BMI,

MP-H, and the excessive volume of the soft palate in upright position.
Conclusion: This study suggests that the evaluation of the amount of fat tissue beneath submaxilla and the morphology of soft palate may be useful to estimate CPAP pressure in patients with OSAHS.

0530

NOCTURIA AND SLEEP-DISORDERED BREATHING IN THE SLEEP HEART HEALTH COHORT

Parthasarathy S,[1] Fitzgerald M,[2] Goodwin J,[3] Budhiraja R,[3] Resnick H,[4] Quan S[5]
(1) United States Department of Veterans Affairs, Tucson, AZ, USA, (2) Loyola University of Chicago, IL, USA, (3) University of Arizona, AZ, USA, (4) DC, USA, (5) University of Arizona, Tucson, AZ, USA

Introduction: Nocturia has been independently associated with falls and all-cause mortality in large cohort studies. A comprehensive and systematic study of the association between nocturia and sleep-disordered breathing has not been performed in a large sample.
Methods: We set out to determine whether nocturia is independently associated with sleep-disordered breathing. In order to achieve this objective we analyzed data from the first exam of the Sleep Heart Health Study cohort.
Results: In 6342 participants (age 63 ± 11 [SD] years, 53% women), 3625 (57.2%) reported frequenting the bathroom often – at least 5 to 15 occasions per month or more – which we considered to be a significant level of nocturia. Univariate logistic regression identified the following covariates for the presence of nocturia: greater age, higher body mass index, more alcoholic drinks consumed per day, lower forced expiratory volume in one second, more cups of coffee per day, and the presence of sleep-disordered breathing (SDB) based on a thresholds of 5, 10, or 15 events per hour for the respiratory disturbance index (RDI; $p < 0.05$). Multiple logistic regression, with nocturia as the dependent variable, revealed that greater age (OR 1.03; 95%CI, 1.02-1.03), higher body mass index (OR 1.02; 95%CI, 1.02-1.03), more alcoholic drinks per day (1.01; 95%CI, 1.00-1.01), and the presence of SDB based upon overall RDI greater than 15 per hour (4% desaturation)(OR 1.28; 95%CI, 1.11-1.49) were independently associated with the presence of nocturia. In this cohort, history of diabetes mellitus or diuretic intake was not independently associated with nocturia. Multinomial or linear regression techniques did not change these results significantly.
Conclusion: In conclusion, nocturia is independently associated with sleep-disordered breathing.
Support (optional): HL53938

0531

COMPLEX SLEEP APNEA SYNDROME MAY PERSIST ON TREATMENT WITH CONTINUOUS POSITIVE AIRWAY PRESSURE

Kuzniar T,[1] Morgenthaler T[2]
(1) Division of Pulmonary and Critical Care Medicine, Evanston Northwestern Healthcare, Evanston, IL, USA, (2) Mayo Clinic, Rochester, MN, USA

Introduction: Patients with complex sleep apnea syndrome (CompSAS) have obstructive sleep apnea but develop troublesome central sleep apnea activity or Cheyne-Stokes breathing when provided continuous positive airway pressure (CPAP) therapy. We examined whether CompSAS activity persists with long-term treatment with CPAP.
Methods: We retrospectively analyzed all consecutive polysomnograms (PSGs) performed at our Sleep Disorders Center between 2003-2005. Among patients who had two PSGs in this period, we identified those who had CompSAS on the first PSG, followed by another PSG at least 1 month later. Initial PSG variables were compared with the PSG variables during the follow-up therapeutic study. Mann-Whitney U test and Fisher´s exact test, as appropriate, were used for comparisons.
Results: Of 200 patients who had two PSGs, 13 patients (11M, 2F) aged 65 (56 - 71, median, interquartile range) had CompSAS on their first therapeutic PSG with a residual AHI of 26 (23 - 40). Most follow-up PSGs were ordered after an abnormal result of overnight oximetry on CPAP, or due to CPAP intolerance. On the repeat therapeutic PSG performed after 195 (49 – 562) days, the AHI had decreased in all but one patient to 7 (3 – 21.5). However, only 7 patients reached AHI<10 ("CPAP responders"), and 6 had AHI 10 ("CPAP non-responders") on repeat testing. "CPAP non-responders" had a higher initial sleepiness (Epworth Score 13 (12.5 - 14) vs 9 (6 - 9.5), p=0.03), and a trend towards lower BMI (29.7 (28.6 - 31.6) vs 34.3 (32.5 - 35.1), p=0.06) than "CPAP responders". Both groups were equally compliant with CPAP therapy.
Conclusion: Although the AHI tends to improve over time in CompSAS patients treated with CPAP, in this retrospective study nearly half maintained a persistently elevated AHI. A prospective trial is merited to determine the optimal treatment for these patients.
Support (optional): Mayo Clinic Foundation

0532

DAYTIME DRIVING PERFORMANCE AND SLEEPINESS IN OSAS PATIENTS

Pizza F,[1] Contardi S,[2] Mondini S,[3] Ferlisi M,[4] Cirignotta F[1]
(1) University of Bologna, Bologna, Italy, (2) University of Bologna, AE (Europe), (3) Italy, (4) University of Bologna, Bologna, AE (Europe), Italy

Introduction: Sleepiness and accidents are common in OSAS patients. Even if the increased risk of road traffic accidents is associated with disease severity and excessive daytime sleepiness, none of the common OSAS markers can detect patients at higher risk of having a crash.
Methods: We studied 30 OSAS patients with subjective (subjective sleepiness scales) and objective (Multiple Sleep Latency Test, MSLT) sleepiness measurements, associated with driving simulation test (DST), previously validated in young healthy subjects. The results of the different tests were compared between them and with the history of previous accidents and sleepiness at the wheel to establish the relations between sleepiness, simulated driving performance and accident risk. Statistical analysis included Oneway ANOVA, Wilcoxon signed rank test, Pearson´s correlations and receiver operating characteristic (ROC) curves to assess the ability of the driving simulation task to distinguish subjects with objective excessive daytime sleepiness.
Results: Subjective and objective sleepiness measurements were significantly correlated with driving performance on the simulator. The most significant correlates of sleepiness were the measures of the primary vehicle control task on the simulator: lane position variability, number of crashes and time from the beginning of the test to the first crash. The comparison of DST and MSLT results suggested our driving simulated approach could be used to evaluate performance decrements associated with sleepiness in the clinical setting of OSAS patients. None of the sleepiness and performance results was significantly associated with previously reported road traffic accidents.
Conclusion: Our DST is a suitable objective tool to detect sleepiness in OSAS patients, and could be useful in the clinical setting of sleep medicine and research. Further studies will establish whether the DST has a predictive value with respect to real driving.
Support (optional): RFO funds of the University of Bologna.

0533

THE IMPACT OF COMPLAINTS AND SLEEP DISORDERS IN THE QUALITY OF LIFE

Mello M, Esteves A, Lopes C, Tufik S
Univ Fed Sao Paulo, Sao Paulo, Brazil

Introduction: The quality of sleep is intrinsically linked to quality of life. For some patients, the improvement of sleep and consequently of its quality of life is the main reason of tack to the treatments for riots of sleep. Of this form, the objective of the study was to evaluate the complaint impact foresaw of riots related to sleep in the quality of life.
Methods: We evaluated 2304 patients with complaints of sleep, being 1610 (69,88%) of masculine and 694 (30,12%) of the feminine. The patients who set appointments for polissomnograph were guided for fulfilling of questionnaires of Standard of Sleep, Sleepiness Scale of Epworth and the MOS-Quality of Life SF-36.
Results: The results showed 1611 (79,20%) patient with apnea, being 1272 of masculine and 339 of the feminine. The results showed 1611 (79,20%) patients with sleep apnea, 1272 man and 339 woman, been 631 (39%) with light apnea, 447 (27%) with moderate apnea 534 (34%) with severe apnea. Also a reduction was presented in props up them of quality of life in patients who had only presented the complaint of the riot of sleep.
Conclusion: It had a reduction in all the dominions of the SF-36 in the patients who had presented scores in the questionnaire of Sleepiness (Epworth>10), since vitality 43,89 ±22,56 followed of mental health 60,29 ±20,53 had more presented an accented reduction. The results gotten in the present study had demonstrated a reduction in the quality of life in a population of individuals that present complaints and riots of sleep. Our results demonstrate that the simple complaint of sleep already significantly modifies the perception of its quality of life.
Support (optional): AFIP, FAPESP (CEPID), CEPE, FADA, CNPQ.

0534

EFFECTS OF OBSTRUCTIVE SLEEP APNEAS ON COGNITIVE FUNCTIONS: A COMPARISON BETWEEN YOUNGER AND OLDER OSAS PATIENTS

Mathieu A,[1] Mazza S,[2] DéCary A,[2] Massicotte-Marquez J,[3] Petit D,[2] Gosselin N,[4] Malo J,[2] Montplaisir J[1]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) Sleep Research Society, Montreal, Quebec, Canada, (3) Montreal, Quebec, Canada, (4) Sleep Research Society, Montreal, Canada

Introduction: Patients with obstructive sleep apnea syndrome (OSAS) present cognitive deficits similar to those observed with aging. The aim of the study was to assess the effects of age on cognitive functions in OSAS patients. It was hypothesized that older OSAS patients will exhibit significant cognitive dysfunction relative to younger OSAS patients and controls.
Methods: Younger and older OSAS patients were compared to younger and older control subjects (age cut-off set at 50 years). Participants underwent a PSG and neuropsychological evaluation. Variables were analyzed by two-way analyses of variance (ANOVAs) with 2 factors: Group (control and OSAS) and Age (younger and older). Additionally, we evaluated the contribution of attentional deficits to cognitive dysfunction for each sub-group of patients by using Spearman correlation coefficients.
Results: Younger OSAS patients were aged between 24-50 years and older patients between 53-74 years and younger controls between 25-50 years and older controls between 53-76 years. No Group by Age interaction was found for any neuropsychological variable. However, for vigilance and attentional testing, main Group ($28.3 > F > 4.5 = 0.4 > p > 0.000002$) and Age ($15.1 > F > 4.3 = 0.04 > p > 0.001$) effects were found. Similarly, memory (including short-term, long-term and procedural) and executive functions (only similarity sub-test for OSAS patients was significant), indicated main Group ($10.2 > F > 4.7 = 0.04 > p > 0.002$) and Age ($13.0 > F > 4.0 = 0.05 > p > 0.0008$) effects. Correlations indicated that attentional deficits contributed importantly to a poorer cognitive performance in younger OSAS patients only ($0.756 > r > 0.637 = 0.002 > p > 0.01$).
Conclusion: Our results are in agreement with those of the literature for both OSAS-related and aging-related cognitive deficits but shows that age can add to the effect of the OSAS condition to worsen cognitive deficits.

0535

PREFERRED TIDAL VOLUME SETTING FOR NON-INVASIVE VENTILATION IS DIFFERENT FOR SLEEP AND WAKEFULNESS

Parthasarathy S,[1] Lowman X,[2] Kuo M,[2] Quan S[3]
(1) United States Department of Veterans Affairs, Tucson, AZ, USA, (2) University of Arizona, AZ, USA, (3) University of Arizona, Tucson, AZ, USA

Introduction: In patients requiring non-invasive ventilation at home, selection of the tidal volume (Vt) setting for either volume-control or volume-assured pressure support modes is unclear. We set out to determine the preferred Vt for non-invasive ventilation with volume assured pressure support.
Methods: We performed a prospective study wherein 24 patients were assigned to recive two 30-minute periods of different Vt settings in random order: 8 ml/kg ideal body weight (IBW) and 110% of the average Vt that was determined over a separate 30-minute period of EEG-documented calm wakefulness. At the end of each 30-minute period, patients rated their preference of Vt on the modified Borg dyspnea scale. Subsequently, sleep was objectively measured by overnight polysomnography. During polysomnography, patients were assigned to the target Vt they preferred -- either 8 ml/Kg IBW or 110% of the average Vt determined during calm wakefulness.
Results: Tidal volume during calm wakefulness demonstrated large variability between patients (7.3 ± 1.8 ml/Kg IBW; range 4.4 to 11.4 ml/Kg IBW; n=24). During wakefulness, dyspnea scores tended to be lower in patients while receiving 110% of resting Vt than while receiving 8 ml/Kg IBW (P=0.1; n=24). However, sleep efficiency during polysomnography was lower in patients receiving 110% of resting Vt (78 ± 15%; n=14) than Vt set at 8 ml/Kg IBW (89 ± 6%; n=10; P=0.03). Apnea-hypopnea index was not different for the two Vt settings (P=0.2; n=24).
Conclusion: In patients requiring volume-assured pressure support, tidal volume preference during wakefulness does not predict the tidal volume preferred during sleep.
Support (optional): Respironics, Inc

0536

ASSOCIATION OF PHASIC REM SLEEP AND TONIC REM SLEEP IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

Lahey M, Goldstein D, Friedman N
Sleep Disorders Center of New Jersey, Scotch Plains, NJ, USA

Introduction: It has been reported that sleep disordered breathing is more prevalent in phasic REM sleep (PREM) than in tonic REM sleep (TREM.) Hypotheses for this finding have included bursts of phasic activity in REM resulting in a further decrease in EMG activity. REM is a heterogeneous stage of sleep with differing activity occurring during

the tonic and phasic periods. The purpose of this study was to determine the relationship of phasic REM in initiating an apnea or hypopnea. Does the amount of phasic activity and its timing during a respiratory event affect the overall AHI?
Methods: Patients in the study with suspected OSA were referred from their primary physician to the sleep disorders center for the purposes of a sleep evaluation. A complete sleep history was obtained. A full nocturnal polysomnogram was performed on all patients using a standard 16-channel montage. Patients included in the study had an apnea-hypopnea index greater that 40 episodes per hour and were required to have a REM AHI greater than non-REM AHI. Patients selected also were required to have had at least 20% REM of TST. The NPSG was scored using standard protocol. The REM periods were then rescored twice. The first scoring defined a PREM respiratory event as one containing any phasic activity (P-ANY). The PSG was subsequently rescored counting an event as a Phasic Initiated Event (PIE) if a phasic burst of activity occurred either within two seconds preceding a respiratory event or in the first two seconds of the respiratory event.
Results: The following table lists how the breakdown of REM AHI is affected by how we define a phasic vs. tonic respiratory event. PREM% is the percentage of the REM AHI that is comprised of phasic events and TREM% is the percentage of the REM AHI that consists of tonic events.

EVENTS	P-ANY	PIE
PREM %	78	11
TREM %	22	89

Conclusion: The vast majority of episodes of sleep disordered breathing in our patients were not associated with phasic initiated events. Therefore, the study was unable to substantiate phasic bursts as initiating apneas or hypopneas. There was a very high percentage of respiratory events that contained at least 1 phasic burst, the significance of which needs to be better defined in future investigations.

0537

WOMEN AND SLEEP-DISORDERED BREATHING

Tantrakul V, Won C, Guilleminault C
Stanford University, Stanford, CA, USA

Introduction: We questioned the clinical presentation of women, 18 to 55 years, referred to sleep clinic for suspicion of sleep-disordered breathing (SDB).
Methods: Systematic compilation of clinical presentation and polysomnography (PSG) were done. Comparison between premenopausal and menopausal women was also performed.
Results: 251 women (40.8 ± 9.89 years) were seen, which included 178 premenopausal (36.9 ± 8.8 years) and 73 menopausal (50.5 ± 3.9 years) women. They consulted for complaints of decrease of alertness and daytime fatigue. Between premenopausal and menopausal women, there was no significant difference in daytime sleepiness (89% vs. 88.6%), and Epworth Sleepiness Scale (11.16 vs. 10.0). Reports of sleep-onset insomnia (32.8% vs. 36.1%), sleep maintenance insomnia (18.4% vs. 19.4%), myalgia (7% vs. 10.3%), fibromyalgia (5.8% vs. 7.4%) were similar. Premenopausal women complained significantly more of daytime fatigue (64.4% vs. 50%, p=0.04); postmenopausal women complained significantly more of depression (40.4% vs. 60.9%, p=0.004) and anxiety (18.3% vs. 23.2%, p=0.034). The body mass index was similar in both groups (28.0 ± 8.9 vs. 29.9 ± 9.1). But the apnea-hypopnea index (AHI) were significantly less in premenopausal women (22.5 ± 28.7 vs. 31.06 ± 27.5, p=0.042) as was the respiratory disturbance index (RDI) (23.4 ± 27.9 vs. 32.7 ± 26.7, p=0.017).
Conclusion: Referred women with SDB are still predominantly overweight, and complain predominantly of excessive daytime sleepiness. But insomnia and fatigue complaints are also common reports. Menopausal women have more anxiety and depression. Premenopausal women, despite many similar complaints to menopausal women, have much lower AHI and RDI on PSG. Premenopausal women have less pathological PSG findings but complaints of equal severity as those reported by post-menopausal women.

0538

ALTERNATIVE MANAGEMENT STRATEGIES FOR SLEEP APNEA IMPROVE ACCESS TO CARE IN VETERANS

Hannah C,[1] Imran A,[2] Budhiraja R,[2] Quan S,[3] Parthasarathy S[1]
(1) United States Department of Veterans Affairs, Tucson, AZ, USA, (2) University of Arizona, AZ, USA, (3) University of Arizona, Tucson, AZ, USA

Introduction: Long wait times for sleep evaluation have been suggested in veterans. To shorten wait times, alternative management (AM) strategies – screening pulseoximetry and automatic-positive airway pressure (APAP) therapy – have been performed in the hospital and in the home settings. However, whether such strategies improve access to care within the Veterans Healthcare System is unknown. We studied whether AM strategies (home- or hospital-based) in veterans with possible OSA can decrease wait times when compared to conventional management (CM; overnight polysomnography).
Methods: Veterans with high probability for OSA – presence of witnessed apneas, Epworth sleepiness score > 10, and desaturation index by overnight pulseoximetry > 5 per hour – underwent either hospital- or home-based APAP therapy. Veterans who did not meet all 3 of the above-mentioned criteria, or who failed APAP therapy, underwent overnight polysomnography. In a separate validation data set of 215 veterans, we found a positive predictive value of these 3 criteria to be 100% for diagnosing OSA.
Results: Of 187 consecutive male veterans (age 59 ± 10 [SD] years) referred for possible OSA, 153 patients were eligible for AM strategy. The wait times between referral and initiation of PAP therapy was different among the 3 groups of patients: median of 245 days (interquartile range [IQR] 142, 311) for CM, 164 days (IQR 97, 303) for hospital-based AM strategy, and 161 days (IQR 98, 229) for home-based AM strategy (Kruskal-Wallis test; P=0.009). Drop-out rates from the management protocol were greatest for hospital-based AM strategy with 31 (47%) of 66, and least for home-based AM and CM strategies (8 and 9%, respectively)(Chi square, P<0.0001).
Conclusion: Alternative management strategy without full polysomnography in veterans with possible OSA was associated with more rapid initiation of PAP therapy.
Support (optional): SAVAHCS Research Award

0539

AROUSALS DURING SLEEP AND THE LEVEL OF DEPRESSION PREDICT NEUROPSYCHOLOGICAL DEFICIT IN OBESE APNEA PATIENTS

Valencia-Flores M,[1] Resendiz M,[2] Juarez S,[3] CastañO A,[1] Santiago V,[1] Garcia E,[1] Aguilar C,[1] Ostrosky F[4]
(1) Instituto Nacional de Ciencias Medicas y Nutrición Salvador Zubirán, Mexico, D.F., Mexico, (2) Instituto Nacional de Ciencias Medicas y Nutrición Salvador Zubiran, México, D.F., Mexico, (3) Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico, D.F., Mexico, (4) Universidad Nacional Autonoma de Mexico, Mexico, D.F., Mexico

Introduction: The neuropsychological deficits of obstructive sleep

apnea syndrome (OSAS) are
often attributed to the rate of respiratory disturbance. However, sleep disordered breathing is not the only factor that might account for waking deficits in obese patients with OSAS.
Methods: Eighty-five obese patients (BMI = 51.4±11.2) with OSAS (IAH=41.0±36.3) were evaluated by a standardized neuropsychological test "Neuropsi" (validated for the Mexican population). After two nights of polysomnographic recording the MSLT was performed and patients completed Beck Depression Inventory (BDI). Odds ratios (ORs) and 95% confidence intervals (CIs) were obtained from multiple logistic regression models to evaluate the association between neuropsychological deficits and risk factors.
Results: Neuropsychological evaluation showed that15.3% of the sample had no cognitive deficit despite the presence of SAOS (IAH=37.2±30.7), the rest of the sample had cognitive deficit in attention and memory functions (IAH=34.02±37.3). Level of sleepiness did not differed between the groups: group without cognitive deficit (mean MSLT 5.5±3.1) and group with cognitive deficit (mean MSLT 5.2±3.7). Multiple logistic regression model allowed to determine that total number of arousals (OR=1.2, CIs 1.02-1.2) and BDI Score (OR=1.1, CIs 1.02-1.20) were the main independent predictors of neuropsychological deficits.
Conclusion: Total number of arousals during sleep and depression level are predictors of cognitive deficit in obese apnea patiens.
Support (optional): This work was supported by CONACYT-46257/H

0540

OBJECTIVE CPAP COMPLIANCE IN THE OLDER ADULT POPULATION

Doerr C,[1] Mcleland J,[1] Kampelman J,[2] Boero J,[2] Duntley S[2]
(1) Washington University in St. Louis, St. Louis, MO, USA, (2) Washington University in St. Louis, Saint Louis, MO, USA

Introduction: Research has shown that the prevalence of obstructive sleep apnea (OSA) dramatically increases with age. Studying compliance with continuous positive airway pressure (CPAP) therapy in the aging adult is important due to the prevalence of OSA in this population. Given the high rate of occurrence, this study highlights the importance of understanding the health consequences and the causes behind noncompliance in older adults.
Methods: Data was collected retrospectively from the charts of 44 patients (24 males). Age >55, diagnosed with OSA (baseline AHI 37.6 ±30.2), during a split night study and titrated to an optimal pressure. Groupings were classified by age: Group 1, 55-59 (29%); Group 2, 60-64 (34%); Group 3, 65-69 (20%); and Group 4, >70 (15.9%). Objective CPAP usage was assessed by downloading compliance data from a Smart Card in each patient´s CPAP machine. Compliance with CPAP treatment was defined as >4 hours use on >70% of nights.
Results: Baseline AHI varied somewhat between the groups 44.0±42.3, 34.4±24.4, 42.5±23.1, 26.6±23.8. The percent of days with CPAP device usage were as follows: 88.3%±18.6, 79.1%±29.5, 83.0%±24.9, and 81.9%±36.5. Average CPAP use between groups declined with age 6.1 hrs, 5.6 hrs, 5.7 hrs, and 5.0 hrs. Residual AHI was similar between groups 0.7±0.8, 2.4±2.3, 3.3±2.5, 2.9±3.7, 2.2±2.4. Optimal pressure was similar between the groups 11.0±2.8, 10.4±2.9, 9.2±1.9, 8.9±1.1, 10.1±2.6. The highest pressures attempted on CPAP were also close in proximity 11.5±2.8, 10.9±2.8, 9.4±2.4, 9.4±1.5, and 10.6±2.6. Arousal indices at optimal pressure were as follows 6.2±6.5, 4.6±4.1, 3.4±3.1, 6.1±3.7, 5.1±4.7.
Conclusion: CPAP compliance is negatively correlated with increasing age with 23%, 27%, 33%, and 42% rates of noncompliance. Factors associated with worsening compliance are unknown and require further investigation.

0541

EVALUATION OF THE BIPAP AUTO M-SERIES WITH BI-FLEX DEVICE FOR THE TREATMENT OF OSA

Wylie P,[1] Grover S,[2] Cain C,[3] Lotz G,[3] Greg M[4]
(1) Arkansas Center for Sleep Medicine, Little Rock, AR, USA, (2) Sleep Center of Greater Pittsburgh, Pittsburgh, PA, USA, (3) Respironics, Inc., Murrysville, PA, USA, (4) Respironics, Inc., Monroeville, PA, USA

Introduction: Previously our labs validated the BiPAP® Auto with Bi-Flex (Respironics, Inc.) device, which demonstrated that this device was essentially equivalent to manual fixed bi-level titration during PSG. This study was undertaken on OSA patients to validate that the new BiPAP Auto with Bi-Flex on the M-Series platform (BAM) provides a clinically stable level of therapy and performs essentially equivalent to the Legacy BiPAP Auto with Bi-Flex (LBA).
Methods: 20 subjects previously diagnosed with OSA and objectively compliant with bi-level therapy were enrolled into this study. Subjects were required to complete 3 non-consecutive overnight PSG studies. Subjects were blinded to the treatment modality each night.
Night 1 and Night 2:
Randomly assigned to either BAM or LBA with Bi-Flex enabled. All patients used humidification.
Device Settings:

MaxIPAP=25cmH2O
MinEPAP=4cmH2O
MaxPS=8cmH2O
Bi-Flex setting=2

Night 3:
Manual in-lab titration to re-establish treatment pressures.
Results: Gender 12 males 5 females
Age (years) 57±11.4
BMI (kg/m2) 37.4±7.7
Diagnostic AHI (hr-1)-Untreated=57.2 ±33.5
BAM AHI (hr-1)=5.3±3.9
LBA AHI (hr-1)=4.7±4.4
Manual titration AHI (hr-1)=8.2±7.0
Conclusion: Data from 17 completed subjects showed no statistically significant difference between BAM and LBA for all sleep variables. There is no statistically significant difference between gender for Age, BMI or diagnostic or treated AHIs. Data from 3 subjects were excluded from analysis due to poor sleep architecture from inconsistencies in protocol execution, and various co-morbitities. Among the device parameters, 90% IPAP and EPAP values for M-Series track within 0.7cmH2O of those from the legacy device.

These data again demonstrate that the BiPAP Auto with Bi-Flex compares favorably with manual titration, and that there is essentially no difference between the BiPAP Auto in the new M-Series platform as compared to the legacy platform.

0542

IS ONE NIGHT OF LABORATORY POLYSOMNOGRAPHY SUFFICIENT TO ASSESS TREATMENT OUTCOMES?

Levendowski D,[1] Zack N,[2] Rao S,[2] Gendreau M,[2] Kranzler J,[2] Zavora T,[1] Westbrook P[1]
(1) Advanced Brain Monitoring, Carlsbad, CA, USA, (2) Cypress Bioscience, CA, USA

Introduction: Variability in PSG results has been attributed to scoring reliability and differences in the time supine and sleep latency/efficiency. This report inspects the variability of repeated-measures PSG results.
Methods: Fourteen patients completed two PSG studies (one–month interval, designated PSG1 and PSG2) at one of four sleep centers in Sidney, Australia. Both studies were conducted at the same sleep center using the same standard, PSG equipment. All PSG data were scored at a central scoring facility by the same rater. Patients were allowed to consume their usual daily amount of alcohol prior to lights out.
Results: The between session correlation for the AHI was 0.18. Using the AHI to assign patients into OSA severity groups (i.e., AHI: normal=0–5, mild=6–20, moderate=21–40, and severe=>40), seven patients fell into the same diagnostic category in both PSG studies. In the most significant change, the diagnostic category changed from mild to severe. There was a strong correlation across the two nights for the percent of time supine ($r=0.73$, $p<0.05$) and supine AHI ($r=0.81$, $p<0.05$). T-tests revealed statistically significant differences in the percentage of time supine for PSG1 and PSG2. The strong correlation between the total sleep time length ($r=0.60$, $p<0.05$) and sleep efficiency ($r=0.82$, $p<0.001$) suggest that patients slept relatively consistently during the two studies. T-tests reveals a slight improvement in sleep efficiency during PSG2 compared to PSG1 ($p<0.01$).
Conclusion: These results confirm that a single night study is most likely insufficient for characterizing the change in a subject´s sleep disordered breathing as a result of treatment. Given the documented night-to-night variability, these findings bring into question the weight that should be assigned to a single night laboratory PSG when it is held up as the gold standard for measuring the accuracy of alternative diagnostic devices or assessing OSA treatment outcomes.

0543

A COMPARISON OF POLYSOMNOGRAM TO LEVEL III HOME TESTING IN ADULT WOMEN

Gjevre J, Reid J, Skomro R, Taylor-Gjevre R, Stiles M, Mink J, Cotton D
University of Saskatchewan, Saskatoon, Saskatchewan, Canada

Introduction: Women with sleep disordered breathing are often under-represented in sleep research. The Embletta device is a level III test well validated in men. We evaluated whether Embletta is comparable to PSG for women.
Methods: 71 consecutive women, referred to the sleep lab for possible obstructive sleep apnea (OSA), were recruited to compare PSG to Embletta. Complete data was available in 45 women who underwent diagnostic PSG followed by a home Embletta test. The PSG was scored by an RPSGT and interpreted by a sleep physician. The Embletta was computer scored.
Results: The average age was 52.24 years (SD 10.84)) with an average BMI of 35.25 (SD 9.46). The average Epworth score was 9.56 (SD 4.42) and the average total Pittsburg score was 8.35 (SD 3.76). Patients preferred the Embletta with an average visual analog score of 33.65 (SD 36.93) with Embletta=0 and PSG=100. The average apnea-hypopnea index (AHI) for PSG was 16.01 (SD 16.26, range 0.50-80.90) while the average RDI for Embletta was 17.69 (SD 14.77, range 1.0-68.60). Paired samples t-test revealed a mean difference of 1.69, $p = 0.442$, 95% CI (-6.07, 2.70) thus indicating no significant difference between PSG and Embletta. Pearson´s correlation was significant at 0.561 ($p<0.001$), thus showing a good correlation between this two tests in the overall data. Using a AHI PSG cutoff of 5 for normal versus OSA, our population consisted of 13 normal and 32 OSA patients. The PPV of Embletta for RDI > 5 was 90.6% with a NPV of 61.5%. The overall accuracy was 82.2%. Using an AHI PSG breakpoint of 30 to distinguish the severe OSA patients, of which there were 8, the PPV of Embletta (RDI > 30) was lower at 50%.
Conclusion: We found that Embletta home testing was preferred by the women and acceptably accurate at distinguishing normal from OSA.
Support (optional): We gratefully acknowledge the Saskatchewan Health Research Foundation for providing funding for this study.

0544

CORTICOTROPH AXIS IS RECOVERED BY N CPAP IN OBSTRUCTIVE SLEEP APNEA PATIENTS

Togeiro S,[1] Carneiro G,[2] Flecha F,[2] Zanella M,[2] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, SP

Introduction: There is increasing evidence that obstructive sleep apnea syndrome (OSAS) increases the risk of cardiovascular events probably due to noturnal activation of sympathetic nervous system and hypothalamic-pituitary-adrenal (HPA) axis .The literature varies regarding the effects of OSAS on HPA axis. Since nasal continuous positive airway pressure (nCPAP) treatment improves nocturnal hypoxia and sleep fragmentation in patients with OSAS, we HPA axis before and during nCPAP to confirm an etiologic link.
Methods: Nine obese patients with severe OSAS (AHI 79 ± 7,2) underwent CPAP treatment. Insulin resistance index, 24-Hour Ambulatory Blood Pressure Monitoring (24h-ABPM), overnight salivary cortisol suppression test with low dose of Dexamethasone (0,25mg) and plasma inflammatory cytokines were measured before and after 3 months of successful CPAP treatment (AIH 21.2 ± 15.2).
Results: Participants had a diminished heart rate (82.6 bpm ± 4.2 vs 74.1 bpm± 4.0; p=0,04), with a significantly improvement in salivar cortisol responsiveness to dexamethasone (438.6 ng/dl ±70.4 vs 168.1 nd/dl ± 41.4; p=0,009).Insulin resistance tended to decrease (HOMA: 7.15±1.48 vs 4.9±1.36; p=0,068) and adiponectin tended to increase (9.45± 2.4 ± 16.8 ±4.0; p= 0.129). The average body mass index did not change (44.3 kg ± 2.4
vs 37.9 kg ± 5.1;p= 0.337).
Conclusion: Corticotroph axis and hypersympathetic activity are recovered by n CPAP in obstructive sleep apnea patients. Further studies are needed to elucidate the changes of adipokines and insulin resistance during nCPAP treatment.
Support (optional): AFIP, FAPESP

0545

ROLE OF OSA AND ORAL PARAMETERS ROUTINELY USED BY ANESTHESIOLOGISTS ON ASSESSMENT OF ORAL INTUBATION PROBLEMS.

Machado C,[1] Togeiro S,[1] Poyares D,[2] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil

Introduction: Specific protocols and approaches related to the anesthesia should be recommended in patients with high risk for OSAS, since they present more complications during and after this procedure such as hard oral intubation, prolonged respiratory sleep events and

extubation difficulties. However, no protocols have been suggested in order to evaluate the risk for OSA during the anesthesia. It has not also been established whether or not OSAS impairs the oral intubation during this procedure. Additionally some facial skeletal and upper airway abnormalities are routinely evaluated by the anesthesiologists, and might be considered to estimate risk for OSA.We sought to evaluate the effect of oral parameters routinely applied by anesthesiologists, and of a validated OSA questionnaire on the degree of difficulty intubating patients during anesthesia.
Methods: 170 patients (60 female and 110 male) were consecutively selected from elective surgical procedures at a general hospital of Brusque-Santa Catarina, Brazil, during a 6-month period, 2006.The risk for OSA was evaluated using Berlim questionnaire; difficulty for intubation was evaluated trough the numbers of attempts for this procedure, the anestesiologist subjective score of difficulty, and by the Comark-Lehane grade (I to IV).
Size and position of the tongue, oral –pharynx, and enlargement of tonsils were respectively evaluated, and Malampati level (I to IV) and Brodsky grade (I to V) were both obtained
Neck circumference and presence of retrognathia were also evaluated for all patients.
Results: Patient´s age ranged from 24 to 75 years and BMI from 18,9 to 48,8 kg/m2 .
The number of intubation attempts significantly correlated with Comark- Lehane grade (beta=.354 p=0.00009); and with presence of retrognathia (beta=.31, P=0.0004).
The subjective impression level of difficulty of intubation also significantly correlated with neck circumference (beta=.26 p=0.02); Brodsky grade(beta=.19 p=0.009); Comark Lehane grade (beta=.56 p<0.00001); and retrognahia (beta=.27 p=0.001).
All other parameters analyzed were non significant in both regressive models.
Conclusion: This data suggest that facial skeletal and oral abnormalities were helpful to predict intubation difficulties during surgery. Neither OSA questionnaire nor sleepiness degree were significant in our model to predict oral intubation difficulties.
Support (optional): AFIP AND FAPESP

0546

DO MALLAMPATI SCORES CORRELATE WITH OPTIMAL CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) DETERMINED BY CPAP TITRATION DURING FULL-NIGHT POLYSOMNOGRAPHY?

Oropello J,[1] Ostrovskaya M,[2] Freeman J,[3] Lund S[3]
(1) Sleep Disorders Institute, Clinilabs, Inc., New York, NY, USA, (2) Clinilabs, Inc., New York, NY, USA, (3) Sleep Disorders Institute, New York, NY, USA

Introduction: The optimal CPAP (OCPAP), determined by CPAP titration (CPAPT), is the lowest effective pressure that eliminates apneas, hypopneas, respiratory-related arousals, desaturations, and snoring. Prediction of OCPAP might be helpful to guide attended CPAPT, allowing more rapid pressure titration when there is limited time due to poor sleep efficiency or split-night studies. The Mallampati score (MS), a noninvasive assessment of tongue size relative to oral cavity, has been associated with the risk of obstructive sleep apnea (OSA) independent of body mass index (BMI) or apnea/hypopnea index (AHI). We explored whether MS correlated with the OCPAP level determined by full-night CPAPT.
Methods: A retrospective chart review of patients ≥ 18 yr. with OSA by polysomnogram (PSG) followed by successful full-night CPAPT from 1/1/06 until 11/1/06 were eligible. Successful CPAPT was defined as completion of manual CPAPT with sleep efficiency > 50% and AHI < 5. Exclusion criteria included primary central sleep apnea, previous ENT surgery, and lack of MS. PSG scoring and OCPAP determination were made by personnel unaware of the study. Data collection included age, gender, BMI, initial AHI, lowest desaturation (low SaO2), MS, and OCPAP.
Results: Ninety-six patients, (56M, 40F) aged 45.3 (±12.7) years with BMI 31.2 (±6.8) and AHI 40.5 (±20.0) were identified. The mean ± SD optimal CPAP levels for each MS were MS I: 9.4±2.9, MS II: 10.0±2.5, MS III: 10.5±2.3, and MS IV: 9.6±1.3 and were not significantly different (ANOVA p = 0.38). Univariate linear regression demonstrated a significant but weak correlation between AHI and OCPAP (r = 0.40, p <0.001) and low SaO2 and OCPAP (r = 0.24, p = 0.02).
Conclusion: No correlation between OCPAP and MS was found. AHI and low SaO2 are weakly correlated with OCPAP.

0547

RANDOMIZED CROSSOVER STUDY OF TREATMENT COMPLIANCE AND SATISFACTION IN NON SLEEPY PATIENTS WITH OBSTRUCTIVE SLEEP APNEA: CPAP WITH PRESSURE RELIEF DURING EXHALATION VS. CONVENTIONAL CPAP

Gfüllner F,[1] Montalvan S,[2] Weber G,[2] Füchtenbusch M,[2] Pfeifer M[2]
(1) Klinik Donaustauf, Universität Regensburg, Donaustauf, Germany, (2) AE (Europe)

Introduction: Continuous positive airway pressure (CPAP) is the standard treatment for obstructive sleep apnea (OSA). However, non sleepy patients with OSA (ESS<11) often demonstrate poor compliance to this therapy. CPAP with pressure relief during exhalation (prCPAP) is a new mode of therapy that is more comfortable than conventional CPAP (cCPAP) and may lead to higher compliance. The aim of this study was to evaluate treatment compliance and satisfaction in non sleepy patients with OSA treated by prCPAP vs. cCPAP.
Methods: A cross-over randomized single-blind study design was used, in which 18 newly diagnosed non sleepy OSA patients were enrolled. Patients were treated with either prCPAP or cCPAP for 30days and then crossed over to the alternative treatment for a further 30day period. Compliance (hours of use/night) was measured using the technology provided with the PAP machines. Satisfaction with therapy, treatment comfort and interface comfort were evaluated using visual analog scales (0-10 cm), with higher scores indicating more favorable ratings.
Results: 18 non sleepy patients with OSA were recruited: 15 men, 56,8+/-9,6 years old, BMI 35,6+/-6,7kg/m2, diagnostic AHI 41,4+/-19,6/h, titration AHI 2,1+/-1,6/h, titration pressure 9,8+/-1,5mbar. 15 patients completed the study.
There was no significant difference in hours of use/night between patients when using prCPAP (5:31+/-1:59h) or cCPAP (5:32+/-1:48h), in satisfaction with therapy (7,3+/-2,8 vs. 7,7+/-2,4), treatment comfort (6,9+/-2,8 vs. 6,0+/-3,1) or interface comfort (6,9+/-2,5 vs. 6,6+/-2,1). The ESS increased in both groups (from 6,6+/-2,0 to 9,1+/-2,9 when using prCPAP and 8,5+/-2.9 when using cCPAP).
Conclusion: We demonstrated high compliance on both modes of therapy in non sleepy patients with OSA. Because compliance was already high in this cohort, it is unlikely that prCPAP would have improved this further. The mode of therapy also had no significant effect on satisfaction with therapy, treatment or interface comfort. The increase in ESS on both therapies needs further investigation.
Support (optional): This study was supported by Respironics, Inc

0548

INHIBITION OF NADPH OXIDASE PREVENTS INTERMITTENT HYPOXIA INDUCED SPATIAL LEARNING DEFICITS.

Row B,[1] Cheng Y,[2] Serpero L,[3] Dayyat E,[3] Gozal D[3]
(1)Louisville, KY, USA, (2) University of Louisville, KY, USA, (3) University of Louisville, Louisville, KY, USA

Introduction: Exposure to intermittent hypoxia (IH), such as occurs in sleep-disordered breathing (SDB), is associated with cognitive impairment and oxidative neural injury in rodents. Enhanced activity of the enzyme NADPH oxidase has been shown to underlie the carbonylation, lipid peroxidation, and proinflammatory responses seen in the brain after long-term intermittent hypoxia exposure in rodents, suggesting that this enzyme plays a critical role in IH-induced oxidation injury and cognitive morbidities.
Methods: The selective NADPH oxidase inhibitor apocynin (40 mg/kg/day) was administered in drinking water to male Sprague-Dawley rats (250-300 g) for 3 days prior and continued throughout the duration of the experiment, which consisted of exposure to either 14 days of IH (alternating 90 second episodes of 10% and 21 % O2 during the light cycle), or normoxia (RA, 21 % O2). All rats then underwent cognitive assessments in the spatial, reference version of the Morris water maze, after which brain tissues were removed for assessment of lipid peroxidation.
Results: Untreated rats exposed to IH were found to require significantly longer times (latency) and distances (pathlength) to locate the hidden platform ($p<.05$ for both latency and pathlength), compared to rats treated with apocynin and exposed to IH, as well as their respective RA controls. On probe trials administered after completion of training, apocynin-treated rats exposed to IH displayed significantly greater spatial bias for the hidden platform position, as assessed by percentage of swim path ($p<.03$) in the target quadrant, than non-treated rats exposed to IH. Treatment with apocynin was also associated with significant reductions in malondialdehyde (MDA) production, an indicator of lipid peroxidation, in both hippocampus and cortex.
Conclusion: These data indicate that oral administration of apocynin is capable of attenuating IH-induced spatial learning deficits and reducing oxidative stress in sensitive brain regions. Inhibition of NADPH oxidase may therefore be a viable strategy to prevent oxidative stress-related morbidities in obstructive sleep apnea.
Support (optional): NIH grants 2P50HL60296-06 and HL69932

0549

COMPLIANCE TO POSITIVE AIRWAY PRESSURE TREATMENT IN OBSTRUCTIVE SLEEP APNEA SYNDROME

Walter R,[1] Guerrero M[2]
(1) Walter Reed Army Medical Center, Laurel, MD, USA, (2) WRAMC, DC, USA

Introduction: Continuous positive airway pressure (CPAP) is currently considered to be the cornerstone of therapy for obstructive sleep apnea (OSA) syndrome. The objectives of this study are to determine if scheduled clinic follow-up improves CPAP compliance, and to determine the appropriate time for follow up clinic visit.
Methods: We performed a retrospective review of 52 randomly selected patients (37M, 15F; mean age=51y, range 22-83 y; mean BMI=31, range17- 48kg/m2). Patients who undergo sleep studies at WRAMC Sleep Center are provided with CPAP device the day after titration or within a week for weekend sleep studies. The device are equipped with smart card that records hourly usage per day, number of days with device usage, percent of days with device usage, average time usage, and percent of days with usage >= 4 hours. Compliance was defined as percentage of days of >= 4 hours usage. Comparisons were made using one way ANOVA test and Bonferroni test for the multiple comparisons post Hoc.
Results: There was no significant difference in percentage of days usage before and after clinic follow-up visit (74.1 vs 77.5% p=0.33 n=44). There was a significant increase in percent of days with usage>= 4 hours before and after follow up visit (53.5% vs 77.5% p=0.02 n=44). Overall compliance was noted to be lower during the first 3 months of therapy (52-58%).
Conclusion: Clinic follow-up visit did not increase daily usage but did greatly increase effectiveness of CPAP therapy based on definition of compliance being >= 4 hours daily CPAP usage. The best follow-up interval appears to be within the first 3 months of initiation of therapy.

0550

FATIGUE IN OSA: THE ROLE OF DEPRESSIVE SYMPTOMS AND SLEEP QUALITY

Palau J,[1] Marler M,[2] Stepnowsky C[3]
(1) VA San Diego Healthcare System, San Diego, CA, USA, (2) CA, USA, (3) University of California, San Diego*, San Diego, CA, USA

Introduction: Recent studies have found that depressive symptoms account for upwards of 10 times more variance in fatigue than OSA severity. We sought to both replicate and extend these findings by including important covariates and a measure of sleep quality to better understand those factors that drive fatigue in OSA patients.
Methods: 75 patients newly diagnosed with OSA and prescribed CPAP were studied. OSA severity was measured by the apnea-hypopnea index (AHI); depressive symptoms by Center for Epidemiologic Studies Short Depression Scale (CES-D 10); sleep quality by the Pittsburgh Sleep Quality Index (PSQI); and fatigue by a 10-point visual analog scale. Data were analyzed using a hierarchical regression analysis using SPSS v14.0.
Results: After inclusion of the covariates (age, BMI: body mass index), OSA severity variables (AHI: number of apneas and hypopneas per hour of sleep, and time spent at < 90% SaO2) accounted for 10% of the variance in fatigue ($R2=0.096$; $F(2,70)=3.73$; $p=.029$) while depressive symptoms accounted for 21% ($R2=0.206$;$F(1,71)=20.75$; $p<.001$). A second model was then tested: step 1: age, BMI; step 2: OSA severity; step 3: PSQI; step 4: CESD. PSQI on step 3 accounted for 25% of the variance in fatigue ($R2=0.253$; $F(1,66)=25.8$; $p<.001$), while the amount of variance accounted for by CESD on step 4 was reduced to 5% ($R2=0.050$; $F(1,65)=5.44$; $p=023$). The full model explained a total of 40% of the variance in fatigue ($R2=0.402$; $F(6,65)=7.28$; $p=<.001$).
Conclusion: Our findings are consistent with previous findings that depressive symptoms contribute more to daytime fatigue than measures of OSA severity. However, the inclusion of sleep quality appears to explain a substantial portion of the relationship between depressive symptoms and fatigue. Future research should focus on better understanding the relationship between depressive symptoms and fatigue in OSA patients by focusing on the role of sleep quality.
Support (optional): VA HSRD IIR 02-275.

0551

HYPOXEMIA AND HIGHER SLEEP FRAGMENTATION AFTER ACUTE CPAP WITHDRAWAL WERE DETERMINANTS IN THE RECURRENCE OF OBSTRUCTIVE RESPIRATORY EVENTS DURING SLEEP

Silva R,[1] Ackel-D´Elia C,[2] Garbuio S,[2] Silva A,[2] Rotella L,[1] Truksinas E,[2] Bittencourt L,[2] Sergio T[2]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao

Paulo, Sao Paulo, Brazil

Introduction: CPAP treatment can effectively maintain upper-airway patency, eliminate nocturnal oxygen desaturation and decrease arousals (Kushida, 2006). It has been demonstrated that one night of CPAP withdrawal results in a return of sleep-disordered breathing (Grunstein, 1996; Yang, 2006). However, we lack understanding of whether that effect occurs in all patients after acute CPAP withdrawal and which factors could determine that condition. The aim of this study was to investigate the effect of one night of CPAP withdrawal on sleep parameters.
Methods: Our sample comprised 19 men with OSA. Polysomnograms (PSG), Epworth Sleepiness Scale (ESS), and Profile of Mood State Scale (POMS) were performed on night 1, before the beginning of CPAP treatment; night 2, after 2 months of CPAP optimal therapy; and on the following night, night 3, without CPAP. According to the apnea-hypopnea index (AHI) observed on night 3, compared with night 1, participants were divided into 2 groups: Group I, those who presented AHI decreased in over 50% (n=6), and Group II, participants who did not present AHI change or presented AHI increased in over 50% (n=13).
Results: Comparing groups I and II, participants were similar regarding age, body mass index, neck circumference, ESS, POMS, and PSG data on night 1. The comparison among the 3 nights (1 vs. 2 vs. 3) showed differences in SaO2 min (Group I = 87 vs. 90 vs. 83, $p>0.05$; Group II = 76 vs. 88# vs. 79#, $p<0.01$#) and arousals index (Group I = 22 vs. 13 vs. 15, $p>0.05$; Group II = 29 vs. 9# vs. 35#, $p<0.01$#), i.e. Group II presented lower SaO2 and higher arousals index after acute CPAP withdrawal.
Conclusion: The worsened hypoxemia and higher sleep fragmentation after acute CPAP withdrawal were determinants in the recurrence of obstructive respiratory events during sleep.
Support (optional): AFIP, FAPESP/CEPID

0552

REDUCED USEFUL FIELD OF VIEW IN DRIVERS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

Tippin J,[1] Rizzo M,[1] Sparks J,[2] Boyle L[1]
(1) University of Iowa, Iowa City, IA, USA, (2) University of Iowa, IA, USA

Introduction: Drivers with obstructive sleep apnea syndrome (OSAS) have an increased risk of motor vehicle crashes. Sleepiness-associated inattention may play an important role in these crashes. Performance on the useful field of view (UFOV) task, which depends upon attention, has been shown to correlate with increased crash risk. Our goal was to determine if drivers with OSAS have a reduction in UFOV.
Methods: Subjects consisted of 108 drivers (mean age 43.3 +/- 10.1 years), 56 with OSAS based upon ICSD clinical criteria, and 52 controls with no neurological or sleep disorders. All OSAS subjects underwent polysomnography (PSG) on the night following UFOV testing. There were 44 with an AHI > 5 events/hour (PSG+) and 12 with an AHI of < 5 (PSG-). Subjective sleepiness was indexed by the Epworth Sleepiness Scale (ESS). UFOV was assessed in all subjects using the Visual Attention Analyzer, Model 3000 (Visual Awareness, Chicago). Subtests 3 and 4, which assess selective attention, and total score were used. The dependent measure in each task was a threshold score at which the subject acheived 75% correct target identification. Higher scores indicate poorer performance.
Results: PSG+ OSAS subjects showed significantly reduced UFOV compared to controls for subtest 3 (130.841 vs. 92.077, $p = 0.0441$), subtest 4 (267.273 vs. 217.077, $p = 0.0421$), and total score (457.318 vs. 351.231, $p = 0.0242$). There were no statistically significant differences for PSG- subjects. No significant correlations were found in PSG+ subjects between UFOV and AHI, minimum O2 saturation, and ESS.
Conclusion: Drivers with PSG proven OSAS have reduced UFOV, which is known to be associated with increased crash risk. UFOV reduction was not predicted by ESS or PSG data. UFOV may prove to be a useful means of identifying those OSAS drivers who have a greater risk for crashing.
Support (optional): CDC R49 CCR 721682 and NIH/NIA R01 AG017177

0553

REM RELATED OBSTRUCTIVE SLEEP APNEA-PROGRESSION OVER TIME

Siddiqui F,[1] Osuna E,[2] Walters A,[3] Chokroverty S[4]
(1) University of Toledo, Toledo, OH, USA, (2) Bogota university, Bogota, Colombia, (3) New Jersey Neuroscience Institute, Edison, NJ, USA, (4) NJ Neuroscience, NJ, USA

Introduction: Rapid eye movement (REM) related obstructive sleep apnea (OSA) REM OSA has been described recently as a distinct entity specific to stage REM. A reduced percentage of REM sleep can superficially inflate the AHI and give a higher REM AHI index. The prevalence, clinical and polysomnographic features specific to this disorder have been described in a sleep apnea population. We studied the clinical and polysomnographic progression of a group of these patients over a period of time. To our knowledge the progression of this disorder over a period of time has not been described before.
Methods: We studied the characteristic of REM OSA in our sleep apnea population and followed 8 patients over a period of 15.9 ±7.8 Months. We selected REM related OSA patients with the following inclusion criteria : AHI >5/hr, NREM AHI<10/hr. REM AHI>15/hr and REM% >12.
Results: We reviewed 972 polysomnographic (PSG) recordings for sequential patients older than 18 years and found 99 patients- 12.5 % (58.5% F avg age 47.8 yr and 41.5% M 45.9 yr) with REM related OSA. There were five females and three males (avg. age 49.7 ±10 yr) who had repeat PSG. Despite the fact that one patient lost 60 lbs and two gained 25 lbs and one had surgery, the AHI on repeat PSG for all four patients remained in the mild range and remained predominately REM related. The other four patients had no change in BMI, medical conditions and medications, and the repeat PSG had shown no progression of the REM OSA.
Conclusion: We conclude that REM OSA is a specific entity that remains stable over a period of time and can be used as a parameter for monitoring OSA patients in research studies.

0554

IMPROVEMENT OF SLEEP DISORDERED BREATHING AFTER OROFACIAL MUSCLE EXERCISE

Shimizu M,[1] Goto M,[2] Yukioka M[3]
(1) Hino Hospital, Sakai, Osaka, Japan, (2) Toin University of Yokohama, Yokohama, Japan, (3) Yukioka Hospital, Osaka, Japan

Introduction: Patients of a rheumatology clinic were encouraged to exercise orofacial muscle and the effects on sleep were examined using polysomnography.
Methods: Twenty three patients studied were suffering from various rheumatic diseases such as rheumatoid arthritis (13), polymyositis (3), systemic lupus erythematosus (2), and an each case of systemic sclerosis, mixed connective tissue disease, fibromyalgia, sarcoidosis. Seventeen were female and 6 were male. PSG was performed in a sleep laboratory using a standard 14-channels apparatus. Recording were

analyzed manually by fully trained technicians. Orofacial muscle exercise (OME) were done using itraoral rubber spring(Patakara), originally developed and widely sold in Japan, 3~10 times daily for more than a year. Lip closing force (LCF) was measured using a strain-gauged assembly attached with two lip holders and the LCF value was expressed by Newton (N).
Results: After more than 12 months of OME, the mean LCF of these 23 patients increased from 11.9N (SD;3.3N) to 14.5N (SD;4.0) . The mean value of apnea hypopnea index (AHI) decreased from 13.1 (SD;16.3) to 9.3 (SD;13.7). The mean value of arousal index (ArI) also decreased from 28.4 (SD;17.0) to 23.3 (SD;15.7). All of these changes were statistically significant ($p<0.03$) when examined by paired t test.
Conclusion: OME, when continued over a year using an adequate method, is very likely to improve sleep disordered breathing.
Support (optional): none

0555

NIGHT TO NIGHT VARIABILITY OF IN-HOME SLEEP STUDIES – IS ONE NIGHT ENOUGH?

Westbrook P,[1] Levendowski D,[1] Zavora T,[1] Scarfeo D,[1] Berka C,[1] Popovic D[2]
(1) Advanced Brain Monitoring, Carlsbad, CA, USA, (2) University of Southern California, CA, USA

Introduction: This restrospective analysis of an existing database of sleep studies acquired with an ARES Unicorder investigates the night-to-night variability to assess the utility of multi-night studies.
Methods: A total of 477 subjects with >4-hours of recording time on each of two-nights were analyzed. Auto-scoring rules identified apneas (10-s cessation in flow)(AI), and hypopneas with 4%-desaturation (AHI-4%), or with 1%-desaturation plus at least one arousal indicator (AHI-1%). Inter-class correlations were computed between N1 and N2 data. AHI-4% and AHI-1% were stratified into normal (<5), mild (5-20), moderate (21-40) and severe (>40) diagnostic categories for N1 and N1+N2 combined.
Results: Strong interclass correlations were observed ($p<0.001$) between N1 and N2 for the overall recording time ($r=0.75$), percent time supine ($r=0.79$), AHI-4% ($r=0.90$) and AHI-1% ($r=0.89$). The supine AI ($r=0.55$), AHI-4% ($r=0.57$) and AHI-1% ($r=0.52$) were not as strongly correlated ($p<0.001$).
For AHI-4%, the percentage of patients with the same diagnostic category for N1 vs. N1+N2 were normal=89%, mild=87%, moderate=77% and severe=90%. Patients with mild OSA shifted equally between normal and moderate. Twice as many patients with moderate OSA on N1 were reclassified as mild for N1+N2.
For AHI-1%, the percentage of patients with the same category for N1 vs. average of N1+N2 were normal=77%, mild=89%, moderate=78% and severe=86%. Ten-percent of the patients who were mild on N1 shifted to moderate. Fourteen-percent of the moderate patients were mild and 8% were severe across two-nights.
For AHI-4% and AHI-1%, patients who were normal or severe never changed more than one diagnostic category.
Conclusion: The difference in the N1 vs. N2 correlations for supine AHI and percent-time supine suggest unexpected variability. Patients with mild to moderate OSA are more likely to change diagnostic categories, such that models that predict or assess treatment outcomes may benefit from multi-night studies.

0556

ADAPTIVE SERVO VENTILATION AND ENHANCED EXPIRATORY REBREATHING SPACE FOR COMPLEX SLEEP APNEA TREATMENT

Rawlins S,[1] Vigneault K,[2] McGeehan B,[2] Gilmartin G,[1] Thomas R[1]
(1) Beth Israel Deaconess Medical Center, Boston, MA, USA, (2) Total Sleep Holdings, MA, USA

Introduction: Complex sleep apnea (complex SA) is a newly recognized subset of SA, characterized by induction, by the application of positive airway pressure (PAP), central apneas and periodic breathing in patients appearing to have obstructive SA on the diagnostic polysomnogram. Adaptive Servo Ventilation (ASV) is the only currently approved therapy for central and complex SA. We have previously described a method of adapting dead space to the use of PAP, Enhanced Expiratory Rebreathing Space (EERS) to treat complex SA. We present the data of the first 54 patients treated with ASV alone and with EERS (50-150 cc).
Methods: Patients with complex SA were evaluated first with ASV and then with ASV + EERS of 100-150 cc on the same night. Mask pressure and flow (pneumotachograph) were obtained during full polysomnography. End expiratory pressure was adjusted to overcome obstruction.
Results: The average age was 53.5 years, there were 12 females and 42 males. Patient characteristics included diabetes (6), renal failure (0), heart failure (3), depression (20), atrial fibrillation (3), and hypertension (19). Hypnotic use (21) was frequent. Seventeen out of 54 (32%) patients had a better response to continuous or bilevel PAP with EERS, while 8 patients had a complete response with ASV alone. Twenty-nine subjects (54%) had the best response with ASV plus EERS. Additional oxygen was necessary in 37 patients (66%).

ASV use was associated with specific polysomnographic features when control was inadequate - continuous pressure cycling, single large breaths, and rapid consecutive breaths. These occurred with ASV alone in all but 8 patients, contributed to patient- ventilator dyssynchrony, and were eliminated by minimizing hypocapnia with EERS.
Conclusion: ASV and EERS have complementary benefits in the treatment of complex SA. Monitoring of mask pressure during ASV evaluation demonstrates unique patterns that have clinical significance.
Support (optional): None

0557

EFFECT OF THERAPY IN PATIENTS ON OPIOID MEDICATIONS WITH CENTRAL SLEEP APNEA.

Veeramachaneni S,[1] Mador M,[2] Desai H,[1] Rohilla R,[3] Khan M,[3] Webster L,[4] Grant B[2]
(1) University of Buffalo, Buffalo, NY, Buffalo, NY, USA, (2) Veteran Affairs Medical Center and University of Buffalo, Buffalo, NY, Buffalo, NY, USA, (3) University of Buffalo, Buffalo, NY, NY, USA, (4) Med One Medical Sleep Laboratory and Lifetree Pain Clinic, Salt Lake City, Utah., Salt Lake City, UT, USA

Introduction: The purpose of this study was to determine the effect of supplemental oxygen and bilevel positive airway pressure (BPAP) therapy in patients on around the clock opioids who had central sleep apnea (CSA) defined at a central apnea index (CAI) ≥5 events/hr.
Methods: We studied 37 consecutive patients on opioids between March 2005 and May 2006 who underwent a therapeutic sleep study in whom a baseline period was obtained before a trial of therapy was initiated with oxygen and/or BPAP for central sleep apnea, with or without concomitant obstructive sleep apnea. Adequate therapy was

defined for sleep apnea as an overall apnea-hypopnea index (AHI) <5 events/hr, and for central sleep apnea as a CAI <5 events/hr on therapy for at least a period of 20 min.
Results: Eight patients with CSA from a diagnostic study had a CAI <5 events/hr during the therapeutic study before therapy was initiated. Four patients without demonstrable CSA in a diagnostic study had a CAI ≥5 events/hr during the baseline period of the therapeutic study. Therefore, there was significant night to night variation in the demonstration of CSA in 32% (95%CI: 18-50%). Supplemental oxygen was effective in treating CSA in 53% (95%CI: 28-77%). BPAP treated CSA effectively in all 20 patients in whom it was tested: 100% (95%CI: 83-100%). The overall AHI was controlled adequately in 10 patients: 50% (95%CI: 27-73%). Therefore, further titration studies were required in 27% (95%CI: 14-44%) of the patients.
Conclusion: We conclude that patients on opioid medications with CSA: (1) have marked night to night variation of their condition, (2) supplemental oxygen adequately controls central apneas about half of the time, (3) central apneas can be eliminated by BPAP but (4) additional titration studies are often needed to optimize therapy.
Support (optional): Divisional funds

0558

PREVALENCE AND FACTORS AFFECTING REM REBOUND ON CPAP TITRATION STUDY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

Osuna E,[1] Siddiqui F,[2] Walters A,[3] Chokroverty S[4]
(1) Bogota university, Bogota, Colombia, (2) University of Toledo, Toledo, OH, USA, (3) New Jersey Neuroscience Institute at JFK Medical Center, Edison, NJ, USA, (4) NJ Neuroscience, NJ, USA

Introduction: In patients with obstructive sleep apnea syndrome (OSAS), treatment with CPAP results in an increase of REM sleep and slow wave sleep(SWS). This increase in REM sleep has been referred as REM rebound (RR) in literature. The definition and factors affecting RR has not been described before.
Methods: We included 179 patients > 18 years with Apnea hypopnea index(AHI) > 10/hr on the baseline polysomnogram(bPSG), who had an adequate CPAP polysomnogram (cPSG) done in the same laboratory. We collected the demographic features, the percentage of REM sleep, AHI, REM AHI, oxygen desaturation of these patients during bPSG and cPSG. We compared and analyzed the increase in REM sleep percentage in bPSG and cPSG and looked for factors affecting RR.
Results: 179 patients were enrolled (M/F: 118/61), with a mean age of (M =48.6 ± 4yr and W= 51.6 ± 12.9yr). The mean interval between the bPSG and cPSG was 1.45 months. The mean body mass index (M= 33.65 ± 7.77 & W= 38.93 ± 8.28), mean AHI was (M= 50.05 ± 27.45/hr & F 34.7 ± 24.9/hr) and mean REM-AHI was (M= 50.29 ± 25.08/hr & W= 50.05 ± 23.37/hr). The mean REM rebound was 6.27 ± 9.97 % for men and 5.1 ± 11.09 % for women. The correlation matrix of REM rebound showed a significant correlation with body mass index (p 0.0042), bPSG stage REM (p 0.000) and bPSG AHI (p 0.000). The multiple regression model showed that the variables that contribute more to the REM change are: REM sleep during bPSG (-0.56), AHI (0.24) and the body mass index (0.081). There was no significant difference by gender in REM rebound (p: 0.47).
Conclusion: We suggest that an increase greater than 6 % in REM sleep should be considered REM rebound, since 6.15 % was the statistical significant difference between bPSG REM sleep and cPSG.

0559

BRAZILIAN INTRA-ORAL MANDIBULAR REPOSITIONER APPLIANCE: TITRATION STUDY

Machado M, Juliano L, Zortea F, Lentini-Oliveira D, Carvalho F, Rufino C, Carvalho L, Prado L, Prado G
Federal University of Sao Paulo, Sao Paulo, Brazil

Introduction: The efficacy of mandibular advancement appliances for mild and moderate OSAS has been proved by many studies, but most of predictor factors of success are still unknown. In the present study we have analyzed the amount of mandibular advancement achieved with ARMIO-BR protocol and what the difference it can make.
Methods: 81 consecutive patients with polysomnographic diagnosis of OSAS were referred for ARMIO-BR protocol between 2004 and 2005. Two groups were formed according to the status achieved with ARMIO-BR: a treated group (AHI<5/h) with 7F/40M, mean age 49.5±11.8 years, BMI 27.5±3,9kg/m2, baseline AHI 22.7±11.8/h and 1.8±1.4/h with ARMIO-BR titrated, and a untreated group (AHI>5) with 6F/28M, mean age 51.5±12 years, BMI 27.3±4kg/m2, baseline AHI 26.5±14/h and 9.7±5/h with ARMIO-BR. We analyzed the amount of mandibular advancement before ARMIO-BR protocol achieved by each patient voluntary, and the total mandibular advancement achieved with ARMIO-BR titrated. The T-test was used to determine statistical significance ($p<0.05$).
Results: The treated group presented a larger voluntary mandibular advancement (11.7±2.6mm) than the untreated group (10.7±2mm) achieved by each patient before the ARMIO-BR protocol (p=0.042). The total mandibular advancement in the end of the ARMIO-BR protocol was larger in the treated group (11.2±1.9mm) compared with the untreated group (10.3±2mm) (p=0.043).
Conclusion: Patients with greater possibility of voluntary mandibular advancement before ARMIO-BR protocol achieved better outcomes. In our opinion, an important aspect that can define the level of success of this type of treatment is the final titration of mandibular protrusion which should be always individually assessed, exploring maximal possibilities and at the same time respecting the limits of each patient.
Support (optional): Uniter-Sono

0560

CORRELATION BETWEEN SUBJECTIVE SLEEP TENDENCY AND OBJECTIVE SLEEP LATENCY

Aurora R,[1] Neubauer D,[2] Punjabi N[2]
(1) Mount Sinai School of Medicine, New York, NY, USA, (2) Johns Hopkins University, Baltimore, MD, USA

Introduction: Subjective sleepiness scales have been utilized in both clinical and research applications. The most widely used instrument is the Epworth Sleepiness Scale (ESS). The degree to which the ESS scores correlate with objective sleep latency during the multiple sleep latency test (MSLT) has generated much debate. Available evidence has not always supported a strong relationship between subjective sleep tendency and objective sleep latency. Specifically, previous studies have found no significant relationship or a weak association between the ESS score and the MSLT. This study examined the correlation between ESS scores and the MSLT in a consecutive series of patients attending a tertiary sleep disorders center.
Methods: A cross-sectional study of 699 patients presenting for clinical evaluation was conducted. Assessments included the ESS, overnight polysomnography, and MSLT. Techniques of survival analysis including the proportional hazards model were used to describe the association between the ESS scores and the median MSLT. ESS score was modeled categorically using tertiles (< 11, 11-15, >15) and as a continuous

variable.
Results: The mean age of the patients was 48.8 years (SD=12.2) and the mean MSLT score was 6.4 minutes (SD=4.9). After controlling for age, gender, and body mass index, the adjusted hazards ratio for sleep onset with 20 minutes during the MSLT for the three ESS score categories (< 11, 11-15, >15) were 1.00, 1.43, and 1.97, respectively. These results indicate that the likelihood of sleep onset during the MSLT is two-fold when comparing an ESS score >15 to <11.
Conclusion: The results of the current study indicate that subjective estimates of daytime sleep tendency with the ESS are associated with MSLT-defined sleepiness. Thus, the ESS provides a simple measure of objective sleep latency. Furthermore, survival analysis should be employed to characterize associations with objective sleep latency, which represents time-to-event data.
Support (optional): NHLBI grants HL07578 and AG025553

0561

APPLICATION OF SNORING SEVERITY TO PREDICT EFFECTIVE CONTINUOUS POSITIVE AIRWAY PRESSURE FOR PATIENTS WITH OBSTRUCTIVE SLEEP APNEA PRIOR TO OVERNIGHT POLYSOMNOGRAPHY

Chirakalwasan N,[1] Ashizawa S,[2] Hlebowicz V,[2] Veeravikrom M,[3] Appel D[2]
(1) Albert Einstein College of Medicine, Bronx, NY, USA, (2) Albert Einstein College of Medicine, NY, USA, (3) King Chulalongkorn Memorial Hospital, Bangkok, Thailand

Introduction: Frequently, patients with suspected obstructive sleep apnea (OSA) have prolonged waits for overnight polysomnography (NPSG). Miljeteig and Hoffstein derived an equation to predict effective continuous positive airway pressure (e-CPAP) : = -5.12+ 0.13*BMI + 0.16*NC + 0.04*AHI. Their equation requires apnea hypopnea index (AHI). We propose using snoring intensity to predict e-CPAP.
Methods: We reviewed 125 charts of patients with NPSG confirmed OSA and NPSG-titrated e-CPAP. Body mass index (BMI), neck circumference, technician observed snoring intensity, AHI, NPSG-titrated e-CPAP among other variables were tabulated. We applied simple linear regression and Pearson's correlation co-efficients to explore the bivariate relationship between titrated e-CPAP and other covariates and multiple linear regression analysis to derive an equation to predict e-CPAP. Snoring Severity Score (SSS) (mild, moderate, severe snoring = 15, 30, 75 respectively) was substituted for AHI in the derived equation. For each patient, predicted and NPSG-titrated e-CPAP were compared. When predicted e-CPAP + 2.5 < NPSG-titrated e-CPAP, histograms were reviewed to determine AHI at predicted e-CPAP.
Results: Respectively, 12, 38, and 75 patients snored mildly, moderately, and severely.
Our derived equation, e-CPAP = 0.086*BMI + 0.029AHI + 5.989, and the SSS substitution for AHI predicted e-CPAP within +/- 2.5cm H2O of NPSG-titrated e-CPAP in 67% and 66% of our patients; Miljeteig´s equation in 49%. SSS derived predicted e-CPAP + 2.5 < NPSG-titrated e-CPAP in 25/125 patients. 15 of these 25 patients had AHI < 5 events/hour at predicted e-CPAP.
Conclusion: SSS predicted e-CPAP within 2.5 cm H2O of NPSG-titrated e-CPAP or predicted e-CPAP associated with AHI < 5 events/hour in all but 8% of our study cohort. SSS may prove clinically useful while patients wait for NPSG. SSS is a NPSG measurement, however, derived from technician observation. Prospectively, we are applying our technician´s methods to patients `observations to determine the clinical utility of our equation.

0562

THE ADDITION OF HEATED WALL TUBING PROVIDES MORE HUMIDITY AND COMFORT THAN STANDARD HEATED HUMIDIFIER CPAP UNITS

Almasri E, Kline L
Temple University, Pittsburgh, PA, USA

Introduction: Despite many advances in CPAP delivery, acceptance and adherence have been less than ideal. Heated humidification (HH), integrated into most CPAP units, improves patient acceptance and adherence to therapy, by suppressing annoying nasal symptoms. However, the levels of humidity provided by these devices vary greatly, and can only deliver humidity levels that ambient temperatures will allow. Adding more humidity results in "rainout" where excess moisture condenses in the tube. Even with HH, a sub-population continues to complain of nasal congestion. Heated wall circuits, used in ventilators, eliminate issues of inadequate humidification, providing physiological levels of heat and moisture. We wondered if patients on CPAP, provided with heated wall tubing (HWT) and a physiological level of HH would demonstrate higher acceptance and adherence rates than current HH systems
Methods: Twelve sleep apnea patients (RDI>15/h) were randomized after a titration PSG to receive CPAP either via a HWT/HH CPAP (Fisher & Paykel, SleepStyle 600, > 27 C), or a HH CPAP (Respironics REMstar, < 21 C, adjusted below tube “rainout.”). Patients were monitored for four weeks, and then crossed over to the alternate system for four weeks. After each month, compliance data (average h/night) and questionnaires gauging perceptions of treatment were obtained (21 realms; scale 1-5, worst to best).
Results: Patients reported significant reductions in nasal symptoms with HWT/HH vs. HH alone (nasal dryness 4.3 vs. 3.7, stuffiness 4.2 vs. 3.0, sinus pain 4.4 vs. 3.7; p<.05), and decreased claustrophobia (4.7 vs. 4.1), dry mouth (3.5 vs. 3.0), and tube “rainout” (4.1 vs. 3.5); (p<.05). Standard HH was not significantly better in any realm. However, compliance was not different in either treatment arm (3.4 h/night HWT/HH, 3.7 h/night HH; p>.05)
Conclusion: Compared with standard CPAP heated humidity, the addition of heated wall tubing provides a more physiologic and comfortable CPAP experience.
Support (optional): Fisher & Paykel Healthcare

0563

LIGHT-TO-MODERATE ALCOHOL DRINKING, SLEEP DISTURBANCE, AND SNORING

Baik I, Joo S, Kim S, Shin C
Korea University Ansan Hospital, Ansan, Gyeonggido, South Korea

Introduction: The effect of light-to-moderate alcohol drinking on sleep disturbance and snoring is unclear. We examined the association between alcohol drinking, sleep disturbance, and sleep-related events including snoring.
Methods: A cross-sectional study included 6,327 male and female Koreans aged 40 to 69 years from the Korean Genome Epidemiology Study. All individuals were free of major diseases, which are related to alcohol drinking or sleep disturbance, and did not habitually drink alcohol or caffeine-containing beverage before sleep. From May 2001 to February 2003, information was collected by interviewer-administrated questionnaires. Outcomes were sleep disturbances, snoring, sleep-related events, and daytime performance.
Results: We observed that light-to-moderate alcohol drinking (5.1-30g/day) was associated with insomnia, in particular difficulty getting back to sleep after awakening; the multivariate odds ratios [ORs] (95%

Confidence Interval [CI]) were 1.38 (1.06, 1.79) for insomnia and 1.45 (1.17, 1.80) for having sleep latency of 30 minutes and longer after awakening among light-to-moderate alcohol drinkers compared with never-drinkers. Light-to-moderate drinkers were more likely to snore, wake up due to the snoring, and disturb other persons due to the snoring than never-drinkers; the multivariate ORs (95% CI) were 1.26 (1.06, 1.48) for being called a snorer, 1.26 (1.04, 1.52) for disturbing other persons due to the snoring, and 1.37 (1.09, 1.71) for waking up due to the snoring. Similar associations were observed among heavy drinkers (>30g/day). Among light-to-moderate drinkers, no significant association was observed for subjective insufficient sleep, daytime performance, and sleep-related events such as teething, breathing difficulty, sweating, and shouting.
Conclusion: Alcohol drinking was associated with difficulty getting back to sleep after awakening, snoring, and awakening due to the snoring even among light-to-moderate drinkers who did not habitually drink alcohol or caffeine-containing beverage before sleep. These findings suggest that light-to-moderate drinking could be a modifiable risk factor for sleep disturbance and snoring.

0564

INCREASED CIRCULATING CELL-FREE DNA CONCENTRATION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

Kim J,[1] Lee S,[2] Kim J,[3] Jung K,[3] Kim S,[3] Yoon D,[1] Shin C[4]
(1) Pulmonary Sleep Disorder Center, Ansan Hospital, Korea University Medical Center, Ansan, Gyeonggi-do, South Korea, (2) Department of Clinical Laboratory Science, Korea University, Ansan, South Korea, (3) Korea University Medical Center, Ansan, Gyeonggi-do, South Korea, (4) Korea University Ansan Hospital, Ansan, Gyeonggido, South Korea

Introduction: Obstructive Sleep Apnea (SDB) is characterized by repetitive obstruction of the upper airway during sleep, has emerged as a significant and highly prevalent public health problem. Exposure to intermittent hypoxia/reoxigenation, occurring in association with OSA, has been proposed to be enhanced production of reactive oxygen speices (ROS) and the rapid oxidative stress propagation can result in molecular and cellular damage.
Circulatory cell-free DNA is increased in a variety of clinical pathologic condition such as sepsis, trauma, stroke, and cardiovascular disease. Although the exact mechanism for this reason, it is likely that cell death is one of the major factors.
These markers could be widely used as marker for detecting and monitoring several disorders. However, there is no study of clinical usefulness in patients with obstructive sleep apnea.Therefore, the purpose of our study was to examine the utility of plasma DNA as plasma based screening tool for the detection of OSA.
Methods: Totally, 186 subjects were participated in this study. All of them were performed full polysomnography. Mild to moderate OSA patients (n=35) were defined by 5< AHI<30nd severe OSA (n=51) by AHI≥30. Each of DNA extracted from plasma of subjects was analyzed for the beta globin gene with a fluorecense-based real time polymerase chain reaction (RT-PCR) for the quantification of plasma DNA concentration.
Results: As a result, patients with severe OSA have a significantly higher plasma DNA concentration than non-OSA (severe OSA vs.non OSA (median): 9.5 ug/L vs. 31ug/L,p<0.0001) Moreover, AHI was significant correlated with plasma DNA concentration (r=0.338, p<0.001)
Conclusion: Plasma DNA concentrations were correlated with OSA and may be a useful predictable marker of OSA.

0565

NEUROPSYCHOLOGICAL AND POLYSOMNOGRAPHIC CHARACTERISTICS IN SLEEP BREATHING DISORDER PATIENTS WITH INSOMNIA SYMPTOMS

Shin W,[1] Lee K,[2] Cha H,[3] Jang E,[1] Jung K[1]
(1) Department of Neurology, School of Medicine, Kyung Hee University, Seoul, South Korea, (2) School of Medicine, Kyung Hee University, Seoul, South Korea, (3) East-West Neo Medical Center, Seoul, South Korea

Introduction: Sleep breathing disorder patients commonly complains sleep maintenance insomnia or recurrent awakening with concomitant difficulty returning to sleep. Especially, obstructive sleep apnea-hypopnea syndrome (OSAS) patients associated with insomnia symptom experienced significantly more psychiatric disorder, cognitive-emotional symptoms, and physical and mental symptoms that disrupted or prevented sleep. We compared the clinical data and nocturnal polysomnography characteristics between OSAS patients with insomnia and without insomnia.
Methods: We reviewed the neuropsychological test and polysomnographic finding of 88 patients (81 men) with OSAS. All patients completed an overnight polysomnography with nasal pressure transducer, several sleep questionnaires, including Stanford Sleepiness Scale (SSS), Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), insomnia severity index and Beck Depression Inventory (BDI) and MMPI(Minnesota Multiphasic Personality Inventory).
Results: 38 patients (43.2%) reported clinically meaningful insomnia complaints. Compared to only OSAS patients, OSAS plus insomnia patients reported more prolonged sleep latency; poor sleep efficacy; decreased total sleep time; increased arousal index and body mass index; high Beck depression inventory score. But, there were no group difference in the apnea-hypopnea index and Epworth sleepiness scale.
Conclusion: Our results showed that Insomnia symptom is very common in OSAS patients and likely contributes to the impaired sleep continuity, Because of OSAS patients with insomnia have difficulty adapting to sleep breathing medical equipment, it is needed to have special attention in diagnosis and treatment of OSAS patients with insomnia complaint.

0566

EVALUATION OF A NEW NASAL EXPIRATORY POSITIVE AIRWAY PRESSURE (EPAP) DEVICE FOR THE TREATMENT OF SNORING AND OBSTRUCTIVE SLEEP APNEA SYNDROME.

Colrain I,[1] Brooks S,[2] Black J[3]
(1) SRI International, Menlo Park, CA, USA, (2) Stanford University, Palo Alto, CA, USA, (3) Stanford University, Stanford, CA, USA

Introduction: Many hypotheses have been generated concerning the mechanism(s) whereby CPAP reduces obstructive sleep apnea syndrome (OSAS) severity. Previous clinical studies have demonstrated that adding positive pressure during expiration only (EPAP), rather than throughout the respiratory cycle, is a promising treatment for OSAS. The present study tests this hypothesis using a new investigational device.
Methods: 31 subjects attended one of two sleep laboratories on two non-consecutive nights, one with and one without a nasal EPAP device (Ventus Medical Inc.). Devices were worn in each nostril, calibrated to provide between 6 and 9 cmH2O expiratory resistance. The order of nights was randomized and counterbalanced across subjects. All studies were scored blind to the condition, the design of the study and the nature of the device. Outcome variables included sleep architecture,

shifts to stage 1 and to wakefulness, typical nocturnal breathing measures and the time spent snoring independent of apneas or hypopneas. Two subjects were excluded from the analysis of the breathing variables due to being statistical outliers (Baseline AHI of 70.8 and 83.8 respectively).
Results: All measures of sleep architecture were unaffected by device use. Six subjects had an untreated AHI of <5, 5 subjects between 5 and 10, 12 subjects between 10 and 20 and 6 subjects >20 (maximum of 58 events per hour). t-tests including all subjects showed that time spent snoring decreased from 25±14% to 9±15% of the night (p <.001). AHI (p <.001), and O2DI (p <.01) decreased and minimum SaO2 increased (p<.01) with treatment. In subjects with untreated AHI > 10, AHI decreased from 25.2±16 to 10.0 ±8 (p <.001), SaO2 desaturation index decreased from 13.3±11 to 7.3±7 and SaO2 nadir increased from 81.3±8% to 85.8±7%.
Conclusion: The results indicate a clear therapeutic effect of nasal EPAP for snoring and for OSAS in patients across a wide AHI range.
Support (optional): Centus Medical Inc.

0567

EXPLORATORY FINDINGS: CPAP DEVICE COMPLEXITY IN THE TREATMENT OF SLEEP APNEA

Drummond C
Invacare Corporation, Elyria, OH, USA

Introduction: Continuous positive airway pressure (CPAP) applied to the nose is a standard treatment for patients with obstructive sleep apnea syndrome (OSAS); however, a variety of CPAP devices with a sometimes bewildering array of features and characteristics is available for prescription. Recent journal literature has suggested that inadequate manufacturer CPAP device descriptions and related clinical data has unnecessarily required physicians to become device algorithm experts. The present exploratory effort is an initial step to address: “Is more complexity necessarily better?” We combined subject exit interviews with a small clinical trial to gauge subject preferences for a simpified CPAP providing very-nearly constant pressure (maintained even during exhalation) to the patient. A favorable patient preference for reduced device complexity would simplify the OSAS education process from both the patient and clinical perspective.
Methods: A prospective eight-patient study was launched whereby patient sleep disturbance levels (determined from a full overnight sleep laboratory polysomnograph, PSG) were compared to exit interviews about device comfort and informal exploration of patient understanding of sleep therapy CPAP options. A very-nearly constant CPAP pressure was set in specific cases.
Results: Preliminary exit interview results on system comfort correlated well with PSG measurements of sleep disturbance levels. Patient knowledge of sleep hygiene and sleep disease corresponded with a short-term tolerance for device differences.
Conclusion: Higher patient awareness of sleep therapy options does not necessarily drive a preference for the most technically complex CPAP unit. Preliminary results from the study suggest that a certain patient cohort can indeed experience comfortable sleep with very-nearly constant pressure CPAP delivery. A research prototcol enabling statistically significant outcomes is now being developed.
Support (optional): This study was conducted and funded by the Invacare Corporation.

0568

PRELIMINARY STUDIES ON MAXILLOMANDIBULAR ADVANCEMENT AND UPPP TREAT THE OBESE PATIENTS WITH SEVERE OSAS

Lu X
Shanghai 9th Hospital, Medical Collage of Shanghai Jiao Tong University, Shanghai, Shanghai, China

Introduction: For Far East obese patients with severe obstructive sleep apnea syndrome (OSAS), Maxillomandibular advancement (MMA) procedures may cause craniomaxillofacial deformities after their jaws advancement in large distance though these procedures can resolve the upper airway problem. So combined surgery with uvulopalatopharyngoplasty (UPPP) and MMA in one stage is considered for these patients.
Methods: 7 cases of obese patients with severe OSAS, whose age 53.61±13.47, BMI 36.23±3.52 kg/m2, AHI 80.76±7.83 /h preoperatively. All patients underwent cephalometric analysis, PSG and estimate of velopharngeal closure and speech function preoperatively and 3.6 months postoperatively. All patients underwent UPPP and MMA in same term, which designed with Computer-Assisted Simulation System for Orthognathic Surgery (CASSOS) . Their maxilla advanced 9.34±3.23 mm by LeFort I osteotomy, and mandible moved forward 27.56±4.34mm by bilateral sagittal split ramus osteotomy and genioplasty.
Results: All seven patients' sleep-related breathing disorders was cured successively, whose AHI reduced to 3.36±1.24/h postoperatively, mean follow-up duration is 7.74 months. No speech/ swallow problem occured, meanwhile good teeth occlusion and good facial profile is achieved.
Conclusion: Our surgical procedures have good responds for the obese patients with severe OSAS in Far East People. Long term results need to be followed.

0569

ENDOTHELIAL DYSFUNCTION AND INFLAMMATORY REACTIONS OF OLDER AND MIDDLE-AGED ADULTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

Chung S,[1] Yoon I,[2] Shin Y,[3] Ahn H,[3] Lee C,[3] Kim J[4]
(1) Seoul National University Bundang Hospital, Seongnam, Gyeonggi, South Korea, (2) Department of Neuropsychiatry, Seoul National University Bundang Hospital, Seongnam, Gyeonggi, South Korea, (3) Seoul National University Bundang Hospital, South Korea, (4) Seoul National University Bundang Hospital, Seongnam, Kyunggi-do, South Korea

Introduction: To investigate whether endothelial dysfunction and inflammatory responses in obstructive sleep apnea syndrome (OSAS) were affected by age, we studied flow-mediated dilatation (FMD) and C-reactive protein (CRP) in older and middle-aged adults with OSAS.
Methods: This study enrolled 116 male subjects who were referred to a sleep laboratory to undergo nocturnal polysomnography (NPSG). After they finished NPSG, FMD was measured on the brachial artery and blood samples were obtained to determine serum CRP levels. All the subjects fasted at least 8 hours. We compared NPSG findings and determinant variables of FMD and CRP between the middle-aged (35-49 years old) and the older patients (>60 years old).
Results: There was no difference in the severity of OSAS between two age groups (X2=2.4, p=0.13). Between the middle-aged and the older patients, there were significant differences in FMD and diastolic blood pressure but not in BMI, systolic blood pressure, AHI, percentage of time below 90% O2 saturation, or serum CRP level. In the middle-aged

patients, percentage of time below 90% O2 saturation was a significant determinant of FMD (beta = -0.27, p = 0.02, R2 = 6%), and BMI was a significant variable to explain CRP (beta = 0.35, p<0.01, R2 = 11%,). In the older patients, hypoxemia-related variables such as oxygen desaturation index, average O2 saturation, and percentage of time below 90% O2 saturation were significant determinants of CRP (beta=1.25, beta=0.50, beta=-0.42, R2=55%). No variable was significantly correlated with FMD in the older patients.
Conclusion: In older adults with OSAS, nocturnal hypoxemia was strongly associated with CRP, which suggests that inflammatory responses in older adults are sensitive to hypoxic damage. That FMD is an early marker of endothelial dysfunction and endothelial function is impaired with aging itself might explain the finding that FMD was not associated with any parameter in the old adults with OSAS.

0570

RELATIONSHIP OF OCCURANCE OF FLOW LIMITATIONS AND AMOUNT OF PRESSURE RELIEF IN AN EXSPIRATORY PRESSURE RELIEF SYSTEM

Jerrentrup A,[1] Canisius S,[1] Jerrentrup L,[1] Becker H,[2] Kesper K,[1] Thomas P,[1] Vogelmeier C[1]
(1) Philipps-University Marburg, Internal Medicine, Marburg, Hessen, Germany, (2) Asklepios Klinik Hamburg-Barmbek, Hamburg, Germany

Introduction: Compliance with nasal continuous positive airway pressure (nCPAP) treatment may be reduced due to difficulties when exhaling against a positive pressure. The C-Flex system therefore lowers the expiratory pressure proportional to the patient´s airflow. To evaluate the theoretical concern that this might induce flow limitations during inspiration, we measured the occurrence of flow limitation during sleep.
Methods: 24 subjects (mean age 52.7 ± 8.5 years, mean cpap pressure 9.7 ± 1.7 cm H2O) with optimally treated obstructive sleep apnea (according to conventional polysomnographic criteria) were studied with polysomnography including respiratory flow and oesophageal pressure measurement. Conventional CPAP and the three pressure relief settings of C-Flex were applied in a randomised order both during NREM and REM sleep. Inspiratory flow limitation was measured with inspiratory pressure:flow relationships and defined as a period of decreasing flow rate with negative pressure dependence.
Results: 46669 breaths were analysed in total. The mean percentage of flow limited breaths in NREM sleep was 19.2% in CPAP mode and 18.4% in C-Flex mode. In C-Flex mode (all pressure relief settings) the average pressure reduction was 1.31 cm H2O in the expiration phase before an inspiratory flow limited breath vs. a 1.28 cm H2O pressure reduction before a non flow limited breath (difference not significant). In REM sleep the average pressure reduction was 1.44 cm H2O before an inspiratory flow limited breath vs. 1.27 cm H2O pressure reduction before a non flow limited breath (difference not significant).
Conclusion: These findings suggest that a CPAP therapy with a mean expiratory pressure relief of about 1.3 cm H2O is safe and sufficient compared with conventional CPAP therapy with regard to the occurrence of inspiratory flow limitations.
Support (optional): This study was supported by an unrestricted grant from Respironics, Inc.

0571

THE EFFECT OF NASAL SURGERY VIEWED IN MORPHOLOGICAL ANALYSIS IN PHARYNGEAL PORTION ON OBSTRUCTIVE SLEEP APNEA PATIENTS

Nakata S,[1] Noda A,[2] Morinaga M,[2] Yasuma F,[3] Nakashima T[2]
(1) Nagoya University, Nagoya, Aichi, Japan, (2) Nagoya University, Aichi, Japan, (3) National Hospital Organization Suzuka Hospital, AA

Introduction: The aim is to determine the effect of nasal surgery viewed in morphological portion on obstructive sleep apnea patients.
Methods: The inferior tubinectomy and/or submucous resection of the nasal septum were performed in 35 patients with OSAS (Male n=34). We classified and scored palate position and tonsil size according to Friedman's classification (Laryngoscope 109 1999), fauces according to Tsai's classification (Am J Respir Crit Care Med 167 2003), and retrogllosal portion according to Woodson's classification (Otoraryngol Head Neck Surg 120 1999) before nasal surgery. We investigated the relation between the improvement ratio of apnea-hypopnea index after nasal surgery and the score with upper airway in pharyngeal portion morphologically. A successful nasal surgery (responder) was defined as an apnea-hypopnea index improvement ratio of >=50%.
Results: There were 8 cases in responder group and 25 in non responder group. Averaged body mass index, age and nasal resistance after surgery in responder group were not significantly different from those in non responder group respectively. The grades of palate position, tonsil size, width of fauces and retrogllosal portion were not significantly different between responder group and non responder respectively. However, total score of 4 morphological cllasifications in grade was different between responder group and non responder significantly.
Conclusion: We suggested that the responder has the wider space in pharyngeal portion than the non respnder.
Support (optional): none

0572

THE CORRELATION BETWEEN NECK CIRCUMFERENCE AND SEVERITY OF OBSTRUCTIVE SLEEP APNEA IN ASIAN SUBJECTS

Lin C,[1] Christian G[2]
(1) Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taipei, Taiwan, (2) Stanford University, CA, USA

Introduction: Previous research has shown that male neck circumference over 43 cm and female neck circumference over 38 cm are more prone to have obstructive sleep apnea in White. This study want to discuss the relationship between neck circumference, age, body mass index (BMI), and severity of obstructive sleep apnea in Asian.
Methods: Subjects included male adults (n=1187, mean age 48.22±13.38) and female adults (n=355, mean age 50.91±14.72) evaluated with whole night laboratory polysomnography from 2005 to 2006. Obstructive sleep apnea (OSA) was defined as an apnea hypopnea index (AHI)≥5. Simple and multiple logistic regression analysis of Gender, BMI, age, neck circumference and severity of AHI were done.
Results: Male is higher than female in RDI(32.85±26.08, 20.75±25.65), BMI(27.26±5.41, 25.97±5.61), and neck circumference(40.46±3.53, 35.60±3.78) except age. Asian OSA male patients are less obese(75.3% BMI<30), less aging related(18%>60 years old), thick neck related(45% neck circumference>41cm). Asian OSA female patients are also less obese(74.2% BMI<30), more aging related(38.7%>60years old), less thick neck related(53% neck circumference<37cm). We found BMI>30 (27.96)had more chance to have OSA compare to Neck circumference>41 cm(11.74), age>60 years old(3.21), male(3.74) in Asian. Female patients were more prone to affected by age >60 years compare to male (14.97:1.82).
Conclusion: In this study, Asian male neck circumference over 41cm was more prone to have OSA, neck circumference of most Asian female OSA patient were below 37cm. Obesity (BMI>30) was the most important risk factor than old age(>60 years old), thick neck(>41cm), male sex. Female OSA patient seemed to be affected more by old age than male OSA patient.

0573

CAP ANALYSIS IN PATIENTS WITH CONTINUOUS FLOW LIMITATION COMPARED TO OBSTRUCTIVE SLEEP APNEA

Palombini L,[1] Lopes M,[2] Pereira D,[3] Guilleminault C,[4] Tufik S,[2] Yagihara F[5]
(1) Univ Fed Sao Paulo, São Paulo, Brazil, (2) Univ Fed sao Paulo, Sao Paulo, Sao Paulo, Brazil, (3) Univ Fed Sao Paulo, SP, Sao Paulo, Brazil, (4) Stanford University, Stanford, CA, USA, (5) Univ Fed Sao Paulo, SP

Introduction: CAP (Cyclic Alternating Pattern) has been recognized as an important tool for evaluation of sleep instability in normal sleep, as well as, to describe different sleep disorders. It has been suggested that Obstructive Sleep Apnea (OSA) and Upper Airway Resistance Syndrome (UARS) are sleep breathing disorders with distinct pathophysiology. The purpose of this study was to evaluate the role of CAP analysis parameters to describe the differences between OSA and UARS.
Methods: A group of 50 patients (25 UARS, 25 mild OSA) was analyzed. UARS was indicated by periods of continuous flow limitation and RDI <5 events/h . CAP analysis was performed with automatic analysis. Polysomnographic parameters: sleep architecture, sleep fragmentation (arousal index, WASO), respiratory parameters (AHI, lowest oxygen saturation) and CAP analysis (CAP rate, CAP subtypes A1, A2, and A3). CAP rate analysis was performed by automatic analysis (Somnologica Program-Embla System). Patients were matched by age and BMI. Statistical analysis: T test for independent samples.
Results: Patients were matched for age and BMI. Age: 30 to 50 years old, BMI: 25 to 27 mg/Kg2 .Polysomnographic Group 1 (UARS): CAP rate 61, 5 ± 20. Group 2 (mild OSA): 56 ± 3, 7. A1 subtype was also increased in UARS compared to OSA. UARS: 49, 6 ±19, 8, OSA: 43, 1 ±18.
Conclusion: UARS patients characterized by periods of continuous flow limitation present increased CAP rate compared to mild OSA. They also show an increase in CAP A1 subtype, which is constituted of predominant synchronized EEG pattern. It may be suggested that the increase in A1 subtype may indicate a “defense mechanism” from sleep function to maintain sleep and prevent sleep fragmentation in these patients, which decrease its efficiency with increased severity the sleep breathing disorder during sleep.
Support (optional): Supported by AFIP/FAPESP/CEPID

0574

THE REDUCTION IN END-EXPIRATORY LUNG VOLUME AT SLEEP ONSET IN OBSTRUCTIVE SLEEP APNEA

Jordan A,[1] Yim S,[2] Schory K,[2] Smith S,[2] Malhotra A,[3] White D[4]
(1) Brigham and Women's Hospital, Boston, MA, USA, (2) MA, USA, (3) Brigham and Women's Hospital, MA, USA, (4) Boston, MA, USA

Introduction: End expiratory lung volume (EELV) has previously been shown to fall approximately 400mls below the waking level by 15 minutes after sleep onset in healthy individuals. Experimentally induced reductions in EELV have been shown to worsen obstructive sleep apnea (OSA), increase the CPAP level required to eliminate flow limitation and compromise pharyngeal mechanics. Thus the sleep related fall in EELV may contribute to airway collapse during sleep. However, the transition from wakefulness to sleep is of particular interest since OSA events often occur at this time. In this study we aimed to measure the reduction in EELV in OSA patients and healthy controls at the transition from wakefulness to sleep.
Methods: To date 13 patients with previously diagnosed OSA have been studied in the supine position overnight. Electroencephalogram (EEG), electro-oculogram and chin electromyogram were recorded to stage sleep and identify the transition from wake (3 to 5 breaths of alpha EEG activity) to sleep (2 to 5 breaths/respiratory efforts with theta EEG activity). Changes in EELV were assessed with chest and abdomen magnetometers that were calibrated with a mask and pneumotachograph.
Results: Analysis is complete on 5 patients with OSA (Mean ± SEM; AHI = 51.5 ± 11 events/hr). EELV was assessed over 4-8 transitions from stable wakefulness to sleep in each subject. The EELV fell 68 ± 20 mls by the second respiratory effort/breath during sleep (compared to the 3rd breath prior to the sleep onset transition). However, this reduction was quite variable (range 5-113mls) and appeared to be related to BMI ($R^2 = 0.58$) with heavier subjects having greater reductions in EELV at sleep onset.
Conclusion: Although more data are clearly required, these findings suggest abrupt changes in lung volume at the alpha-theta transition may have important implications for sleep apnea pathogenesis.
Support (optional): NIH P50HL60292, NCRR GCRC RR01032 and American Heart Association 0635318N.

0575

ARE SURGICAL PATIENTS WITH DIFFICULT INTUBATION CANDIDATES FOR SLEEP CLINIC REFERRALS?

Chung F,[1] Yegneswaran B,[1] Herrera F,[2] Shenderey A,[2] Shapiro C[3]
(1) University of Toronto, Toronto, Ontario, Canada, (2) , (3) University Health Network, Toronto, Ontario, Canada

Introduction: Upper airway abnormalities are described with obstructive sleep apnea (OSA) and difficult tracheal intubations. Both conditions contribute to significant clinical problems and have increased morbidity and mortality. In a small retrospective study of 15 patients, Hiremath et al found the prevalence of sleep apnea syndrome was 53% in patients with difficult intubation. We hypothesized that patients who present with difficult intubation may have a very high incidence of OSA and patients with difficult intubation should be referred to sleep physicians for polysomnography (PSG).
Methods: Hospital ethics approval was obtained. Patients classified as grade 3 and 4 according to Cormack and Lehane direct laryngoscopic view or patients who required two or more attempts for successful endotracheal intubation were referred by anesthesiologists at four hospitals. Informed consent for overnight polysomnography was obtained from these patients when they had recovered from surgery. Data on Apnea-Hypopnea Index (AHI) and postoperative events were collected. Patients with AHI > 10 per hour were considered positive for OSA. Clinical and polysomnographic variables were compared between difficult intubation with and without OSA using t-tests. $P < 0.05$ was considered as statistically significant.
Results: Over a fifteen-month period, 83 patients with difficult intubations were referred by anesthesiologists. Thirty two patients agreed to participate and 48 patients refused, 3 had a previous diagnosis of sleep apnea. 56% (18/32) of the patients with difficult intubation were diagnosed to have AHI > 10. There were no significant difference in age and ASA status between the OSA group and non-OSA group. There was significant difference in gender, BMI, neck size and postoperative complications between the OSA group and non-OSA group.
Conclusion: Fifty six percent of patients with difficult intubation were diagnosed to have OSA. Thus surgical patients with difficult intubation are worthy candidates for sleep clinic referrals for PSG.

0576

POLYSOMNOGRAPHIC VARIABLES ON DIAGNOSIS DO NOT PREDICT PAP ADHERENCE

Freitas J,[1] Arnedt J,[2] Millman R,[3] Hoyt B,[1] Lee-Chiong T,[4] Aloia M[1]
(1) National Jewish Medical and Research Center, Denver, CO, USA, (2) University of Michigan, MI, USA, (3) Brown Medical School, RI, USA, (4) National Jewish Center, Denver, CO, USA

Introduction: Positive Airway Pressure (PAP) is the most commonly used form of treatment for OSA, but adherence is poor. Previous studies have attempted to predict adherence using sleep variables, self-reported outcomes, and psychological constructs associated with behavior change. One study found that adherence was best in those patients with the greatest sleep improvement on the CPAP titration night. We examine whether standard polysomnography (PSG) variables on the diagnostic night predicted long-term adherence.
Methods: One hundred seventy-eight medically and psychiatrically healthy OSA patients (62 women, mean age 50.4 (sd 10.9) years, mean AHI 44.3 (sd 24.8)) were recruited. All participants were PAP naïve. Participants underwent a full-night diagnostic PSG ,which was followed by an additional full night for PAP titration. Adherence was monitored objectively using an internal microprocessor housed within the PAP device, which was capable of monitoring nightly PAP use at the prescribed pressure. Visual stage scoring was conducted according to standard criteria. Average 6-month use was calculated and used as the dependent variable.
Results: Average PAP use at 6 months was 3.98 hours per night (sd 2.40). The average minutes spent in various stages were: stage 1, 13.3 (sd 11.3); stage 2, 214.3 (sd 60.3), stages 3/4, 55.0 (sd 34.0), REM 54.3 (sd 31.0). Total sleep time, percentage time spent under 90% oxygen saturation, and arousal index were also scored following standard criteria. No single PSG variable correlated significantly with 6-month adherence.
Conclusion: Standard PSG variables on the diagnostic night do not predict long-term adherence to PAP. It is possible that more refined analysis of EEG variables would reveal different findings. The primary differences between this and the previous study were that this study only examined diagnostic PSG variables and the previous study used adherence over a shorter time period.
Support (optional): This research was supported by a grant from the National Heart, Lung and Blood Institute (R01 HL67209)

0577

WHAT IS THE BEST OBSTRUCTIVE SLEEP APNEA (OSA) SCREENING TOOL FOR PRE-SURGICAL PATIENTS?

Yegneswaran B,[1] Chung S,[2] Khajehdehi A,[1] Islam M,[1] Shapiro C,[2] Chung F[1]
(1) University of Toronto, Toronto, Ontario, Canada, (2) University Health Network, Toronto, Ontario, Canada

Introduction: The American Society of Anesthesiologist (ASA) has identified the need for anesthesiologists to screen patients for OSA preoperatively to reduce the risk of perioperative adverse outcome. However polysomnography (PSG) is not feasible for the screening of all surgical patients. The ASA taskforce classifies OSA as AHI>5 and has suggested a checklist to identify undiagnosed OSA. The Berlin questionnaire (BQ) was developed for OSA screening in primary care patients. The OSA questionnaire (OSAQ) is a new short-form screening tool. The purpose of this study was to validate the BQ, the OSAQ and the ASA checklist in surgical patients.
Methods: Hospital ethics approval was obtained. All preadmission clinic patients, age>18 yrs, ASA I-IV, were screened with the BQ, OSAQ and ASA checklist. The ASA, a 16-item checklist, has 3 categories: predisposing physical characteristics, symptoms, and complaints that encompass the common features of OSA. The validity of the BQ, OSAQ, and ASA checklist was assessed by comparing their sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) using AHI as the gold standard. McNemar's test was used to analyse the agreement between the 3 instruments and the AHI data.
Results: 94 patients were studied with the BQ, OSAQ, ASA checklist and PSG. The BQ, OSAQ and the ASA checklist had a sensitivity of 0.65, 0.65, 0.68; specificity of 0.5, 0.54, 0.39; PPV of 0.75, 0.77, 0.73 and NPV of 0.38, 0.39, 0.34, respectively, at an cutoff of AHI>5. Using McNemar's test to analyse the measure of agreement between AHI and the 3 screening instruments separately, all 3 instruments agreed with the AHI in diagnosing OSA patients ($p>0.05$).
Conclusion: Using PSG as the gold standard in OSA diagnosis, the BQ, OSAQ, and ASA checklist concur with AHI results and are equally able to identify patients with OSA in the preadmission clinic.

0578

COMBINATION OF TRANSPALATAL ADVANCEMENT PHARYNGOPLASTY AND UVULOPALATOPHARYNGOPLASTY FOR OBSTRUCTIVE SLEEP APNEA

Jingying Y,[1] Biao Y,[2] Jingming L,[3] Guo-Ping Y,[3] Xiao-Yi W,[3] Liman W,[3] Xinli S[3]
(1) beijing tongren hospital, Beijing, China, (2) peking university hospital of stomatology, Beijing, China, (3) Beijing, China

Introduction: Patients with OSAHS and bony nasopharynx cavity narrowing were underwent H-UPPP plus concomitant transpalatal advancement pharyngoplasty, the effects of the operations and the causes of failure were investigated.
Methods: Thirty two male patients, aged 39.09±7.75 in mean, were included in the study. Their mean BMI was 29.02±3.57 kg/m2, preoperative AHI was averaged 61.75±21.92 times/hr, the mean nadir oxygen saturation was 0.64±0.13. Bony nasopharynx cavity narrowing was confirmed by preoperative endoscopies and Cephalometry studies. All patients had H-UPPP and concomitant transpalatal advancement pharyngoplasty. 14 patients who had tongue-base obstruction underwent chin advancement. Patients combined with nasal disorders had endoscopic sinus surgery in one month after operation. All patients were followed by polysomnography six month after operation. The criterion to estimate effects was as follow: effective, the decrease percent of AHI reach or more than 25%; significant effective, the decrease of AHI reach or more than 50% or postoperative AHI was less than 20/h; cure, postoperative AHI reach or less than 10/h.
Results: Twenty seven patients(84.4%) were effective and 22 of them were significant effective(68.8%),15 patients were cured(46.9%),including 8 patients with AHI less than 5/h after operation. The other 5 patients were ineffective (15.6%).
Conclusion: Combination of transpalatal advancement pharyngoplasty and H-UPPP can improve the responding rate and improve cure rate in some patients with pure retropalatal airway narrowing. Of the 15.6% patients who were ineffective, their retropalatal airway sizes were also enlarged markedly. the failure may due to the neuromuscular disorder of upper airway dilator muscles in these patients.

0579

OSA QUESTIONNAIRE: DEVELOPMENT OF A NEW SHORT-FORM SCREENING TOOL FOR OBSTRUCTIVE SLEEP APNEA (OSA) PATIENTS

Yegneswaran B,[1] Chung S,[2] Islam M,[1] Khajehdehi A,[1] Shapiro C,[2] Chung F[1]
(1) University of Toronto, Toronto, Ontario, Canada, (2) University Health Network, Toronto, Ontario, Canada

Introduction: Anesthesiologists are concerned about the implications of obstructive sleep apnea (OSA) among surgical patients. Therefore a concise screening tool for OSA would better serve busy anesthesiologists. The Berlin Questionnaire (BQ) was developed for OSA screening in primary care. The OSA questionnaire (OSAQ) is a new short-form screening tool developed for pre-surgical OSA screening. The objective of this study was to compare the OSAQ and BQ for OSA screening in surgical patients by validating these questionnaires against AHI obtained from polysomnography (PSG).
Methods: Hospital ethics approval and informed consent was obtained. All eligible preadmission clinic patients, age ≥18 years, ASA I-IV, were screened for OSA with the BQ and OSAQ. The BQ consists of 9 items regarding snoring, witnessed apneic events, daytime sleepiness and falling asleep while driving. The OSAQ contains 4 questions: “Has anyone noticed that you stop breathing during sleep?”, “Do you snore loudly?”, “Do you feel tired during the daytime almost every day?”, “Do you have or are you being treated for hypertension?” Based on these questionnaires, all participants were stratified into high or low risk OSA groups.
Results: 2426 patients were screened with the BQ and OSAQ. The BQ identified 23.4% (567/2426) whereas the OSAQ identified 22.3% (541/2426) as being at high risk for OSA. 2003 patients were invited to undergo PSG study, 223 patients gave informed consent and 1704 patients refused. 94 patients completed the study. Mean age 57± 13 years (range18-86 yrs), 51% male, 44% female and ASA I: 7.4%, II: 50%, III: 40.4%, IV: 2.2%.With PSG, 43.6% (41/94) of patients were diagnosed to have AHI >10 /hr. The sensitivity and specificity of BQ was 0.66 and 0.46 and of OSAQ was 0.68 and 0.51.
Conclusion: OSA questionnaire is more concise and it has similar sensitivity and specificity to BQ.

0580

DO COGNITIVE FUNCTIONS PROVIDE EVIDENCE FOR A "VERY SEVERE" GROUP AMONG SEVERE OSA PATIENTS?

Hoyt B,[1] Freitas J,[1] Arnedt J,[2] Millman R,[3] Lee-Chiong T,[4] Aloia M[1]
(1) National Jewish Medical and Research Center, Denver, CO, USA, (2) University of Michigan, MI, USA, (3) Brown Medical School, RI, USA, (4) National Jewish Center, Denver, CO, USA

Introduction: Traditional severity categories in OSA leave a wide range of individuals in the severe group (AHI 30 or greater). This group may possibly be divided further based on functional abilities. Our goal was to see if this was possible using cognitive functions.
Methods: One hundred sixty-nine medically stable, PAP naïve severe OSA patients (AHI >=30, 59 women, mean age 50.5 (sd 11.6)) were recruited. Participants underwent a full-night diagnostic PSG and full-night PAP titration. Baseline cognitive measures of attention, memory, executive functions, and motor coordination were administered prior to treatment. The group was divided based on distribution of AHI scores and compared on baseline cognitive measures to determine the need for a very severe categorization.
Results: Participants were categorized into mildly severe (AHI 30-44), moderately severe (AHI 45-65), and very severe (AHI 66-125) groups. Groups were similar in subjective sleepiness, functional outcomes of sleepiness, education, and estimated verbal IQ. The very severe group had a significantly higher body mass index (BMI) than the other two groups (very severe 38.3, moderately severe 34.6, mildly severe 34.3, $p < .01$). The mildly severe group was significantly older than the other two groups (very severe 47.7, moderately severe 49.5, mildly severe 54.2, $p < .01$). Using T-scores to control for age, group differences were observed only on measures of initial verbal learning ($p < .01$) and a timed executive function task (trend $p = .07$), with the very severe group performing worse than the other two groups. Group differences remained after controlling for BMI.
Conclusion: Little evidence distinguished among severe OSA patients based on cognition, although some individuals with an AHI over 65 demonstrated greater difficulty with initial learning and executive functions. Further division among severe OSA patients may be possible based on other outcome variables, such as cardiovascular disease markers.
Support (optional): This research was supported by a grant from the National Heart, Lung and Blood Institute (R01 HL67209)

0581

EXPLORING THE EXPERIENCE OF PATIENTS NEWLY DIAGNOSED WITH OBSTRUCTIVE SLEEP APNEA (OSA) AND INITIATING CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) THERAPY.

Moore W, Dose A, Olson E, Slocumb N, Sikkink V, Heim-Penokie P, Ryan K, Tucker S
Mayo Foundation for Medical Education and Research, Rochester, MN, USA

Introduction: OSA is a chronic condition in which enhancement of patient self-efficacy is important for successful long-term management. We are in the process of developing a patient education video geared to promote self-efficacy and knowledge of chronic management of OSA. As part of that development process, we have been collecting data on the perceptions of newly diagnosed OSA patients about to embark on a trial of CPAP. Herein, we report the data on patients´ insights into their initial sleep evaluation, effects of OSA on health, and of CPAP.
Methods: Patients with newly diagnosed OSA starting on CPAP were approached to participate in our prospective larger study developing an education video for chronic management of OSA. As part of the qualitative arm in the pilot process, subjects underwent semi-structured, audiotaped interviews at the time of their 1 month CPAP recheck visit. Verbatim transcript responses were coded and grouped into themes to reflect experiences of participants.
Results: Twelve individuals (7 males, 5 females) participated in the interviews. As for expectations about their sleep center visit, most (67%) hoped for improvements in their overall quality of life. Patients reported varying effects of OSA on overall health, such as exhaustion (83%). Others thought their current health status was normal (33%), and some recognized links with cardiovascular status (25%). Reactions to CPAP initiation ranged from outright fear (25%) and disappointment (17%), to seeing it as the lesser of two evils (42%) or being open (50%) and hopeful (42%) about therapy.
Conclusion: Study participants recognized the impact of sleep apnea on their overall quality of life. The significant number of negative initial responses suggests that the ability to effectively educate patients about CPAP is of paramount importance.
Support (optional): This study was funded by the Education Research Committee and the Department of Nursing Research. Mayo Clinic College of Medicine, Rochester, MN.

0582

RESPIRATORY COMPLICATIONS AMONG OBSTRUCTIVE SLEEP APNEA (OSA) PATIENTS WHO UNDERWENT SURGERY

Liao P, Yegneswaran B, Vairavanathan S, Zaki A, Chung F
University of Toronto, Toronto, Ontario, Canada

Introduction: Obstructive Sleep Apnea (OSA) is presumed to be a risk factor for perioperative morbidity and mortality. At present the data quantifying the magnitude of perioperative complications due to OSA is very limited to make any major correlations. This retrospective study is designed to document the occurrence of perioperative respiratory complications among surgical patients with OSA.
Methods: Hospital ethics approval was obtained. All OSA patients age >18 years who underwent surgeries other than uvulopalatopharyngoplasty in 3 hospitals of University Health Network for 15 years from1990 to 2005 were selected. Chart review and data analysis was focused on respiratory complications which included desaturation (mild: SaO2 ≤ 95%, severe: SaO2 ≤ 90%), pulmonary edema, bronchospasm and re-intubation. The treatments for the complications were also documented.
Results: 275 charts were reviewed: age: 55 ± 13 years; male: 75%; female: 25%; BMI: 34.9 ± 9.6 kg/m^2 and ASA status I: 2%, II: 35%, III: 50%, IV: 13%. The major pre-existing diseases were: hypertension (47%), GERD (27%), coronary artery disease (26%), obesity (24%) and diabetes (22%). 64% OSA patients were on home CPAP.
The incidence of respiratory complications was 32% (n = 88).The most common was desaturation which was seen in 84 (26.6%) patients (Mild: n=42, Severe: n=42). Other complications were pulmonary edema (2.6%), bronchospasm (2.2%), and pneumothorax (0.7%). As a result of the complications, 36.4% patients needed prolonged oxygen therapy during their postoperative period; 26% patients who had not be on home CPAP required CPAP postoperatively; 6 patients had unplanned ICU admission of whom 1 patient had to be re-incubated and 2 patients had episodes of hypercapnea.
Conclusion: OSA surgical patients had a high incidence of perioperative respiratory complications (32%) and extra treatment was often required.

0583

IMMEDIATE EFFECT OF ACUPUNCTURE ON THE SLEEP ARCHITECTURE OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

Freire A,[1] Sugai G,[2] Togeiro S,[2] Yamamura Y,[2] Mello L,[2] Tufik S[2]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, SP

Introduction: The objective of this study was to investigate the immediate effect of manual acupuncture and electro acupuncture (EA) 2Hz and 10Hz on the sleep pattern of 40 patients, aged 30-68 years, with obstructive sleep apnea assessed by polysomnography.
Methods: It was a randomised, placebo-controlled, single blind study, with blinded evaluation. 40 patients presenting an apnea-hypopnea index (AHI) of 15 to 30 per hour, assessed by polysomnography participated in the study. All procedures were done in the Public Hospital of the Universidade Federal de Sao Paulo, Brazil, in the Division of Sleep Biology and Medicine of the Department of Psychobiology, between July 2005, and October, 2006. Patients were randomly assigned to four groups: manual acupuncture group (n= 10); electro acupuncture 2Hz group (n= 10); electro acupuncture 10Hz group (n= 10), and the control group, receiving no treatment (n= 10). The patients received manual acupuncture or electro acupuncture (2Hz or 10Hz) just before the polysomnography study at 9 pm.
Results: The AHI (P= 0.005), the apnea-index (P= 0.007) and the number of respiratory events (P= 0.005) decreased significantly in all treated groups when compared to the non treated group, but the electro acupuncture 2Hz group had significant improvement compared with the other treated groups.
Conclusion: Both manual acupuncture and EA 2Hz and 10Hz applied in the night of the polysomnography diminished the AHI of patients with moderate OSAS.
Support (optional): AFIP, FAPESP/CEPID

0584

EFFECT OF CARDIAC RESYNCHRONIZATION THERAPY ON SLEEP ARCHITECTURE AND SLEEP QUALITY IN PATIENTS WITH CHRONIC HEART FAILURE AND SLEEP DISORDERED BREATHING AND PREDICTIONS FROM THE REM AHI

Burschtin O,[1] Rapoport D,[1] Chinitz L,[1] Ferrick K,[2] Magnano A,[3] Stahl L,[4] Kwok J,[5] Pu Y[6]
(1) New York University, New York, NY, USA, (2) Montefiore Hospital Medical Center, NY, USA, (3) Columbia University, NY, USA, (4) Boston Scientific, MN, USA, (5) Boston Scientific, Minneapolis, MN, USA, (6) Minneapolis, MN, USA

Introduction: CRT is an established therapy for drug refractory congestive heart failure (CHF), which is often associated with central sleep disordered breathing (SDB). CRT can improve cardiac function, cardiopulmonary capacity, depression and quality of life, and would be expected to reduce central but not obstructive SDB. However, distinguishing between central and obstructive events (particularly hypopnea) may be difficult on standard polysomnography. One differential point is that central events tend to disappear during REM, whereas obstruction tends to worsen. The present study evaluated the impact of CRT on sleep architecture, sleep quality and stage specific AHI in patients with CHF and SDB.
Methods: Patients with indications for CRT had device implantation and underwent full lab polysomnography (including the use of nasal cannula) prior to and after 3 months of CRT pacing. Apnea and hypopnea were scored manually to calculate AHI-total, AHI-central and AHI-obstructive for total and REM sleep. Other sleep variables assessed for change included time in bed (TIB), total sleep time (TST), sleep efficiency (SE), %time in each sleep stage and measures of hypoxia.
Results: 22 patients completed the 3-month follow-up. Group means for AHI-total, AHI-central, AHI-obstructive, mean and min SpO2, time of SpO2<85% did not change. Only patients who at baseline had a fall in AHI during REM showed significant improvements in AHI-total with CRT. However, TST and SE increased significantly ($p<0.05$) as did %stage2 ($p<0.001$) while %wake decreased significantly ($p<0.05$) for the entire group and %stage1, %delta and %REM did not change significantly.
Conclusion: While mean apnea indices and hypoxic condition of the cohort were unchanged after CRT, sleep quality and architecture improved. The effect of REM on AHI may be a useful predictor of patients in whom CRT improves SDB, as it may identify central control mechanisms (susceptible to suppression by REM) which differ from those affecting obstructive events. Confirmation of these findings is required.
Support (optional): Boston Scientific

0585

SPLIT NIGHT STUDIES- PASS OR FAIL?

Brown T, Johnson S
St. Joseph Memorial Hospital Sleep Disorders Center, Murphysboro, IL, USA

Introduction: Split studies have been used in many sleep facilities. The method is to let the patient sleep at least 2 hours during the diagnostic part of the study, then institute the CPAP titration. Splits have advantages and disadvantages. Split studies may fail to give us an adequate baseline Apnea/Hypopnea index since our criterion of Apnea/Hypopnea index greater than or equal to 5 is traditionally defined as over longer than 2 hours of sleep.
Methods: We defined a successful split study as follows: 1) The patient slept at least two hours (Medicare rule) during the diagnostic part of the study, and clearly met criteria for sleep apnea (Apnea/Hypopnea index greater than or equal to 5), and 2) A pressure was determined that reduced Apnea/Hypopnea index to < 5. We chart reviewed 50 consecutive split studies performed in our lab between 1/1/05 and 12/1/06 to determine success rate.
Results: 56% (28) of splits were successful according to the criteria. 44% (22) split studies were not successful. 34% (17) met only criteria 1. 2% (1) met criteria 2 only. 8% (4) met neither criteria. Number of patients who met both criteria, but had no REM sleep during titration were 4% (2). 52% (26) met both criteria and had REM sleep. All splits showed an Apnea/Hypopnea index of 40 or greater during the diagnostic portion.
Conclusion: In our studies performed by registered polysomnographic technicians in an accredited lab, splits were successful only 56% of the time. Several of these studies were made successful by allowing the patient to sleep longer than the usual termination of testing time. Some patients are unable to do this. Clearly having enough titration time is an issue with splits. Rarely the tech may not realize that the patient has not slept 2 hours before CPAP is begun.

0586

OVERNIGHT CHANGES IN EXHALED NITRIC OXIDE: EFFECT OF SLEEP FRAGMENTATION AND BODY MASS INDEX

Sethi J,[1] Givelber R,[1] White A,[2] Robinson L,[2] Arena V,[1] Choi A,[2] Zhang Y,[2] O'Donnell C,[2] Kelley D,[2] Sanders M[1]
(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Introduction: We assessed the effects of sleep fragmentation and BMI on end-expiratory nitric oxide (EE-NO), a marker of oxidative stress, in subjects without Sleep Disordered Breathing (SDB).
Methods: 17 healthy subjects, 8 with normal weight (ages 20-56; BMI 18.8-24.6) and 9 overweight subjects (ages 19-47; BMI 27.8-35.2) underwent a 4 night, 3 day protocol. Polysomnography: Nights (N)1-4. N1: SDB screening, acclimatization. N2: Undisturbed sleep. N3 and N4: Induced sleep fragmentation. EE-NO was measured prior to sleep on N2 and N4, and the next mornings. Changes in EE-NO were evaluated for statistical significance with the Wilcoxon signed rank test; the Wilcoxon Mann-Whitney test assessed differences between normal and overweight groups.
Results: Polysomnography Variables (mean±SD):
Apnea+Hypopnea Index: N2 = 1.4 ± 1.1; average N3-4 = 2.8 ± 2.5 (p < 0.001).
Arousal Index: N2 = 8.8 ± 3.2; average N3-4 = 26.4 ± 4.6 (p <0.0001).
Total Sleep Time, min.: N2 = 424.0 ± 74.4; average N3-4 = 389.4 ± 65.8 (p < 0.005).
Mean SpO2 during sleep: N2 = 97.2%, average N3-4 = 97.1% (p < 0.373).
EE-NO (median values):
EE-NO increased significantly across N2 (2.3 ppb, p=0.017) and N4 (1.4 ppb, p=0.035). The overnight increase in EE-NO did not differ between N2 and N4 (p=0.712).
Normal and overweight subjects did not differ with regard to the magnitude of change in EE-NO either on N2 (p=0.606) or N4 (p=0.743).
There was no significant difference in the magnitude of EE-NO increase over N2 vs. N4 in either the normal (p=0.312) or overweight (p=0.164) subjects.
Conclusion: In subjects without clinically significant SDB, overnight sleep is associated with increased EE-NO, perhaps related to increased oxidative stress. Moderate sleep fragmentation and higher BMI do not modify these increases.
Support (optional): RO1 AG023977, M01-RR000056.

0587

PREVALENCE OF RESIDUAL EXCESSIVE SLEEPINESS IN OBSTRUCTIVE SLEEP APNEA PATIENTS TREATED BY CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

Pepin J,[1] Escourrou P,[2] Meslier N,[3] Sapene M,[4] Levy P,[5] Krieger J,[6] Dervaux B,[7] Lenne X,[8] Mallart A[7]
(1) Sleep Laboratory and EFCR, Grenoble University Hospital, Grenoble, France, GRENOBLE CEDEX 09, France, (2) other fields, Clamart, France, (3) other fields, Angers, France, (4) Other fileds, Bordeaux, France, (5) Other fields, Grenoble, France, (6) Other fields, Strasbourg, France, (7) other fields, Lille, France, (8) Other field, Lille, France

Introduction: Sleepiness is a common symptom in apneic patients usually relieved by CPAP treatment. The percentage of compliant CPAP-treated patients who continue to experience excessive sleepiness has not been precisely established.
Methods: This cross sectional observational study measured the prevalence rate of residual excessive sleepiness (RES) as defined as an Epworth Sleepiness Scale (ESS) score ≥11. OSA patients using CPAP >3 h per night referred for their usual one-year follow-up visit were eligible. ESS and polysomnographic data at diagnosis as well as anthropometric items, symptoms, quality of life and depression scales and objective CPAP compliance were collected.
Results: A total of 502 patients from 37 French sleep centres were included. Sixty patients remained sleepy on CPAP (ESS = 14.3 ± 2.5) leading to a prevalence rate of RES of 12.0% (CI 9.1-14.8%). Patients with RES were younger (age: 56 ± 12 vs. 60 ±11 years, p < 0.008) and more sleepy at diagnosis (ESS: 15.8 ± 4.6 vs. 11.3 ± 4.8, p < 0.01). Conversely, there was no difference in terms of BMI or CPAP compliance (6.1hrs ± 1.3 vs. 6.5hrs ± 2.9). After having excluded clinically or by polysomnography restless leg syndrome, major depression and narcolepsy as confounding diseases, the final prevalence rate of RES was 8.4% (CI 5.9-10.8%). Excepted pain domain, all the others Nottingham Health Profile domains were two fold more impaired in patients with RES (p < 0.01). In a subgroup of 361 who completed ESS before and after treatment 59% of the patients had an ESS ≥11 before CPAP and among them 10.8% had RES after CPAP treatment. The relative risk for having RES is 5.3 ([CI: 1.6-22.1] p<0.0001, MacNemar Test) when ESS before treatment was ≥11.
Conclusion: As 160 000 OSA patients are currently treated in France by CPAP, one can estimate that more than 13 000 of them still suffer of residual excessive sleepiness and could benefit from an adjunct therapy.

0588

ASSESSMENT OF CEREBRAL SENSORY PHARYNGEAL PROJECTIONS BY FUNCTIONAL MRI: APPLICATION TO THE PATHOPHYSIOLOGY OF OBSTRUCTIVE SLEEP APNEA

Dematteis M,[1] Bootz A,[1] Lamalle L,[2] Tropres I,[2] Krainik A[2]
(1) Sleep and HP2 Laboratories - INSERM ERI17 UJF EA3745, Grenoble, France, (2) MRI Department, IRM 3T, IFR1, Grenoble, France

Introduction: Obstructive sleep apnea syndrome is associated with cerebrovascular morbidity and is characterized by pharyngeal occlusions caused by anatomical and/or functional factors compromising the pharyngeal dilator reflex (PDR). Pharyngeal sensitivity participates to the control of pharyngeal patency and has been shown to be impaired in apneic patients. While pharyngeal neuropathy, a peripheral cause of decreased pharyngeal sensitivity, has been investigated, impairment of the cerebral integration of pharyngeal sensory informations that may contribute to PDR dysfunction has been poorly assessed due to methodological limitations. To specifically address these concerns, we present a new method assessing cerebral sensory pharyngeal projections using functional magnetic resonance imaging (fMRI).
Methods: Functional MRI using BOLD method (3Tesla, gradient-echo EPI sequences) was performed in five healthy volunteers and in one apneic subject who were unilaterally stimulated at the soft palate using a device previously developed for measuring pharyngeal sensation. The oral device was combined to an air source delivering small air puff stimuli according to a block-design paradigm alternating rest and sensory stimulations. Functional images were superimposed over 3D-MPRAGE anatomical T1-weighted images and analyzed using Matlab7 and SPM5 softwares.
Results: Localized stimulations of one hemivelum led systematically to bilateral and symmetrical BOLD activation of the insular and opercular cortices. Except for the cerebellum which also exhibited significant bilateral activations, other brain regions were either less or only unilaterally activated. Compared to healthy subjects, the operculo-insular activation was unilateral and greatly reduced in the apneic subject. Different stimulation and acquisition modalities were assessed allowing to increase BOLD activation of the operculo-insular cortices without further activation of the other brain regions.
Conclusion: This study is the first allowing specific assessment of the cerebral sensory pharyngeal projections using fMRI. This novel method may contribute to further investigations of the pathophysiology of upper airway dysfunction.
Support (optional): Supported by: ANTADIR and Agir@dom

0589

RECURRENT OBSTRUCTIVE APNEAS INDUCE LONG-TERM FACILATATION OF UPPER AIRWAY MOTOR OUTFLOW IN SPONTANEOUSLY BREATHING RATS IN-VIVO

Tadjalli A,[1] Duffin J,[2] Peever J[1]
(1) University of Toronto, Toronto, Ontario, Canada, (2) University of Toronto, Ontario, Canada

Introduction: Respiratory long-term facilitation (LTF) is a persistent, long-lasting increase in respiratory motor outflow that is induced by episodic but not continuous hypoxia. While three 5-minute periods of hypoxia have been shown to induce LTF, it is unknown if brief periods of asphyxia produced by apneas that are physiologically relevant (as in obstructive sleep apnea, OSA) also induce LTF. Therefore, the aim of this study was to determine whether recurrent airway occlusions evoke LTF in spontaneously breathing adult rats.
Methods: Experiments were performed on anesthetized, tracheostomized, spontaneously breathing adult rats. Respiratory motor activity was determined by recording the EMG activity of both diaphragm (DIA) and genioglossus (GG) muscles. Apneas were induced by obstructing tracheal airflow using a specially-constructed device. Two experimental protocols were executed. Protocol 1 (control): rats were not exposed to apneas, and respiratory motor activity was recorded for 120 minutes. Protocol 2 (intervention): respiratory motor outflow was recorded for 60 minutes before and after exposure to a cluster of ten 15-second airway obstructions, each separated by 1 minute. This protocol was hypothesized to evoke LTF.
Results: Protocol 1: Both DIA and GG muscle EMG activity remained stable during the 120-minute recording period (n=8; $P>0.05$). During obstructions the inspiratory amplitude of both DIA and GG muscles increased. After recurrent airway obstructions, the amplitude of the GG inspiratory motor outflow transiently returned toward baseline levels and then over the subsequent 60 minutes, increased to levels significantly greater than baseline (n=9; 168 ± 12%; $P<0.05$). Respiratory frequency, the amplitude of DIA inspiratory activity and end-tidal CO_2 levels remained stable and were unchanged during the 60 minute period following obstructions.
Conclusion: These results demonstrate that repeated airway obstructions evoke LTF in GG motor activity. We suggest that LTF may be a protective mechanism for maintaining airway patency, which may play a role in OSA.
Support (optional): Research was supported by grants from the Canadian Institutes of Health Research and the National Science and Engineering Research Council of Canada

0590

THE EFFECTIVE USE OF AUTO TITRATING CPAP IN PATIENTS WITH A LOW APNEA HYPOPNEA INDEX

Daley Barsch L, Foran K, Katzoff M, Meyer M
Aurora Health Care, Milwaukee, WI, USA

Introduction: In our clinical experience, multiple patients with a low AHI on PSG, respond well to a trial of auto titrating CPAP. Current Medicare criteria for reimbursement require symptomatic patients to have an AHI > 5.0. This study questions the adequacy of the current criteria of scoring for the diagnosis of SDB.
Methods: We retrospectively reviewed the charts of 37 symptomatic patients who were placed on an auto titrating CPAP unit following a PSG. All patients had AHI´s between 0 and 14.7. Medicare ineligible patients (AHI < 5.0, n = 20) were compared to Medicare eligible patients (AHI > 5.0, n = 17). Data reviewed included; age, gender, BMI, pre treatment Epworth, arousal index, RERA index, PLM index, neck size, total hours on auto CPAP, usage per day (hrs), number of usage days, pressure at the 95th percentile (primary clinical indicator), median pressure, pressure range, L/sec mask leak at the 95th percentile, maximum leak, and the auto CPAP download parameters of AHI, AI, and HI.
Results: The auto CPAP pressure at the 95th percentile delivered (CPAP pressure) in the group that had an AHI < 5.0 averaged 10.3 cm H2O with a range of 6.9 to 14.0. The auto CPAP pressure at the 95th percentile delivered (CPAP pressure) in the group that had an AHI > 5.0 averaged 10.7 with a range of 6.2 to 13.6. The difference between the groups was not statistically significant ($P = 0.45$). Using the same clinical endpoint, rank correlations of the measured indices suggest statistical significance for BMI ($P = 0.03$) and AI ($P = 0.05$), but not AHI, Epworth, RERA index, PLM index and neck size (all $P > 0.05$).
Conclusion: When symptomatic patients with an AHI < 5.0 and > 5.0 were compared, auto CPAP pressures delivered were above baseline in every case. We conclude that the current threshold for Medicare

approval of CPAP therapy needs to be reconsidered. Conventional PSG and current criteria of scoring may fail to adequately diagnose patients with SDB and prohibits CPAP reimbursement.

0591

MANDIBULAR ADVANCEMENT DEVICE TITRATION SLEEP STUDIES

Freedman A,[1] Stark T,[2] Scoles V,[1] Scoles T,[1] Smith-Cappucci J,[1] Disanto S[1]
(1) Pulmonary and Critical Care Associates, Inc., East Brunswick, NJ, USA, (2) Thomas Stark, DMD, Somerset, NJ, USA

Introduction: Mandibular advancement devices (MADs) provide an excellent alternative to CPAP for the treatment of sleep disordered breathing (SDB) by expansion of the retrolingual space and preventing the collapse of the upper pharyngeal airway. Unfortunately, most devices are adjusted empirically by trial and error without ever objectively establishing an optimal position. This can lead to over advancement with discomfort and tension on the temporomandibular joint or under treatment with ineffective resolution of SDB. CPAP generally is adjusted with a CPAP titration study to an optimal pressure based on reduction of the apnea-hypopnea index (AHI). The present study describes a method of titrating MADs to optimal position with the use of the EMA Titratable Device.
Methods: Patients who elected to try a MAD, due to failure of CPAP or inability to tolerate CPAP, were fitted with the EMA Titration Device (Frantz Design) by the dentist. Neutral position (NP) and the patient´s most comfortably advanced position of the mandible (MA) were established and indicated on the EMA. The patient then underwent full-night polysomnography wearing the device, which was advanced in 3 mm increments from NP to MA in order to establish a point of optimal SDB resolution.
Results: 14 patients had a mean AHI from a previous diagnostic study of 35.4 ± 16.5 (SD). Mean AHI at MA was 5.5 ± 2.9 (SD), an 83.8% ± 7.9 (SD) reduction from the baseline, with $p<0.001$ by a paired test. Mean MA was 7.1 mm ± 2.5 (SD). Subjectively, there were minimal patient complaints regarding discomfort wearing the device or with the technician making the adjustments.
Conclusion: MADs are an effective means of treating SDB and can easily be titrated in the sleep lab to an optimal position to provide guidance to the sleep dentist.

0592

GENDER AND AGE DIFFERENCES IN THE INITIAL ACCEPTABILITY OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) IN OBSTRUCTIVE SLEEP APNEA (OSA)

Bhola A,[1] Mouskourie E,[1] Freeman J,[1] Lund S[2]
(1) Clinilabs, Sleep Disorders Institute, New York, NY, USA, (2) Sleep Disorders Institute, New York, NY, USA

Introduction: Patients diagnosed with OSA by nocturnal polysomnogram (PSG) that require CPAP, may reject treatment from the outset. We examined the influence of gender, age and other variables that might affect initial CPAP acceptability. This is different from CPAP compliance which is defined as long term use. Prediction of these differences in variables may help devise methods to improve acceptability.
Methods: A retrospective chart review of PSGs was performed between 8/1/06 and 10/1/06 to identify new adult patients diagnosed with OSA (AHI≥20), after exclusion criteria were met. Successful CPAP titration (CPAPT) was defined as completion of overnight CPAPT with AHI.≤5. Exclusion criteria included unsuccessful CPAPT resulting in AutoPAP, h/o COPD, major depression, insomnia, and previous ENT surgery. Acceptability was defined as consent to CPAPT, tolerance of CPAPT, subjective improvement and/or likelihood of choosing CPAP as indicated on post CPAPT questionnaire and CPAP order placed within 1 month of successful titration. Data collection included gender, age, AHI, CPAP titration-NPSG interval, sleep latency, sleep efficiency, wake after sleep onset (WASO), subjective improvement, and likelihood to accept CPAP.
Results: Of seventy-two patients (23F, 49M), fifty patients (19F, 31M) underwent CPAPT within 2 months. We divided these subjects into 2 groups: CPAP accepters (CA), n=42 (12F, 30M,) and CPAP rejecters (CR), n=8 (6F, 2M). Groups differed with respect to mean age (CR: 59±13, CA: 46±12, p=.006) and gender (p=.012). Logistic regression analysis indicated that age accounted for 52% of variance whereas gender accounted for 28%. Although subjects reporting subjective improvement after CPAPT had lower sleep latency, WASO and higher sleep efficiency these polysomnographic differences did not contribute to CPAP acceptance.
Conclusion: Due to the limited number of subjects, it is hard to draw conclusions at present, although the trend towards CPAP acceptability was higher in younger males. Further exploration appears warranted.

0593

EVALUATION OF THE EFFICACY OF GENIAL BONE ADVANCEMENT TREPHINE IN THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA SYNDROME

Balaicuis J, Doghramji K, Boon M, Jaffe F, Seymour P, Markov D, Friedel M
Thomas Jefferson University, Philadelphia, PA, USA

Introduction: Genial bone advancement trephine (GBAT) is a surgical technique intended to treat obstructive sleep apnea syndrome (OSAS). Our aim was to assess the effectiveness of this procedure in reducing the respiratory disturbance index (RDI) in patients with OSAS.
Methods: Patients were identified as candidates for GBAT based on an RDI of ≥ 5 as determined by nocturnal polysomnography (PSG), with failure of CPAP (continuous positive airway pressure) treatment and manifestation of physical signs that the tongue base was contributing to upper airway collapse. Patients had a PSG prior to surgery and again following GBAT. Ten patients received uvulopalatopharyngoplasty concurrent with GBAT, 5 received concurrent tonsillectomies, 1 received concurrent partial inferior turbinectomy, and 1 received concurrent functional endoscopic sinus surgery.
Results: Thirty-seven patients have undergone pre-surgical evaluation and the surgery to date, ranging in age from 27 to 65. The following mean values pertain to 15 patients (7 males and 8 females) who have returned for post-surgical PSG: age 49.3 (SD 7.1), body mass index 32.7 (SD 7.1), pre-surgical RDI 39.5 (SD 33.3), post-surgical RDI 32.7 (SD 30.3), pre-surgical SaO2 nadir 82.1% (SD 9.2), post-surgical SaO2 nadir 81% (SD 8.5). Paired T-test analysis demonstrated significance at the $p < .001$ level when comparing pre-surgical and post-surgical RDI, as well as when comparing pre-surgical and post-surgical SaO2 nadir. In a multiple linear regression model there is significance for pre-surgical RDI predicting post-surgical RDI while controlling for age ($p < .002$), while in the same model age was not predictive for post-surgical RDI ($p < .089$). Multiple surgical complications (some major) were noted.
Conclusion: These preliminary results indicate that GBAT reduced the RDI in our group of OSA patients. Further study is underway to obtain follow-up PSG evaluation on the remainder of the patients in this study and to assess clinical significance.
Support (optional): This was an unsupported study.

0594

SLEEP APNEA AND NECK CIRCUMFERENCE IN WOMEN

Djekidel K,[1] Dubey A,[2] Harianawalla S,[3] Rahmouni H,[4] Goldberg R[5]
(1) Graduate Hospital, Philadelphia, PA, USA, (2) Graduate Hospital, PA, USA, (3) NY, USA, (4) University of Pennsylvania, PA, USA, (5) Lankenau Medical Research Center, PA, USA

Introduction: Several reports have shown a relationship between age, body mass index, craniofacial anatomy, nasal patency, pharyngeal soft tissue content, menopause and the risk for obstructive sleep apnea (OSA). While studies have implicated neck circumference as a good predictor of OSA, these have included either mixed gender groups or exclusive male groups. To the best of our knowledge no study has demonstrated a similar correlation in women. We aim to determine whether such an association exists.
Methods: This is a prospective study. Women older than 18 undergoing diagnostic overnight polysomnography for evaluation of a sleep disorder qualified for this study and provided informed consent. OSA was defined as an apnea-hypopnea index (AHI)≥ 10. Neck circumference (NC) was measured at the level of the superior border of cricothyroid cartilage.
Results: Forty-five women have been enrolled to date. Mean NC was 14.8 ± 1.7 inches (range 11-19). Mean AHI was 26.2 ± 27.5 (range 0-118). Preliminary analysis by linear regression revealed no statistically significant relationship between female NC and AHI (r2=0.089; ≤p 0.05). The highest likelihood ratio was present for a NC cutoff of 15 inches (correct classification of 64.4%; AUC = 0.75, 95% CI [0.57-0.94]) with a sensitivity of 57.1% and a specificity of 90%.
Conclusion: In this preliminary study, neck circumference does not appear to be a reliable predictor of sleep disordered breathing in adult women. This is an ongoing study however, and additional data may yet allow for further stratification.

0595

INTERMITTENT HYPOXEMIA, SLEEP-DISORDERED BREATHING AND CARDIOVASCULAR DISEASE

Murphy S,[1] Punjabi N[2]
(1) Johns Hopkins University Applied Physics Laboratory, Laurel, MD, USA, (2) Johns Hopkins University, Baltimore, MD, USA

Introduction: Previous results from the Sleep Heart Health Study (SHHS) have shown that the respiratory disturbance index (RDI) is independently associated with prevalent cardiovascular disease. Although the RDI is a useful metric for quantifying the severity of intermittent hypoxemia in sleep-disordered breathing (SDB), it does not fully capture the `intermittent´ nature of oxygen desaturation during sleep. The purpose of this study was to determine whether a metric of intermittent oxyhemoglobin desaturation would be associated with prevalent CVD independent of RDI.
Methods: Polysomnographic data from the SHHS were used to assess the correlates of prevalent CVD. The standard deviation of the oxygen saturation (SaO2) recording was used to characterize the fluctuations in SaO2 recording during sleep. Multivariable logistic regression models were used to determine whether the standard deviation of the SaO2 signal (std-SaO2) was independently associated with prevalent CVD.
Results: The study sample consisted of 5,673 subjects with high quality SaO2 tracings and complete data on measures of body composition and cardiovascular disease. The prevalence of cardiovascular disease in the study sample was 17.3%. After adjusting for age, body mass index, waist and neck circumference, prevalent hypertension, and RDI, std-SaO2 was independently associated with prevalent CVD. The adjusted odds ratios for the tertiles of std-SaO2 were 1.00 (reference), 1.22 (1.00–1.48) and 1.39 (1.11–1.74), respectively.
Conclusion: The results of this study confirm that, although the RDI is independently associated with CVD, parameters that reflect the intermittent nature of oxygen desaturation during sleep have additional ability to correlate with CVD. The implications of these findings are that intermittent hypoxemia may be an important determinant of SDB-related cardiovascular disease.
Support (optional): National Institutes of Health Grants HL07578 and AG025553

0596

IMPACT OF INTERTRIGEMINAL REGION AMPA RECEPTOR BLOCKADE ON RESPIRATORY RESPONSES IN RATS

Isenovic E, Radulovacki M, Carley D
University of Illinois at Chicago, Chicago, IL, USA

Introduction: Respiratory disturbance, including apnea, can be induced by microinjection of glutamate (GLU) into the intertrigeminal region (ITR) of the lateral pons in rats. In a previous study, we blocked this effect by microinjection of kynurenic acid, a broad spectrum GLU receptor antagonist. In this study we hypothesized that functional glutamatergic AMPA receptors are expressed in the ITR and that the blockade of these receptors by a specific antagonist (NBQX) would alter both central GLU-induced apnea as well as vagally mediated reflex apnea induced by intravenous infusion of serotonin.
Methods: Respiration was monitored in 19 ketamine-anesthetized Sprague-Dawley rats by piezoelectric strain gauge. Recordings began with a 5–10 min registration in baseline conditions. Next, three successive infusions (0.5 µl over 5 s) of 5-HT (0.05 M) were made at 5-min intervals into the left femoral vein. In 9 rats, multi-barrel micropipettes were filled with 1mM NBQX, saline, GLU (10 mM), and oil red-O dye. In the other 10 rats, 1mM NBQX was replaced with 10mM NBQX. Microinjection of GLU into ITR produced immediate apnea. After recovery of the breathing pattern, 1mM or 10mM NBQX was microinjected into ITR followed by an additional GLU microinjection. Red dye was microinjected to aid histological verification of injection sites.
Results: Microinjections of NBQX (10mM) shortened GLU apnea duration by 68% (p=0.006), reduced GLU apnea frequency by 82% (p=0.034) and decreased GLU apnea density during the first 30s by 79%. (p=0.006). The same dose of NBQX did not affect vagally mediated reflex apnea induced by intravenous infusion of serotonin.
Conclusion: These results show that functional glutamate AMPA receptors are expressed in the ITR and that their blockade impairs the modulatory role of pontine structures in respiration.
Support (optional): This work was supported by NIH grants HL070870 and AG016303.

0597

COMPUTATIONAL FLUID DYNAMICS ANALYSIS OF UPPER AIRWAY RECONSTRUCTED FROM MAGNETIC RESONANCE IMAGING DATA

Mihaescu M,[1] Murugappan S,[2] Gutmark E,[2] Donnelly L,[3] Kalra M[4]
(1) University of Cincinnati, Cincinnati, OH, USA, (2) University of Cincinnati, OH, USA, (3) Children's Hospital Medical Center of Cincinnati, OH, USA, (4) Children's Hospital Medical Center of Cincinnati, Cincinnati, OH, USA

Introduction: Although the individual role of airway anatomic characteristics and dynamic control of the upper airway muscular tone in the pathogenesis of Obstructive Sleep Apnea (OSA) is well accepted, there is paucity of data addressing the effect of anatomical

characteristics on airway collapsibility. Our objective is thus to investigate the pathophysiology of OSA using an accurate and efficient computational tool able to perform flow computations in complex three-dimensional geometries.
Methods: Transverse MR Sequences (Axial T1) were acquired on a subject with OSA to cover the entire length of the pharyngeal airway extending from the roof of the nasopharynx to the lower mandibular plane. A Matlab code, developed originally for aerospace applications, was modified to identify the boundaries of the airway from MRI images. Cartesian coordinates for airway´s boundary were employed to reconstruct the three-dimensional computational model of the upper airway. 3D steady state Reynolds Averaged Navier-Stokes (RANS) flow simulations were performed for the 3D reconstructed airway model using commercial FLUENT software. The flow pattern inside the airway was computed at two inspiration inlet flow rates (5 and 10 liters per minute). The results were analyzed to determine the velocity, static pressure, and wall shear stress distributions.
Results: The highest axial velocity was observed at the site of minimum cross sectional area (retropalatal pharynx) resulting in the lowest level of wall static pressure. The highest wall shear stresses were concentrated at the same location due to the high velocity gradients. The pressure drop was 3 times larger for the higher flow rate condition as compared to the lower flow rate.
Conclusion: The results indicate that the presence of airway narrowing leads to changes in the flow characteristics, which can potentially increase airway collapsibility at the site of constriction. Further, this predisposition of the airway to collapse is increased at higher flow rates.
Support (optional): AASM/Pfizer's Scholars Grant in Sleep Medicine and Cincinnati Children's Research Foundation Trustee Grant.

0598

EVALUATION OF A SINGLE CHANNEL PORTABLE MONITOR FOR THE DIAGNOSIS OF OBSTRUCTIVE SLEEP APNEA: AN INTERIM ANALYSIS

Passero M, Gupta N, Atwood C, Givelber R, Drumheller O, Peterson J, Rogers S, Strollo P
University of Pittsburgh, Pittsburgh, PA, USA

Introduction: The current reference standard for the diagnosis of obstructive sleep apnea (OSA) is attended polysomnography. This test has limitations that relate primarily to cost and access issues. Our objective was to determine if a portable monitor (PM) that utilizes a one-channel recorder of nasal pressure could accurately diagnose OSA in adults referred to a sleep medicine clinic.
Methods: The study is a prospective cohort design. Consecutive subjects are evaluated in the home with the PM (PMhome) followed by simultaneous data collection with full night diagnostic polysomnography (PSGDx) and the PM in our sleep laboratory (PMlab). The PM allows for full disclosure of the acquired nasal pressure data. For the PM, apneas are defined as an > 80% reduction in airflow from baseline for > 10 seconds and hypopneas as a 50% to 80% reduction in airflow from baseline for > 10 seconds. For the PSGDx, apneas are defined as an > 80% reduction in airflow from baseline for > 10 seconds and hypopneas as a 50% to 80% reduction in airflow from baseline associated with a > 4% oxyhemoglobin desaturation for > 10 seconds. Data are expressed as mean + standard deviation (SD). Prevalence, sensitivity, specificity and likelihood ratios were calculated for PSGDx vs. PMlab. Spearman correlation of PMhome vs. PMlab were calculated.
Results: Study population (to date) – 21 subjects (5 males /16 females), mean age of 43 (SD + 10.4 yrs), and mean BMI of 35.2 (SD + 10.4). The prevalence of an AHI of > 15 in the cohort is 30%. The sensitivity, specificity and likelihood ratio of identifying an AHI of > 15 is 1.0, 0.73, and 3.75 respectively. The Spearman correlation PMhome vs. PMlab is 0.89 ($p < 0.05$).
Conclusion: This PM shows promise as a tool to identify patients with moderate to severe OSA.
Support (optional): ResMed

0599

WEIGHT LOSS AND UPPER AIRWAY COLLAPSIBILITY: COMPUTATIONAL FLUID DYNAMICS ANALYSIS

Kalra M,[1] Donnelly L,[2] Mihaescu M,[3] Murugappan S,[3] Gutmark E,[3] Amin R[2]
(1) Children's Hospital Medical Center of Cincinnati, Cincinnati, OH, USA, (2) Children's Hospital Medical Center of Cincinnati, OH, USA, (3) University of Cincinnati, OH, USA

Introduction: Obstructive Sleep Apnea (OSA) is highly prevalent in adolescents with extreme obesity and resolution of OSA occurs following surgical weight loss. The mechanism of OSA resolution associated with surgical weight loss is, however, not clear. We hypothesized that surgical weight loss is associated with changes in both the cross-sectional area and collapsibility of the pharyngeal airway. We performed Computational Fluid Dynamics (CFD) analysis of airway MRI data in 4 obese female adolescents before and after surgical weight loss.
Methods: Transverse MR Sequences (Axial T1) were acquired to cover the entire length of the pharyngeal airway. Three-dimensional computational model of the upper airway was constructed from the airway MRI data. 3D steady state Reynolds averaged Navier Stokes (RANS) flow simulations were performed during the inspiration phase for the reconstructed airway model using FLUENT commercial software.
Results: The median body mass index (BMI) was 52.6 at baseline and 38.4 at a median interval of 4 months after laproscopic gastric bypass surgery. At baseline, computational analysis revealed an acceleration of the flow at the site of minimum cross sectional area leading to a significant static pressure drop and increased wall shear stress. Surgical weight loss resulted in an increase in airway cross sectional area of the retropalatal pharynx leading to approximately two fold reduction of axial velocities in this region. Also the static pressure and wall shear stress distributions on the airway wall were found to be more uniform. For the same flow rate (20 l/min), the static pressure minimum value after weight loss was found to be 3 times higher as compared to baseline, while the wall shear stress values were 1.5 times lower.
Conclusion: Our results indicate that surgical weight loss, through change in the flow characteristics that result in decreased flow velocity and decreased drop of static pressure, can reduce airway collapsibility.
Support (optional): AASM/Pfizer Scholars Grant in Sleep Medicine and Cincinnati Children's Research Foundation Trustee Grant

0600

FACTORS INFLUENCING GENIOGLOSSUS MUSCLE CONTROL DURING REM SLEEP

Eckert D,[1] Malhotra A,[2] Schory K,[2] David W,[2] Amy J[2]
(1) Brigham and Women's Hospital, Sleep Disorders Program and Harvard Medical School, Boston, MA, USA, (2) Brigham and Women's Hospital, Sleep Disorders Program and Harvard Medical School, MA, USA

Introduction: Sleep-disordered breathing (SDB) is often most severe during REM sleep. Reduced upper airway (UA) dilator muscle activity, eg genioglossus (gg), is likely important in mediating this effect.

However, the underlying mechanisms remain poorly understood. Previous reports in healthy subjects suggest that tonic EMGgg is suppressed during REM sleep only when eye movements are occurring. This study was designed to characterize gg muscle activity during REM sleep and the factors influencing its control with CPAP in place to minimize UA resistance effects on gg activity.
Methods: Data from 8 healthy subjects and 4 OSA patients on CPAP sufficient to eliminate flow limitation have been analyzed thus far. Polysomnography, epiglottic pressure (Pepi), EMGgg and ventilation were recorded. EMGgg (%max) was compared between 1) REM sleep with and without eye movements and 2) REM (as a single state) and NREM. Multiple linear regression exploring the potential factors influencing EMGgg activity in REM sleep (ie V_T, eye movements, EEG power) has been performed in three subjects thus far.
Results: During REM sleep 1) there were no differences in phasic or tonic EMGgg or ventilatory measures for breaths with versus without active eye movements and 2) phasic EMGgg consistently correlated with V_T but not with eye movements or EEG power. Compared to NREM sleep, REM was associated with 1) higher respiratory frequency and lower V_T; minute ventilation unchanged 2) similar nadir Pepi (-1.8±0.3vs. -1.9±0.3cmH2O) and 3) reduced phasic and tonic EMGgg which remained after adjustment for differences in breath timing (0.8±0.3vs. 1.7±0.6%max and 0.6±0.2vs. 1.1±0.4%max, respectively).
Conclusion: REM sleep is associated with reductions in both phasic and tonic EMGgg activity independent of the presence of active eye movements in subjects on CPAP. Reduced EMGgg activity compared to NREM despite similar Pepi supports previous reports that gg muscle responsiveness to negative pressure may be reduced during REM sleep.
Support (optional): NIH HL60292, RR01032 and American Heart Association 0425786T.

0601

OBSTRUCTIVE SLEEP APNOEA IN SINGAPORE: POLYSOMNOGRAPHY DATA FROM A TERTIARY SLEEP DISORDERS UNIT

Lim L, Fook S, Chiou F, Kwok A, Tham K, Puvanendran K
Singapore General Hospital, Singapore, Singapore

Introduction: Comprehensive polysomnography (PSG) data in Asian patients with suspected obstructive sleep apnea (OSA) is generally lacking. We reviewed Sleep Laboratory data with the objective of describing clinical and PSG characteristics of patients evaluated for OSA in Singapore.
Methods: PSG data of patients evaluated for OSA in 2005 at the Sleep Disorders Unit of a public tertiary hospital were retrospectively reviewed.
Results: 584 diagnostic studies were performed in 1 year (January through December 2005), in patients with excessive daytime sleepiness and/or snoring or recurrent unexplained awakenings. There were 449 male patients (76.9%) and 135 female patients (23.1%), with a mean age of 47.5 years (SD 12.7). Men were on average younger than women, 46.1 years versus 52.0 years ($p<0.0005$). The mean body-mass index (BMI) was 27.9 (SD 6.7), with no significant difference between genders. An association was shown between AHI and BMI (Pearson correlation index $r = 0.362$).

Men had overall significantly higher AHI (27.2 vs 18.9), shorter mean sleep onset latency (16.9 minutes vs 22.6), more light sleep (65.5% vs 58.9%), less deep sleep (17.4% vs 22.7%), and more respiratory event related arousals (21.0 vs 12.4) ($p<0.0005$).

Severity was classified: AHI < 5 ("Normal or Primary Snoring")(28.3%), AHI 5-15 ("Mild")(22.3%), AHI >15-30 ("Moderate")(18.3%), AHI > 30 ("Severe")(31.2%). There was no difference in age among the 4 groups. More severe OSA patients were significantly heavier, and had more light sleep, less deep sleep, less REM sleep, more respiratory event related arousals and lower oxygen desaturation.
Conclusion: OSA is predominant in middle-aged, overweight Singapore males and much less common in females who tend to be older. Majority of patients have moderate to severe OSA. The relatively lower BMI compared to other OSA populations may be related to craniofacial characteristics and/or higher percentage body fat for BMI which has been described in Singaporeans.
Support (optional): National Medical Research Council, Singapore

0602

EFFECTS OF EXPERIMENTAL SLEEP FRAGMENTATION AND INTERMITTENT HYPOXIA ON WATER MAZE PERFORMANCE IN RATS

McCoy J,[1] Ward C,[2] McKenna J,[1] Connolly N,[3] McCarley R,[4] Strecker R[1]
(1) Psychiatry, VA Boston Healthcare System and Harvard Medical School, Brockton, MA, USA, (2) Physiological Sciences, University of Florida, Gainesville, FL, USA, (3) Psychology, Wheaton College, Norton, MA, USA, (4) VA Boston Healthcare System and Harvard Medical School, Brockton, MA, USA

Introduction: Animal models of sleep apnea indicate that both sleep fragmentation (SF) and intermittent hypoxia (IH) impair spatial learning & memory in the water maze. Suggested mechanisms include diminished hippocampal (HIPP) LTP for SF and IH, and HIPP apoptosis for chronic IH. Here we perform a head-to-head comparison of 24h SF and 24h IH in order to dissociate their relative contributions to the cognitive impairments of sleep apnea.
Methods: SF: treadmills awakened male Fisher Brown Norway (FBN) rats every 2 min for 24h *before* training or for 24h *after* training. IH: O2 levels cycled between 6 and 19% for 24h immediately *before* training. Water maze: acquisition training took ~3h (3 blocks/4 trial each, 30 min inter-block interval) followed 24h later by a 30s probe trial to assess retention.
Results: SF *after* training robustly impaired retention on the probe trial. However, unlike previous observations in Sprague-Dawleys (SD), SF *before* training did not impair acquisition or retention in FBN rats. IH produced a small acquisition deficit seen only on the 2nd block of training trials; retention was not impaired.
Conclusion: SF findings indicate that, 1) 24h of SF *after* learning had a greater effect on retention than did 24h SF *before* learning, and, 2) 24h SF *before* training impairs acquisition in SD rats, but not FBN rats. The 24h IH effect herein was very modest, suggesting that allowing more time for apoptosis to occur (e.g., multiple days of IH exposure, or a longer interval between IH exposure and testing) produces greater spatial learning and memory impairments.
Support (optional): This research was supported by NIH HL060292, NIMH 39683, NIMH 40999, Dept. of Vet. Aff., NIH T32 HL07901 to JTM, and NIH F32 MH070156 to JTM.

0603

DIAGNOSTIC UTILITY OF ESOPHAGEAL PRESSURE MONITORING IN A CLINICAL SETTING

Hershner S, O'Brien L, Chervin R
University of Michigan, Ann Arbor, MI, USA

Introduction: Esophageal pressure (Pes) monitoring facilitates a diagnosis of upper airway resistance syndrome (UARS), but is rarely

performed at most sleep laboratories. We sought to characterize the utility of Pes monitoring, in a clinical sleep laboratory setting, in terms of the diagnostic impact on otherwise negative studies performed for suspected sleep-disordered breathing.
Methods: Databased reports of adult polysomnograms performed with Pes monitoring (10/2000-4/2003) were classified as normal (apnea/hypopnea index [AHI]<5) or diagnostic of obstructive sleep apnea (AHI>5). Normal studies were further classified as diagnostic of UARS by sleep board-eligible or certified faculty when the number of crescendo increases in esophageal pressure leading to cortical arousals was thought to be clinically significant (e.g., >5 per hour). In a small number of cases, the diagnosis was based on prolonged periods of excessively negative esophageal pressures (e.g., <<-10 cm of water).
Results: Among 272 polysomnograms, 163 showed no obstructive sleep apnea, but 75 (46%) of these were judged to be consistent with UARS. For diagnosis of sleep-disordered breathing, the negative predictive value of a polysomnogram with AHI<5 was 0.54. Among subjects with AHI<5, frequent snoring was noted by technologists in similar proportions of UARS-negative and UARS-positive polysomnograms (10% vs. 17%; Chi-square p=0.2).
Conclusion: Among our polysomnograms performed with Pes monitoring, the procedure demonstrated UARS in nearly half of those with AHI<5. The utility of Pes monitoring in our laboratory, in comparison to others, could no doubt be affected by hypopnea definitions, subjective clinical assessment of EPM tracings, nasal pressure monitoring (often used qualitatively, but not scored in this series), and selection of particular patients for Pes monitoring. However, in the near absence of published data on the frequency with which EPM may be useful in a clinical setting, our data are among the first to suggest that this frequency can be substantial.

0604

CHARACTERIZING MEASUREMENT VARIABILITY IN THE APNEA-HYPOPNEA INDEX: THE WOMEN´S MIDLIFE SLEEP STUDY

Peppard P, Young T, Austin D, Finn L
University of Wisconsin-Madison, Madison, WI, USA

Introduction: In research examining associations between sleep-disordered breathing (SDB) and outcomes such as hypertension or diabetes, measurement variability in the apnea-hypopnea index (AHI, events/hr) can yield underestimates of associations. Using repeated in-home polysomnography (PSG) studies from the Women´s Midlife Sleep Study, we comprehensively characterized AHI measurement variability and reliability.
Methods: Intrasubject measurement variability was characterized in 171 Women´s Sleep Study participants (average age=52, range=38-63 years). All participants had previously experienced polysomnography and had at least two additional in-home PSG studies meeting strict criteria (women experienced <2% weight change and no change in menopausal status or HRT use during a maximum interval of 8 months between repeated studies). Several indices of reliability of the AHI and categorical classification of SDB were calculated. The dependence of intrasubject AHI variability on severity of SDB, age, menopausal status and other characteristics was examined.
Results: Mean AHI was similar between the first and second PSG studies (13.0 vs. 13.2, paired t-test p-value=0.69). The average absolute difference between repeated AHI measurements was 4.4 events/hr. The intraclass correlation coefficient (ICC) between repeat studies was 0.89. Intrasubject variability in the AHI increased with SDB severity. A log(AHI+3) transformation stabilized the intrasubject variance across the severity spectrum while providing a nearly identical ICC (0.89). Percent agreements for classifying SDB severity by AHI cutpoint values of 5 and 15 were 85% (kappa coefficient=0.70) and 90% (kappa=0.76), respectively. Percent agreement using 3 categories of SDB severity (AHI<5, 5=<15, AHI>=15) was 78% (weighted kappa=0.73).
Conclusion: In-home PSG in the Women´s Midlife Sleep Study estimated SDB severity with good reliability characteristics, similar to those reported from the Sleep Heart Health Study (Quan *et al.* Sleep 2002;25{8}:8-14). Our calculated indices of reliability can be used to predict the degree of underestimation of associations between SDB and sequelae in research employing similar SDB assessment methods.
Support (optional): Grants R01HL62252, RR03186, and R01AG14124 from the National Institutes of Health.

0605

CPAP USE IS ASSOCIATED WITH ONGOING INSOMNIA BUT NOT WITH PRE-EXISTING INSOMNIA

Reed B, Balakrishnan K, James K, Weaver E
University of Washington & Harborview Medical Center, Seattle, WA, USA

Introduction: CPAP can cause discomfort and theoretically worsen insomnia when trying to fall asleep. We hypothesized that patients with pre-existing sleep-onset insomnia would have decreased CPAP tolerance and use.
Methods: We enrolled newly diagnosed sleep apnea patients who were recommended CPAP therapy in the Seattle Sleep Cohort. Each patient answered insomnia questions in the Pittsburgh Sleep Quality Index questionnaire immediately prior to diagnostic polysomnography and again six months later. Objective CPAP use was downloaded at six months. We tested whether self-reported average minutes to fall asleep pre-CPAP was inversely associated with the average minutes of nightly CPAP use at six months. We also explored the data for associations of other measures of pre-existing or ongoing insomnia with CPAP use, and then tested the positive associations in an independent sample of patients from the Seattle Sleep Cohort.
Results: We enrolled 272 patients in the original sample: age 47+/-12 years, 58% male, and pre-treatment apnea-hypopnea index 51+/-35 events/hour. The Spearman correlation between minutes to fall asleep pre-CPAP (mean 30+/-36 minutes) and 6-month CPAP use (mean161+/-178 minutes/night) was -0.03, not statistically different from 0.00 (p=0.62). Exploratory analysis revealed no significant association between seven different measures of pre-existing insomnia and subsequent CPAP use (all p>0.10), but did reveal consistent associations between seven measures of ongoing insomnia and CPAP use (all p < 0.05). These associations were confirmed in an independent sample of 232 patients.
Conclusion: Pre-existing insomnia is not associated with subsequent CPAP use in newly diagnosed adult sleep apnea patients. It is possible that some pre-existing insomnia is due to sleep apnea that is treated successfully by CPAP, so that it is not a useful predictor of subsequent CPAP use. However, ongoing insomnia while on CPAP is associated with decreased CPAP use, so future studies should assess the impact of insomnia treatment in this setting.
Support (optional): 1. NIH K23 HL068849.
2. Triological Society Career Development Award.
3. The American Geriatrics Society Jahnigan Award (funded by the John A. Hartford Foundation of NYC and Atlantic Philanthropies).

0606

ANXIETY SYMPTOMS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

Yang C,[1] Wu C,[2] Chen N[3]
(1) National Cheng-Chi University, The Research Center for Mind, Brain, and Learning, Taipei, Taiwan, Taipei City, Taiwan, (2) Fu-Jen Catholic University, Taoyuan, Taiwan, (3) Chang Gung Memorial Hospital, Taoyuan, Taiwan

Introduction: Previous studies have reported anxiety symptoms in patients with obstructive sleep apnea syndrome (OSAS). However, the relationship between OSAS severity and anxiety ratings were not consistent across the studies. The present study analyzed different dimensions of anxiety in OSAS patient and their association with OSAS severity in order to further clarify this issue.
Methods: The participants consist of 56 OSAS patients. Their sleep and OSAS severity were assessed with a nocturnal polysomnography. They were then requested to complete a subjective rating scale for anxiety (Beck Anxiety Inventory [BAI]). The BAI consists of four factors: neurophysiological, subjective, panic, and autonomic symptoms. Pearson correlations were conducted to assess the relationships between OSAS severity (Apnea Hypopnea Index [AHI]) and the different factor scores of the BAI.
Results: The results showed that AHI correlated moderately with the total score of the BAI (r .30, p<.05). In addition, AHI showed significant correlations with anxiety symptoms of more a physiological origin (neurophysiological symptoms: r .34, p<.05; autonomic symptoms: r .36, p<.01), but showed no correlations with anxiety symptoms that are more a subjective feeling or associated with cognitive processes (subjective and panic symptoms).
Conclusion: The results showed that OSAS severity is more associated with the physiological aspect than the subjective/cognitive aspects of anxiety. The findings implied that anxiety in OSAS may reflect primarily the physiological consequences of OSAS. Careful evaluation in the patients is needed to avoid misdiagnosis.

0607

THE THEN TEST IS MORE RESPONSIVE TO CHANGE THAN SERIAL DIFFERENCE MEASUREMENTS OF SLEEP APNEA QUALITY OF LIFE

Weaver E, James K
University of Washington & Harborview Medical Center, Seattle, WA, USA

Introduction: Subjective sleep apnea outcome measurement is vulnerable to the response shift phenomenon, where the patient´s frame of reference changes with therapy. Typically, this shift is due to the patients´ overestimation of their baseline quality of life before they experience improvement with therapy. The Then Test stabilizes the reference frame by comparing the conventional post-treatment quality of life to a post-treatment reassessment of the baseline quality of life instead of to the original baseline assessment. We tested the hypothesis that the Then Test difference in sleep apnea quality of life will be more sensitive to change than the conventional serial difference in quality of life.
Methods: We enrolled newly diagnosed sleep apnea patients who were recommended CPAP therapy in the Seattle Sleep Cohort and followed them for six months. At baseline all patients completed the Sleep Apnea Quality of Life Index (SAQLI). At 6-month follow up, each patient completed a post-treatment SAQLI followed by a reassessment of their baseline SAQLI. We compared Then Test and serial differences. SAQLI scores range 0 – 7 with higher scores indicating better quality of life.
Results: We enrolled 117 patients, age 47+/-12 years, 58% male, and apnea-hypopnea index 55+/-36 events/hour. Baseline SAQLI was 4.3+/-1.0 and post-treatment reassessment of the baseline SAQLI was 3.9+/-1.2 (p<0.001). Serial difference in SAQLI (final – baseline) was 0.3+/-0.9 while Then Test difference in SAQLI (final – reassessed baseline) was 0.7+/-0.9 (p<0.001).
Conclusion: The baseline scores overestimate quality of life relative to the post-treatment reassessment of the baseline scores. Conventional serial differences underestimate the change in quality of life compared to Then Test differences in scores. The response shift phenomenon appears significant, and serial differences may underestimate the benefit achieved with therapy. Sleep apnea treatment benefit might best be measured with Then Test differences rather than conventional serial differences.
Support (optional): 1. NIH K23 HL068849.
2. The Triological Society Career Development Award.
3. The American Geriatrics Society Jahnigan Award (funded by the John A. Hartford Foundation of NYC and Atlantic Philanthropies).

0608

NASOENDOSCOPY DISCLOSES SWALLOWING PROBLEMS IN OSAS PATIENTS VERSUS CONTROLS

Zancanella E,[1] Valbuza J,[2] Osorio C,[3] Machado M,[4] Carvalho L,[5] Prado L,[5] Prado G[4]
(1) Federal University of Sao Paulo, Indaiatuba, Sao Paulo, Brazil, (2) Federal University of Sao Paulo - Brazil, Sao Paulo, Brazil, (3) Federal University of Sao paulo, Brazil, (4) Federal University of Sao Paulo, Sao Paulo, Brazil, (5) Federal University of Sao Paulo, Sao Paulo, Brazil

Introduction: OSAS patients may have subclinical swallowing abnormalities due to progressive mechanical trauma of the pharyngeal tissues caused by snoring.
Methods: We study by nasoendoscopy 11 patients, 6 women, without spontaneous complaints of swallowing, 48±14 years old, with PSG diagnosis of OSAS, IAH 25.78±36.82 and 10 controls. The exams were carried through without anesthetics and nasal vasoconstriction. It was offered to patient diet bolus (5 and 10ml) as thin liquids (L), purée (P), and solids (S). Two examiners had analyzed the anatomical structures and the functional aspects of the swallowing events following the criteria: (1) premature leakage of bolus into the pharynx; (2) laryngeal penetration; (3) traqueal aspiration; (4) bolus residual in the pharynx after swallowing; (5) inefficacious pharyngeal cleanness.
Results: We verified that 64% of the patients presented premature leakage: 8% for L; 9% for S; 9% for L and P; 18% for P and S; and 9% for L, P and S. We did not observed laryngeal penetration and traqueal aspiration. We verified that 55% of the patients had presented bolus residual after swallowing: 18% for P; 18% for L and P; and 9% for L, P and S. Nine percent of the patients presented inefficacious pharyngeal cleanness for L and P; and 9% for P and S. Were also observed that the patient with more severe problems of swallowing was the not fat one and presented the longer illness time (30 years). The controls did not any kind of abnormal swallow.
Conclusion: OSAS patients presented subclinical manifestations of abnormal swallowing by nasoendoscopy possibly associated to neuromuscular injury caused by snoring. The time of illness and severity of the OSAS seem to be associated to the swallowing dysfunctions in our sample.

0609

A PROSPECTIVE RANDOMIZED CROSSOVER TRIAL TO OBTAIN OBJECTIVE COMPARISON BETWEEN INITIAL CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) USE WITH AND WITHOUT EXPIRATORY PRESSURE RELIEF IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA (OSA)

Modrak J,[1] Greenblatt D[2]
(1) University of Rochester, rochester, NY, USA, (2) University of Rochester, NY, USA

Introduction: CPAP has been used to effectively treat OSA for several decades. New modalities such as expiratory pressure relief have been implemented to improve comfort, thereby theoretically improving adherence to prescribed CPAP therapy. This study was conducted to ascertain objective hours of use of CPAP with and without expiratory pressure relief together with subjective findings of comfort, ease of use and self-efficacy.
Methods: A randomized two-arm prospective crossover unblinded repeated mesures comparison study of two commercially available CPAP machines (Puritan Bennett GoodKnight 420S; Respironics REMstar Plus with C-Flex) was conducted on patients newly titrated on CPAP with an apnea hypopnea index of ≥ 20. Polysomnographically titrated pressure was set on each respective device. On the CPAP with expiratory pressure relief,(CPAP-EPR) the lowest expiratory pressure setting was used initially and adapted as needed based on patient preference. Patients were studied for a total of 28 consecutive days, consisting of 2 14 day periods. Data was downloaded from each CPAP machine for each period. Subjects were asked to keep daily logs and complete a questionnaire at the end of each period.
Results: Data were analyzed on twenty-six CPAP naive patients (19 men, 7 women, mean age 56 (range 32-75). The mean hourly use on CPAP-PB was 5.1 vs. the CPAP-EPR 5.4. (p= 0.70)
Conclusion: The results indicate that there is not a significant difference between the two devices in terms of usage. Patients experienced the same amount of "on mask" time with each machine, thus demonstrating that CPAP with expiratory pressure relief in this sample of patients did not improve overall use or initial acceptance of CPAP therapy.
Support (optional): This research was funded by a grant from Puretan Bennett

0610

MR VOLUMETRY OF UPPER AIRWAY STRUCTURES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME IN SOUTH KOREA

Hong S,[1] Joo E,[2] Han S,[3] Cho J,[1] Kim S,[3] Km H[3]
(1) Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, (2) Ewha Woman University Hospital, Seoul, South Korea, (3) Samsung Medical Center, Sungkyunkwan University School of Medicine, South Korea

Introduction: To evaluate volume changes of upper airway structures and air spaces, we measured the sizes of upper airway structures and air spaces in patients with severe OSAHS and age/sex-matched normal volunteers.
Methods: We enrolled 19 severe OSAHS patients and 14 normal volunteers. Upper airway MR imaging obtained three mm thickness axial and sagittal slices of upper airway using a 1.5-T MRI scanner. Upper airway measurements included 1) the airway volumes of the retropalatal (RP) region and the retroglossal (RG) region, 2) minimum cross-sectional area of the RP and RG airway spaces, 3) anterior-posterior and lateral dimensions at the level of the minimum airway in the RP and RG regions, respectively, and 5) the volume of tongue, soft palate, lateral pharyngeal wall, lateral parapharyngeal fat pad, and genioglossus muscle.
Results: Mean apnea-hypopnea index (AHI) of OSAHS patients was 56.9±22.3/hour (range, 31.6 - 103.9). In OSAHS patients, mean airway volumes of RP and RG regions was significantly smaller [RP region, OSAHS 2401.7 vs. normal 3108.8mm3, p=0.038; RG region, OSAHS 5117.3 vs. normal 6464.6mm3, p=0.017]. Mean volumes of soft palate [OSAHS 8242.7 vs. normal 5812.1mm3, p=0.002] and lateral pharyngeal wall [OSAHS 17524.2 vs. normal 13413.6mm3, p =0.003] in OSAHS patients were larger than those of normal volunteers. In cross-sectional area analysis, OSAHS patients showed significantly smaller airway area per slice in RP [OSAHS 62.2 vs. normal 100.2 mm2, $p < 0.001$] and RG [OSAHS 145.1 vs. normal 171.5 mm2, $p = 0.029$] regions. Lateral dimensions of RP [OSAHS 8.1 vs. normal 16.6mm2, $p < 0.001$] and RG [OSAHS 18.4 vs. normal 26.3mm2, $p = 0.003$] regions were definitely shorter in OSAHS patients.
Conclusion: Korean OSAHS patients had significantly larger volumes of soft palate and lateral pharyngeal wall in upper airway structures and shorter lateral dimensions of pharyngeal airways.

0611

SLEEP-WAKE PATTERNS OF GENIOGLOSSAL EMG AT THE BASE AND TIP OF THE TONGUE IN THE RAT

Lu J, Kubin L
Dept. of Animal Biology and Ctr. for Sleep and Respiratory Neurobiology, Univ. of Pennsylvania, Philadelphia, PA, USA

Introduction: In rats, the sleep-wake pattern of lingual EMG is different from that of neck postural muscles: whereas nuchal EMG progressively declines from high and variable during wakefulness to atonia with occasional twitches during REM sleep, lingual muscles become nearly atonic during slow-wave sleep (SWS) and then progressively increase their phasic activity during REM sleep (Lu *et al.*, Respir. Physiol. Neurobiol, 2005). Our goal was to test whether sleep-wake-related changes in lingual EMG differ between the basal and distal compartments of the tongue muscle.
Methods: Four rats were instrumented and adapted for recording of lingual EMG from two locations, nuchal EMG, cortical EEG and hippocampal activity. Data from 2 middle hours of recordings conducted between noon and 4 pm were analyzed, with the records scored and root mean squares of EMG activities determined in successive 10 s intervals. In additional 3 rats, diaphragmatic EMG also was recorded to determine whether some phasic bursts in lingual EMG were bound to inspiration.
Results: Three recording sites within the tongue were during autopsy localized near the base of the tongue and 3 within 4-5 mm from the tip of the tongue (distal). When normalized by the mean levels of activity during wakefulness, the mean lingual EMG near the base of the tongue was 8.7%±4.0(SE) during SWS and 27%±5 during REM sleep. For the distal recording sites, the mean levels were 8.9%±2.2 and 27%±3, respectively (not different from the base of the tongue). Rhythmic activities intermittently occurred in both locations in wakefulness and REM sleep, but the rhythms were not respiratory.
Conclusion: In contrast to upper airway motor tone in obstructive sleep apnea subjects, in normal rats, lingual EMG in both basal and distal compartment of the tongue reaches a nadir during SWS, rather than REM sleep, and is not respiratory-modulated.
Support (optional): HL-071097.

0612

PREOPERATIVE MALLAMPATI SCORE AS PREDICTOR OF SEVERITY OF OBSTRUCTIVE SLEEP APNEA

Paruthi S,[1] Doherty T,[2] Consens F,[1] Naff J,[2] Opp M[1]
(1) University of Michigan, Ann Arbor, MI, USA, (2) MI, USA

Introduction: Mallampati scores (MS) and body-mass index (BMI) have been shown to have positive correlations with obstructive sleep apnea (OSA) as measured by apnea-hypopnea index (AHI) > 5. These variables are routinely evaluated preoperatively by anesthesiologists. We hypothesize MS and BMI may help predict the severity of OSA.
Methods: Sections of two large databases from the University of Michigan were merged: the Sleep Center with 17,005 consecutive polysomnograms (PSGs) between 3/4/85-4/23/03 and the Department of Anesthesia with 17,386 consecutive surgical cases performed from 6/1/04-8/9/05. When multiple PSGs were noted for the same patient, AHI from the earliest study was used, assuming it was the baseline. When more than one surgery was performed, the earliest procedure requiring general anesthesia and an overnight stay was included.
Results: A total of 212 patients, 110 men, had PSGs and peri-operative information during those times. Mean and SD were: age 54.32 (14.5), AHI 24.4 (28.4), minimal oxygen saturation 82.3% (10.9), and BMI 32.9 (8.6). For analysis, AHI was divided into quartiles: 1-4.9, 5-14.99, 15-29.99, and >30 with 20.0%, 31.7%, 22.9% and 25.4% of patients per group, respectively. MS was divided into III/IV, II and I with 14.6%, 56.1% and 29.3% of patients per group, respectively. MS significantly correlated with AHI and BMI for all subjects (p=0.028), more significant for women (p=0.016). A MS of III/IV was found in 31.3% of the women with an AHI >30, vs. 8% of the men. A MS of I was found in 40% of the subjects with an AHI<5.
Conclusion: As previously reported, we confirmed in our larger sample, that MS correlates with BMI and OSA as measured by AHI. This association may have gender differences. The inclusion of these simple measures as part of pre-operative screening may prove to be useful tools to improve surgical care.

0613

IMMUNE RESPONSES TO INFLUENZA VACCINATION ARE IMPAIRED IN PATIENS WITH OBSTRUCTIVE SLEEP APNEA

Consens F,[1] Naff J,[1] Teodorescu M,[2] Opp M[1]
(1) University of Michigan, Ann Arbor, MI, USA, (2) University of Wisconsin-Madison, Madison, WI, USA

Introduction: The impact on immune function of OSA in the population has not been evaluated. The deleterious effects of sleep disorders on the immune system, measured by Ab response to influenza vaccination, have been demonstrated in a partial sleep deprivation study; sleep deprived healthy young adults had a less than half Ab response to immunization than full-night sleepers. We hypothesized that antibody (Ab) titers after influenza vaccination would be reduced in subjects with OSA.
Methods: Screening questionnaires included the SA-SDQ. Volunteers were excluded if they received a flu-shot within 9 months, had a current acute illness or a pre-existing immuno-suppressive disease, or were taking immuno-suppressing medications. Controls reported no sleep problems. Apneics had an SDQ score > 32 for women and > 36 for men and a polysomnogram (PSG) with an RDI >10. Blood samples were taken at baseline (before the flu-shot), 10 and 30 days later. Influenza A serum IgM Ab titers were measured by ELISA.
Results: Thirty-three subjects completed the study. Comparing (mean±SD) 21 controls (6 men) with 12 apneics (6 men), controls were younger (39±11 vs 48±7 yrs), had lower BMI (27±4.3 vs 36±7.7) and lower SDQ scores (25±8 vs. 41±6). PSG comparing controls and apneics showed a mean RDI of 2.2±2.9 vs. 41.9±32.1 (p<0.001), minimal oxygen saturation of 91±3.2% vs. 75.9±9.2% (p<0.001). IgM Ab titers were higher in controls compared with apneics 10 days (13.9±10.5 vs. 6.2±3.0, p=0.027) and 30 days after the flu shot (10.4±8.0 vs. 5.2±2.3, p=0.036) after adjusting for age and BMI.
Conclusion: Apneics have a reduced IgM Ab response to the flu-shot, suggesting that these individuals are less able, or slower, to mount an immune response. This finding may have implications for public health programs aimed at improving effectiveness of vaccinations. Further studies are needed to determine mechanisms whereby OSA negatively impacts immune function.
Support (optional): University of Michigan GCRC M01-RR00042

0614

PHYSICAL EXAMINATION PREDICTORS OF OBSTRUCTIVE SLEEP APNEA IN BARIATRIC SURGERY CANDIDATES

Bae C, Ioachimescu O, Schauer P, Chand B
Cleveland Clinic Foundation, Cleveland, OH, USA

Introduction: It is important to diagnose and treat OSA prior to bariatric surgery to decrease the chance of perioperative complications. However, many morbidly obese patients are not sleepy, do not snore or have witnessed apneas. This study looked at physical exam findings as potential predictors of OSA in morbidly obese patients.
Methods: This was a retrospective chart review between 5/05 and 11/06 of patients who had a PSG before bariatric surgery at the Cleveland Clinic. Demographic and PSG data were collected and correlated with physical exam findings (neck circumference [NC], Friedman tongue position [FTP], BMI). The FTP score provides information about the relationship between the palate and tongue. OSA was classified as mild (5≤AHI>15) or moderate to severe (AHI>15). Univariate and bivariate regressions using JMP5.0.1 (SAS Institute, Cary, NC) were performed.
Results: Seventy-three patients (78% female) were included. Mean age was 46±10.8 (mean±SD). Mean BMI was 50.5±10.5. Mean NC was 44.0cm±5.3cm, and 51 % had a neck circumference≥43.2cm. FTP was 1 or 2 in 24.0% of patients, was 3 or 4 in 76.0% of patients. Mean AHI was 33.7±34.5 (range 0.2-142.0). OSA was mild in 45.0% of patients, was moderate to severe in 55.0% of patients. BMI did not correlate with the AHI (R2=0.006, p=0.48). The probability of having moderate to severe sleep apnea with a NC greater than 43.2cm (23/73 patients) or 46cm (37/73 patients) was 92% and 100% respectively. Moderate to severe sleep apnea was diagnosed in 64% of patients with a FTP score of 3 or 4 (n=55) and in 28% of patients with a FTP score of 1 or 2 (n=18).
Conclusion: The neck circumference and Friedman tongue position may help determine the necessity of a polysomnogram prior to bariatric surgery. A prospective study with a larger number of subjects is needed to validate these findings.

0615

MAXILLOMANDIBULAR ADVANCEMENT FOR OSA IN WOMEN

Li K,[1] Khaja A,[2] Guilleminault C,[3] Faizy R[4]
(1) Stanford University, East Palo Alto, CA, USA, (2) Stanford University, Stanford Sleep Disorders Clinic, Stanford, CA, USA, (3) Stanford University, Stanford, CA, USA, (4) University of California Riverside, Redlands, CA, USA

Introduction: Maxillomandibular advancement (MMA) has been shown to be a highly successful treatment for OSA. However, little is known of the outcomes of MMA in women with OSA. This study evaluated

the objective and subjective outcomes of MMA in women.
Methods: Twenty-eight women were prospectively evaluated. Variables examined include age, sex, BMI, respiratory disturbance index (RDI), lowest oxygen saturation (LSAT), cephalometric data, Epworth sleepiness scale as well as patient-administered questionnaires containing a 10 cm visual analog scale (0 = no change, 10 = drastic change) to subjectively evaluate the patient´s perception of the facial appearance, TMJ symptoms, as well as the overall satisfaction with the treatment outcomes four months following surgery.
Results: Twenty-six patients underwent postoperative polysomonographic evaluation and twenty-four patients completed and returned the questionnaires. The mean age was 46.6 ± 11.9 years and the mean BMI was 25.8 ± 3.1 kg/m2. The mean RDI improved from 49.5 ± 29.2 to 9.1 ±6.0 events/hr, and the mean LSAT improved from 86.5 ± 4.3 to 89.3 ± 2.5%. One patient was defined as incomplete-responder (RDI>20). The ESS improved from 12.8 ± 4.9 to 6.2 ± 4.1 and all of the patients noted significant subjective improvement of daytime sleepiness. Instead of a routine 10 mm MMA, an individualized surgical planning with variable maxillary and mandibular advancement while minimizing midfacial changes was performed in all patients. Despite less advancement of the maxilla, all of the patients achieved a minimum 10 mm advancement of the mandible along with successful objective outcomes. Although all of these patients felt that there were changes in their facial appearance after surgery, all but one patient gave either a neutral or favorable response to their facial esthetic results. One patient reported pain and discomfort of the TMJ which resolved after several months.
Conclusion: MMA is a highly effective treatment for OSA in women objectively as well a subjectively. However, it is important to assess potential facial changes and an individualized surgical planning that is best suited for each patient´s facial appearance should be incorporated to minimize dis-satisfaction after surgery.
Support (optional): None.

0616

PERIODIC LIMB MOVEMENTS IN COMPLEX SLEEP APNEA SYNDROME VS. OBSTRUCTIVE SLEEP APNEA: A RETROSPECTIVE COMPARATIVE REVIEW

Pusalavidyasagar S,[1] Kuzniar T,[2] Olson E,[1] Morgenthaler T[1]
(1) Mayo Foundation for Medical Education and Research, Rochester, MN, USA, (2) Evanston Northwestern Healthcare, Evanston, IL, USA

Introduction: Factors responsible for the development of central apnea events on continuous positive airway pressure (CPAP) in patients with complex sleep apnea syndrome (CompSAS) are not well understood. It seems likely that CompSAS patients have instability of respiratory control at baseline compared with obstructive sleep apnea (OSA) patients. We considered that periodic limb movement (PLM) related arousals may destabilize sleep, and consequently, control of breathing. We hypothesized that the PLM Index (PLMI) and PLM arousal index (PLMAI) would be higher in patients with CompSAS than with OSA, and might play role in destabilizing sleep and thus respiration.
Methods: Retrospective review of patients studied in our Sleep Disorders Center.
Results: There were 112 patients with OSA [median (interquartile range)] age of 59(51-69 years; 85 males, 27 females), and 88 with CompSAS aged 60(47-70 years; 71 males,17 females). Restless legs syndrome was documented in 10 CompSAS patients and 13 OSA patients (p=1.0). During diagnostic polysomnography, the total arousal index (TAI), respiratory related arousal index (RRAI), and PLMAI were similar between CompSAS and OSA patients [40.9 (24.2-53.2) vs. 39.8(26.3-58.9); 26.1(15.0-44.7) vs. 31.2(18.3-50.0); 0 (0-2.3) vs. 0.3(0-3.1); all p>0.05]. In contrast, after CPAP application patients with CompSAS had a higher TAI [27.2(15.5-39.9) vs.16.6(10.7-26.5); p=<0.001], RRAI [12.8 (6.3-23.3)vs.1.1(0.3-3.2); p=<0.001], but lower PLMI [0(0-21.1) vs. 12.6 (0-36.2); p =0.009] and PLMAI [0(0-1.3) vs.0.8(0-4.2) ; p=0.004] than patients with CompSAS. The total sleep time, sleep efficiency and the percent sleep in supine position were similar in both the groups.
Conclusion: PLMS are not more common in CompSAS patients. They do not play a significant role in destabilizing the breathing in CompSAS patients.
Support (optional): Mayo Foundation

0617

RESPONSE TO CPAP THERAPY AMONG SLEEPY OSA PATIENTS

Dolan D,[1] Taylor D,[1] Rosenthal L[2]
(1) University of North Texas, Denton, TX, USA, (2) Sleep Medicine Associates of Texas, Dallas, TX, USA

Introduction: To determine the response to CPAP therapy among sleepy OSA patients during the initial month of therapy.
Methods: Retrospective chart review of 156 consecutive patients (104 male/52 female) diagnosed with OSA who agreed to CPAP therapy. Of those, 127 (83%) were sleepy as defined by the Time of Day Sleepiness Scale (ToDSS). The ToDSS provides 3 sleepiness scores: am, pm and evening and has been shown to provide differential self-reported sleepiness levels across the day. Sleepiness is defined as the presence of one or more elevations at any time of day. The use of the ToDSS has been shown to yield a sensitivity of over 80% in detecting an AHI >10/hour. Patients completed the ToDSS at follow-up and were classified as persistently sleepy (non-responders) and alert (responders) by ToDSS criteria.
Results: Of the initial 83% who were defined as sleepy at baseline, 69% were classified as non-responders and 31% as responders. The two groups were comparable on diagnostic AHI (45.1±31.5 vs. 53.7±30.8), CPAP requirements (8.7±2.5 vs. 8.9±2.6) and follow-up AHI (as derived from the CPAP units: 4.7±3.6 vs. 4.6±2.6). The follow-up interval was comparable for non-responders (31 ± 8 days) and responders (33 ± 11 days). Non-responders had a lower percentage of days used (87 ±16 vs. 93±11; p= .04), and lower average hours of use/night (5.0±2 vs. 5.8±1.9; p= .05) than responders.
Conclusion: The majority of OSA patients experience excessive sleepiness at baseline, which is not resolved after one month of therapy. Strategies to improve adherence with the goal of achieving nightly use of over 5-½ hours/night need to be developed. Finally, the impact of residual sleepiness on activities of daily living in this population requires further investigation.

0618

INFLUENCE OF GENDER ON POSITIVE PRESSURE REQUIREMENTS IN OBSTRUCTIVE SLEEP APNEA.

Subramanian S,[1] Jayaraman G,[2] Surani S,[3] Alridge T[4]
(1) Baylor College of Medicine, Houston, TX, USA, (2) Baylor College of Medicine, TX, USA, (3) Baylor College of Medicine, Corpus Christi, TX, USA, (4) Apnix Sleep Lab, TX, USA

Introduction: Obstructive sleep apnea (OSA) is two to three times more common in men as in women. The mechanisms leading to this difference are currently unclear. Upper airway collapsibility has been shown to be greater in men than in women. We hypothesized that continuous positive airway pressure (CPAP) requirements will be higher in men than in women for a similar severity of OSA.

Methods: This was a retrospective study. We reviewed patient charts of patients with OSA (diagnosed as AHI of > 5) who underwent polysomnography for CPAP titration at our center and recorded the prescribed CPAP pressures. Other data including age, BMI, were also tabulated. Majority of patients were scheduled to undergo bariatric surgery.
Results: A total of 97 charts were analyzed - 59 females and 38 males. The two groups - male and female - were well matched in terms of age (43.97 +/- 13.1 vs 40.52 +/- 9.6; p = 0.164). The BMI was lower in the males compared to the females (42.1 +/- 10.9 vs. 48.4 +/- 11.32; p = 0.014). The AHI in both groups was not statistically different (m - 47.7 +/- 35 vs f - 38.4 +/- 40.3; p = 0.24). Values for daytime sleepiness as assessed by Epworth sleepiness scale was also similar (11.5 +/- 4.8 vs. 11.6 +/- 5.5; p = 0.469). Males were seen to need significantly higher CPAP pressures than females (mean pressure 13.02 +/- 3.49 vs. 10.08 +/- 2.1 respectively; p < 0.0005).
Conclusion: For similar severity of OSA, despite lower values for BMI, males were seen to need higher mean CPAP pressures compared to females. This study serves to reinforce the signifcant influence of gender on upper airway collapsibility and highlights an important clinical relevance.
Support (optional): None

0619

EPISODIC HYPOXIA ELEVATES THE HYPOCAPNIC APNEIC THRESHOLD DURING NON RAPID EYE MOVEMENT SLEEP

Chowdhuri S,[1] Pierchala L,[1] Shanidze I,[1] Maslinski P,[1] Mateika J,[1] Badr S[2]
(1) Wayne State University, Detroit, MI, USA, (2) Detroit, MI, USA

Introduction: Episodic hypoxia is followed by increased ventilatory motor output referred to as long-term facilitation (LTF). The present study was designed to determine whether episodic hypoxia (EH) influences the susceptibility to develop hypocapnic central apnea, ascertained from the $P_{ET}CO_2$ that demarcates the hypocapnic/apneic threshold (HAT) during NREM sleep.
Methods: We studied 9 healthy subjects during stable NREM sleep (6 females and 3 males, age 26.4 ± 1.4 years, BMI 22.3 ± 0.7 kg/m^2). The subjects underwent mechanical ventilation (MV) to determine the HAT. Thereafter, they were exposed to isocapnic EH. The EH protocol was comprised of 15 1-minute episodes of isocapnic hypoxia, separated by 1-minute recovery periods. The mean oxygen saturation achieved was 86.9±0.6%. Ten minutes after EH, the HAT was again determined. EEG, minute ventilation(VE) and supraglottic pressure were measured. HAT was defined as the measured $P_{ET}CO_2$ at which a central apnea closest to the last hypopnea occurred. The $\Delta P_{ET}CO_2$-AT was the change in $P_{ET}CO_2$ between control and the HAT. The ventilatory response was calculated by dividing ΔVE (eupneic V_E –hypopneic V_E) by $\Delta P_{ET}CO_2$.
Results: Results are mean±SEM. The eupneic $P_{ET}CO_2$ declined significantly from pre-hypoxia to post-hypoxia(39.5±1.04 to 38.4±0.24 mm Hg, p=0.002, indicating decreased plant gain), while ΔPETCO2-AT was reduced from -3.3±1.6 to -2.7±1.2 mmHg (p=0.04). Ve increased significantly in the recovery period (6.3±0.3 to 6.6±0.3 L/min, p=0.02).The slope of the ventilatory response was higher in the post-hypoxic recovery period compared to the pre-hypoxic period (1.77±0.30 vs. 3.96±0.96 L/min/mm Hg, p=0.051), indicating increased controller gain.
Conclusion: Following hypoxia, the ventilatory sensitivity to CO_2 below eupnea was increased and $\Delta P_{ET}CO_2$ was reduced significantly below control despite a significant reduction in eupneic $P_{ET}CO_2$ in the recovery period. This indicates that episodic hypoxia may play a destabilizing role by increasing controller gain despite decreasing plant gain.
Support (optional): Department of Veterans Affairs and NHLBI

0620

SCREENING FOR SLEEP DISORDERS IN NORTH AMERICAN POLICE OFFICERS

Rajaratnam S,[1] Barger L,[1] Lockley S,[1] Cade B,[2] O'Brien C,[2] White D,[3] Czeisler C[1]
(1) Brigham and Women's Hospital / Harvard Medical School, Boston, MA, USA, (2) Brigham and Women's Hospital, Boston, MA, USA, (3) Brigham and Women's Hospital / Harvard Medical School / Sleep HealthCenters, Boston, MA, USA

Introduction: Sleep disorders are common, costly, and treatable, but often remain undiagnosed and untreated. Unrecognized sleep disorders adversely affect personal health and may lead to chronic sleep loss, which in turn increases the risk of accidents and injuries. These problems are exacerbated in shift workers, who may experience chronic sleep loss due to their work schedules and also show a high incidence of sleep disorders. The present study sought to examine the incidence of major sleep disorders in a sample of North American police officers.
Methods: Police officers (n=4,471) completed a self-report survey that included screening for obstructive sleep apnea (OSA) alone or for OSA and all of the following: insomnia, restless leg syndrome (RLS), shift work sleep disorder (SWSD), and narcolepsy with cataplexy. Validated screening questionnaires were used for all sleep disorders except for SWSD. For SWSD, the screening questions were based on the International Classification of Sleep Disorders-II diagnostic criteria, but required participants show both insomnia and excessive sleepiness that are temporally associated with a recurring work schedule that overlaps the usual sleep time. Participants were recruited through invitation letters to law enforcement agencies and through visits to police stations during which an education session about sleep and health was presented to officers. Participants who screened positive for one or more sleep disorder were referred to a sleep clinic for formal evaluation. The evaluation was verified in a subset of participants.
Results: The percentage who screened positive for any sleep disorder was 38.4%. The percentages for each disorder were as follows: OSA 35.1%, insomnia 6.8%, RLS 0.7%, SWSD 2.0%, and narcolepsy 0.5%.
Conclusion: Based on these data, sleep disorders appear to be highly prevalent in the present sample of police officers. Sleep disorder screening and treatment programs may potentially improve police officer health, safety and productivity.
Support (optional): This study was supported by the National Institute of Justice (2004-FS-BX-001) and the Centers for Disease Control and Prevention (R01 OH008496).

0621

ACUTE EFFECTS OF INTERMITTENT HYPOXIA ON GLUCOSE METABOLISM IN NORMAL SUBJECTS

Louis M, Punjabi N
Johns Hopkins University, Baltimore, MD, USA

Introduction: Sleep-disordered breathing (SDB) has been independently associated with impaired glucose metabolism and insulin resistance. Whether intermittent hypoxemia or sleep fragmentation are in the putative causal pathway linking SDB and altered glucose metabolism remains to be determined. To explicate the role hypoxia in SDB-related alterations in glucose homeostasis, the current study examined the acute metabolic effects of intermittent hypoxia in normal subjects.
Methods: Six non-smoking, non-obese, healthy young male volunteers

were recruited. Using a cross-over study design, subjects were exposed to 5-hours of normoxia (21% O_2) or hypoxia (5% O_2) during the day. Subjects were randomly assigned to normoxia or hypoxia as the initial exposure. Approximately one week after the initial intervention, each subject was crossed over to the other condition. Intermittent hypoxemia was induced with recurrent but brief exposures to hypoxic gas using tight-fitting nasal mask connected to a manual three-way valve mechanism. A nadir oxyhemoglobin saturation of 85% was targeted with each exposure to the hypoxic gas. Glucose metabolism was assessed with the intravenous glucose tolerance test (IVGTT). The minimal model was used to quantify insulin sensitivity from the IVGTT.
Results: The number of oxygen desaturations in the study sample ranged of 20 to 30 events/hr over the 5-hour period. Compared to normoxic conditions, insulin sensitivity with intermittent hypoxia decreased from 3.8 to 2.6 $(mU/L)^{-1}min^{-1}$ ($p < 0.06$), amounting to 30% change in insulin sensitivity.
Conclusion: Acute exposure to intermittent hypoxia for 5-hours in normal subjects decreases insulin sensitivity. The findings of this study implicate SDB as a causal factor for glucose intolerance and insulin resistance. Ongoing work is focused on the intermediate mechanisms (e.g., inflammatory pathways, sympathetic activation) through which hypoxemia may mediate alterations in glucose homeostasis.
Support (optional): NIH grants HL07578 and AG025553

0622

ALPHA-DELTA SLEEP AND SLEEP APNEA

Faiz S,[1] Mora A,[1] Hamzeh N,[1] Castriotta R,[1] Patel B,[1] Murthy J[2]
(1) University of Texas Health Science Center at Houston, Houston, TX, USA, (2) University of Texas Health Science Center at Houston, TX, USA

Introduction: Alpha-delta sleep has been described with chronic fatigue syndrome, rheumatologic disorders, fibromyalgia, and chronic sleep disruption deprivation. Although demonstrated in patients with UARS, the correlation with OSA is unclear. The purpose of this study is to identify the presence of alpha-delta sleep and its´ associations.
Methods: A retrospective analysis in a county hospital of patients with polysomnography over two months was reviewed for alpha-delta sleep. From a total of 150 studies, alpha-delta sleep was observed in 34 studies (22.6%). The studies included: 13 split night, 14 baseline, 5 titrations, 1 baseline with MSLT, 1 titration with MSLT.
Results: Alpha-delta sleep was identified in 34 patients. There were 6 men and 28 women, with an average age of 47, BMI of 37.6 kg/m2, and Epworth Score of 11.6. Primary sleep disorders were present in 33 patients including 79% OSA(average AHI 23.3), 5.8% OSA during REM sleep(average AHI 20.5), 11.8% UARS(average RERA index 15.8), and 3.2% without any sleep disordered breathing. PLMD co-existed in 17.6% patients(average PLMD index 11.8). Concomitant medical disorders included 64.7% psychiatric disorders (anxiety/depression/bipolar), 11.8% rheumatologic disorder (sarcoidosis/lupus/rheumatoid arthritis), 52.9% pain-related issue (back pain/RLS/arthritis), 14.7% thyroid disorders, 8.8% seizure disorder, and 8.8% hepatitis. Only 26.5% actively smoked, 8.8% consumed alcohol, and 2.9% used illicit drugs. The majority of patients(73.6%) admitted to consuming 1 to 10 caffeinated beverages a day (average of 3.9). Positive pressure was applied in 19 patients, with16 patients on CPAP (average pressure 12.7 cm H20) and 3 on BIPAP.
Conclusion: In this population, alpha-delta sleep is associated with sleep disordered breathing extending beyond UARS. Compliance with treatment could be influenced, for treatment is primarily pharmacologic. Although many patients also consumed caffeine, correlation with illicit drug intake could provide a more valid association. The association of alpha-delta sleep is more vast that originally hypothesized.
Support (optional): Gold, Chest 2003; 123:87-95
Manu, Southern Medical Journal 1994; 87(4):465-70.

0623

EFFECTS OF INTERMITTENT HYPOXIA ON SLEEP ARCHITECTURE IN NORMAL SUBJECTS

Louis M, Punjabi N
Johns Hopkins University, Baltimore, MD, USA

Introduction: Sleep-disordered breathing (SDB) is characterized by episodic decreases in oxyhemoglobin saturation and transient electroencephalographic (EEG) arousals from sleep. The mechanisms through which diminished airflow through the upper airway during sleep elicits an arousal response in SDB are not entirely known. The primary objective of this investigation was to test whether in normal subjects brief but recurrent drops in oxyhemoglobin saturation fragment and disrupt sleep continuity.
Methods: Five non-smoking, non-obese, healthy young male volunteers were recruited. Using a cross-over study design, subjects were exposed to 5-hours of normoxia (21% O_2,) or hypoxia (5% O_2) during sleep. Subjects were initially assigned to normoxia or hypoxia using random allocation. Approximately one week after the initial intervention, each subject was crossed over to the other condition. Intermittent hypoxemia was induced with recurrent but brief exposures to hypoxic gas using tight-fitting nasal mask connected to a manual three-way valve mechanism. A nadir oxyhemoglobin saturation of 85% was targeted with each exposure to the hypoxic gas. Sleep was monitored using full-montage polysomnography under normoxic and hypoxic conditions. EEG arousals and sleep stages were scored using standard criteria.
Results: Total sleep time during normoxic and hypoxic conditions was comparable (471.6 vs. 471.7 min). Sleep stage distribution showed similar amounts of stage 2 sleep (59.1% vs. 57.3% p=0.6); slow wave sleep (14.7% vs. 13.7%, p=0.6), and REM sleep (21.5% vs. 22.1%, p=0.8). Stage 1 sleep was slightly higher with hypoxic than normoxic exposure (4.7% vs. 6.9%, p = 0.05). However, arousal frequencies showed no differences between the two conditions (13.1 vs. 13.0 events/hr, p =0.98).
Conclusion: Acute exposure to intermittent hypoxia for 5-hours during sleep in normal subjects does not disrupt sleep architecture. The findings of this study suggest that mechanisms besides intermittent hypoxemia may underlie the arousal response to upper airway collapse during sleep in SDB.
Support (optional): NIH grants HL07578 and AG025553

0624

NEUROCOGNITIVE FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH OSA: SHORT AND LONG-TERM EFFECTS OF AUTO AND FIXED PAP.

Castronovo V,[1] Marelli S,[1] Aloia M,[2] Fantini M,[1] Kuo T,[3] Manconi M,[1] Giarolli L,[4] Ferini-Strambi L[1]
(1) Sleep Disorders Center University Via-Salute San Raffaele Milano, Milan, Italy, (2) National Jewish Medical and Research Center, Denver, CO, USA, (3) Stanford University, Stanford, CA, USA, (4) Sleep Disorders Center University Via-Salute San Raffaele Milano, Milan, AE (Europe), Italy

Introduction: Sleep fragmentation and intermittent hypoxemia from OSA have been shown to have a negative impact on neurocognitive function. Literature data on improvement after treatment are mixed. A recent study demonstrate that cognitive improvement may be related to type of PAP treatment and to adherence. Aim of this study was to

compare changes in neurocognitive function and quality of life in OSA patients after treatment with Auto and fixed PAP after a short period of therapy (ST- two months) and after a longer follow-up(LT-12/18 months).
Methods: Forty patients with severe OSA (RDI >30), were randomly assigned to one of two treatment groups. Group A received treatment with Auto PAP and group B received treatment with fixed PAP (all patients received RemStarAuto, Respironics Inc. devices set in Auto or fixed PAP mode). All patients were evaluated at Baseline (BL- before treatment), at T1 (after two months) and at T2 (after 12/18 months). Neurocognitive functioning (attention, vigilance, language, memory, executive function, constructional and psychomotor abilities), sleepiness (Epworth), mood (Beck Depression Inventory) and quality of life (SF-36 and FOSQ) were assessed at BL, T1, T2. Results were analyzed by means of Anova by repeated measures.
Results: 38 patients (36 M, 2 F; mean age 54.5 ± 9.5) completed the study. The two groups were similar in terms of demographic and clinical features. All patients showed good objectively measured adherence to PAP therapy (time in minutes of use per night: Group A 345 ± 60 vs Group B 374 ± 75 and % of days of use: Group A 75 ± 31 vs Group B 79 ± 40).
Most of neurocognitive tests showed an effect of time indicating a treatment improvement on cognition over time ($p<0.001$). In particular long term memory (MLT) (Corsi Supraspan Recall, Rey´s Copy, Rey List Learning, Rey List Recall , Rey List Recognition), attention and executive function (PASAT error, Trial A, Stroop , and TEA Flexibility) were significantly better at T2.
Group A showed greater improvement on attention (Divided Attention 722,5 ± 87,8 vs 677,7 ± 73,4; $p=0.045$) and executive function (Stroop 46,4 ± 24,5 vs 33,1 ± 17,8; $p=0.015$) while Group B showed greater improvement on MLT (Rey List Learning 46,6 ± 9,5 vs 48,2 ± 7,8; $p=0.014$ and Rey List Recognition 14,4 ± 0,7 vs 14,5 ± 0,8; $p=0.031$). Results of quality of life showed a significant improvement over time in both groups [FOSQ total $F(1,66; 61,62)=21,226; p<0.001$]. A positive correlation between objectively measured adherence and cognitive performance was also found (MLT r=0,39;p=0,025).
Conclusion: Our data showed that cognitive functions significantly improved over time, regardless the type of PAP. Our long term data suggest a possible plasticity of the brain in recovering cognitive function over time (also after 1 year). The objectively measured adherence should be always measured when assessing cognitive functioning changes.
Support (optional): The study was partly supported by a grant by Respironics Inc.

0625

CHARACTERISTICS OF ASIAN LATERAL FACE WITH OBSTRUCTIVE SLEEP APNEA USING DIGITAL PHOTOGRAPHY

Higami S,[1] Kryger M,[2] Yumiko H,[3] Kitano H[3]
(1) Tottori University, Yonago, Tottori, Japan, (2) University of Manitoba, Manitoba, Canada, (3) Tottori University, Tottori, Japan

Introduction: To use digital photography and to compare anatomic structure between Caucasian and Asian OSAHS. To evaluate the characteristics of Asian lateral face.
Methods: All patients were diagnosed using comprehensive polysomnography. Their lateral facial photographs were taken using a digital camera, with seating upright and taking a relax position according to cephalometrics technique. We set some measuring point on face to evaluate anatomic strictures. These some angles and distances were calculated with computer software.
Results: Thirty-four Caucasians, thirty-eight Asians. Age (50±11 vs 49±10; $p=0.97$), BMI (29.6±2.9 vs 25.7±2.1; $p<0.0001$), AHI (25.7±27.0 vs 43.6±16.7; $p=0.0015$), ANB angle: relation between upper and lower jaw (6.5±3.0 vs 8.3±2.9; $p=0.0072$), NGnH angle: lower jaw position (119.2±7.5 vs 123.4±8.1; $p=0.04$).
Conclusion: Jaw relation (ANB) and jaw position (NGnH) were significantly different between Caucasian and Asian. These angles showed Asian faces have the characteristic of micrognathia and retrognathia rather than Caucasian.
Digital photography can be used to assess anatomic structure of patients with OSA.

0626

WHEN CAN OBJECTIVE CPAP DATA DETERMINE NONCOMPLIANCE?

Doerr C,[1] Mcleland J,[2] Kampelman J,[1] Boero J,[1] Duntley S[1]
(1) Washington University in St. Louis, Saint Louis, MO, USA, (2) Washington University in St. Louis, St. Louis, MO, USA

Introduction: Obstructive Sleep Apnea (OSA) is a serious condition affecting an estimated 18 million Americans. Continuous Positive Airway Pressure (CPAP) continues to be the preferred treatment for OSA. CPAP compliance is imperative for the safety, health, and well being of patients with OSA. Literature suggests that the first 3 months of CPAP use at home is predictive of continued CPAP compliance. We examined CPAP use by downloading objective data from patients´ CPAP machines.
Methods: Compliance data was obtained from 77 recently diagnosed OSA patients. Smart card daily usage was acquired from 64 patients (age 58.3±10.0) who were divided into two groups based on CPAP compliance (>4hrs of use >70% of days). Patients were setup on CPAP at home for an average of 202 days when compliance data was downloaded.
Results: 43 patients (67%) met the criteria for compliant (19 males) while 21 patients (33%) were found to be noncompliant (14 males). Compliant and noncompliant patients did not vary by age (58.5±9.3 vs. 58.1±11.5), disease severity (AHI 38.7±24.0 vs. 39.7±30.4), lowest oxygen desaturation (79.8% vs.78.4%) or by optimal treatment pressure (10.3±2.7 vs. 9.5±2.3 cm H2O). After the first week of CPAP use, 71% of patients categorized as noncompliant were not meeting the requirements for compliance. Over the 3 months, weekly noncompliance rates in this group continued to increase: 66%, 71%, 76%, 81%, 76%, 71%, 81%, 86%, 86%, 90%, and 95% while usage rates in the compliant group fluctuated at 81%, 88%, 79%, 81%, 74%, 70%, 77%, 74%, 67%, 72%, 72%, and 65%.
Conclusion: Findings indicate that initial noncompliance with CPAP during the first week is a predictive factor of overall noncompliance. This suggests that CPAP compliance should be closely monitored and intervention for noncompliance should be performed immediately. This emphasizes that contact and follow up from the sleep center early on is imperative.

0627

EFFECTIVENESS OF MAXILLOMANDIBULAR ADVANCEMENT VIA DISTRACTION OSTEOGENESIS AS A TREATMENT FOR OBSTRUCTIVE SLEEP APNEA

Consens F, Helman J, Palmisano J
University of Michigan, Ann Arbor, MI, USA

Introduction: Distraction Osteogenesis (DO) is a gradual surgical elongation of bone implemented in OSA patients concomitantly in the mandible and maxilla. Previous data showed guarded improvement in

patients with an RDI of >70 and BMI > 32 treated with standard Maxillomandibular Advancement. We sought to evaluate DO as a treatment option for obstructive sleep apnea (OSA) in the above mentioned population. We examined the changes in polysomnographic (PSG) and BMI data in patients before and after DO.
Methods: We evaluated pre- and post-operative RDI in both REM (RDI-R) and NREM sleep (RDI-NR), minimal O2, and Mean body mass index (BMI).
Results: A total of 16 men, underwent DO for OSA at our institution between 8/01 and 8/06. Two cases were excluded due to device failure, and those who had standard MMA. Prior upper airway surgery (UPPP) was performed in 5 subjects. Mean subject age was 45 years ± 8 sd. BMI was 36.7 kg/m2 ±6.5. Polysomnography prior to surgery revealed a mean RDI of 82.3 ±21.6 events/hr and minO2 of 75.3% ±11.6. Post-operative PSG, obtained 33±10 days after surgery, after 17±3.4 mm of advancement showed a significant difference with a mean RDI of 14±11.7 (p=0.003) events/hr and minO2 of 84%±8.8 (p<0.001) and BMI of 33.9±5.5 (p<0.001). The RDI-NR decreased form 68.6±34.7 to 14.9±17 (p= 0.001) in contrast to the RDI-R that decreased from 36±39 to 23±22, which was not significant.
Conclusion: DO is a viable surgical option for OSA, showing significantly lowered RDI, mainly due to improvement in the RDI-NR, increased minO2, and decreased BMI. The lack of improvement in RDI-R suggests that patients with mainly high RDI-R may not benefit as much from this procedure.

0628

CHARACTERISTICS AND SURGICAL RESULTS OF RAPID EYE MOVEMENT(REM) RELATED OBSTRUCTIVE SLEEP APNEA(OSA)

Kim S
Kyunghee University, College of Medicine, Seoul, South Korea

Introduction: Airway resistence is usually increased during REM sleep due to atonia of muscle tone, especially hypotonia of respiratory muscles. REM sleep related OSA(ROSA) is considered as unique disease or one of clinical spectrum of OSA. It is usually considered as poor indication of surgical treatment. But there is a few data about that. The aim of this study was to compare the sleep and anatomic parameters between ROSA and non-ROSA, and define whether ROSA can be surgical candidate or not.
Methods: All patients were classified by two groups, ROSA and non-ROSA by the definition of ROSA;AHI(REM)/AHI(NREM)>2. Sleep parameter, such as polysomnogrphic data, Epworth sleepiness scale score(ESS), daytime and nighttime symptom score using visual analogue scale, were analysed. Also, anatomic evaluation, such as anthropometric parameter, nasopharyngoscopic parameter, and cephalometric parameter were performed. And all the parameters were compared between ROSA and non-ROSA. After the multilevel surgery, surgical results using symptom improvement on postoperative 1 month, and polysomnographic data on postoperative 6 months were evaluated and matched between ROSA and non-ROSA. Success criteria of surgical treatment were AHI less than 20 and more than 50% reduction.
Results: Numbers of ROSA(n=29) were smaller than non-ROSA(n=108). Severity in ROSA were weaker than that in non-ROSA. Most ROSA belonged to mild and moderate OSA. There was no statistical difference in sleep parameters and anatomic parameters between 2 groups preoperatively. And surgical results were similar except small part of symptom improvement when compared in the same degree of severity.
Conclusion: We can conclude that ROSA may not specific disease and ROSA patients can be the candidate for surgical treatment if they have definite obstruction site.

0629

QUANTIFICATION OF SLEEP FRAGMENTATION THROUGH THE ANALYSIS OF SLEEP-STAGE TRANSITIONS

Ivanov P, Lo C
Boston University, Boston, MA, USA

Introduction: We introduce new quantitative approaches to study sleep-stage transitions with the goal of addressing the two following questions: (i) Can the new approaches provide more information of the structure of sleep-stage transitions? (ii) How does sleep fragmentation in patients with sleep apnea affect the structure of sleep-stage transitions?
Methods: We analyze hypnograms and compare normal subjects and sleep apnea patients using numerous measures, including percentage of sleep time for each stage, probability distributions of the duration of each stage, sleep-stage transition matrix, and a measure of the asymmetry of this matrix. 197 normal subjects and 50 obstructive sleep apnea patients recruited in the SIESTA project.
Results: We find that the time percentage for wake stage duration is identical for sleep apnea subjects and for normal healthy subjects. However, subjects from the sleep apnea group have a faster decaying distribution of wake duration. Both healthy and sleep apnea subjects exhibit exponential distributions for the duration of all sleep stages. In contrast, we observe a power law distribution for the wake stage duration in both groups. We also find that there is a loss in the preference of specific transition pathways between sleep stages in the subjects sleep apnea.
Conclusion: The new approaches proposed here enable us to show that the distribution of sleep and wake duration have different functional forms, indicating fundamental differences in the dynamics between sleep and wakefulness control. This difference remains even under conditions of sleep apnea when sleep is fragmented. The fragmentation of sleep in sleep apnea results in shorter wake duration, and interrupts the structure of sleep-stage transitions of sleep apnea subjects, causing the loss of certain transition pathways.

0630

QUALITY OF LIFE DETERMINANTS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

ValençA J,[1] Garcia M,[1] Caeiro F,[1] Monteiro O,[1] Moreira S,[2] Sotto-Mayor R,[1] Bugalho De Almeida A[1]
(1) Santa Maria Hospital, Lisbon, (2) Santa Maria Hospital, Lisbon, Lisbon, Portugal

Introduction: Recent studies demonstrate a decline in life quality of patients with obstructive sleep apnea syndrome (OSAS). Our goal was to analyze the factors that contribute to such decline.
Methods: We studied 161 OSAS patients using polysomnography and the Functional Outcomes of Sleep Questionnaire (FOSQ) test at the date of initiation of CPAP. We correlated the total score and the scores of its different subscales (Pearson Correlation) with age, body mass index (BMI), Epworth Sleepiness Scale (ESS), diurnal PaO2 and PaCO2, and data from polysomnography. We then performed a stepwise multivariate analysis with the variables where we observed correlation.
Results: The impact on activity level (2,8±0,7) correlated with: minimal SaO2, average SaO2, T90, PaO2 , PaCO2, BMI and ESS. The vigilance score (2,4±0,9) correlated with: E3+E4, IAH, total duration of apnea/hypopnea, average SaO2, minimal SaO2, T90, ODI, PaO2 and ESS. The intimacy subscale (2,5±1,2) correlated with: E4, E3+E4, PaO2, age, BMI and ESS. The general productivity subscale score (3,1±0,7) correlated with: E3, E4, E3+E4, average SaO2, minimal

SaO2, T90, PaO2, PaCO2, BMI and ESS. The social outcome subscale (3,2±1,0) correlated with: E4, PaO2, PaCO2, BMI and ESS.
The total FOSQ (14,0±3,7) correlated with: E3, E4, E3+E4, average SaO2, minimal SaO2, T90, PaO2, PaCO2, age, BMI and ESS.
In the multivariate analysis the models that included ESS, BMI, PaO2 explain 27% of the impact in the activity level; ESS, PaO2 explain 44,5% of vigilance changes; age, BMI, ESS 30% of intimacy changes; ESS, PaO2, E3+E4 21,6% of the decline in general productivity; ESS, BMI 14,2% of the social outcome; ESS, PaO2, BMI, age 39,1% of decline in the quality of life as measured by FOSQ.
Conclusion: The factors that contributed the most to the decline in the quality of life of patients with OSAS were excessiveness daytime sleepiness, obesity and hypoxemia.

0631

REPORTED DREAM RECALL FREQUENCY: A MARKER FOR SLEEP ONSET REMS PERIODS (SORP´S) IN HYPERSOMNOLENT PATIENTS WITHOUT OSA

Pagel J,[1] Shocknasse S[2]
(1) University of Colorado Health Sciences Center, Pueblo, CO, USA, (2) Colorado State University, Pueblo, CO, USA

Introduction: Dreaming related phenomena including hypnogognic hallucinations, and sleep paralysis are classically associated with narcolepsy. The current diagnostic requirement for narcolepsy in patients without cataplexy includes a shortened sleep latency and at least two SORP´s in patients that have had polysomnographic evaluation. This study addresses the association of reported dream recall frequency with a positive or negative diagnostis of narcolepsy by MSLT in a hypersomnolent population without the complaint of cataplexy and without OSA (based on a AHI < 5.0 on polysomnography).
Methods: Individuals (N=41) included in this study were being evaluated in a clinical sleep laboratory for hypersomnolence (Mean age 36.9, Range 14-59; Male # 8/ Female # 33). Dream recall frequency was reported on intake questionnaire using a non-continuous Likert scale in which 1=never, 2=1x/month, 3=1x/week, 4=2x/week and 5=every night. Multiple sleep latency testing was done per AASM approved protocols utilizing a 4 nap protocol extended to 5 naps when one SORP was obtained.
Results: For the group reporting dream recall 1x/week or more frequently, 13/28 patients (46.4%) were noted to meet criteria for narcolepsy with at least 2 SORP´s. In the grouping reporting dream recall at 1x/month or less, only 2/13 (15.4%) were noted to have SORP´s. The report of dream recall frequency 1x/week or more has a diagnostic sensitivity in this population of 46.4%, with a diagnostic specificity of 84.6%.
Conclusion: The assessment of reported dream recall frequency has diagnostic value in suggesting whether hypersomnolent patients without OSA and/or cataplexy being evaluated for narcolepsy by MSLT are likely to have SORP´s. Individuals in this population reporting low dream recall (1x/month or less) are less likely to meet criteria for the diagnosis of narcolepsy.

0632

THE DISTRIBUTION AND IMPACT OF NARCOLEPSY SYMPTOMS IN NON-SLEEP-DISORDERED INDIVIDUALS

Ruiter M,[1] Lichstein K,[2] Durrence H,[3] Taylor D,[4] Riedel B,[5] Bush A[6]
(1) University of Alabama, Tuscaloosa, AL, USA, (2) The University of Alabama, AL, USA, (3) Somaxon Pharmaceuticals, CA, USA, (4) University of North Texas, TX, USA, (5) University of Memphis, TN, USA, (6) University of Tennessee, TN, USA

Introduction: Some characteristics of narcolepsy are also observed in the general population. The differences in sleep and daytime functioning in those displaying these most common symptoms compared to those that do not are unknown. The goal of this paper is to compare individuals who endorse experiencing the narcoleptic symptoms of sleep attacks and/or paralysis upon sleep onset (PN, positive for narcolepsy symptoms) to those that do not (NN, negative for narcolepsy symptoms) on demographic, health behavior, subjective sleep, and daytime functioning variables.
Methods: We identified 67 PN and 668 NN, out of 772 participants in an epidemiological survey that did not endorse any other sleep disorders. All participants completed the following questionnaires: two weeks of sleep diaries, a general health questionnaire, and daytime functioning questionnaires including sleepiness, fatigue, insomnia impact, depression, and anxiety.
Results: t-tests between PN and NN were conducted. Results indicate PN had worse daytime functioning on five questionnaires compared to NN ($p<.001$). On sleep variables, PN reported worse sleep on five of six variables compared to NN ($p<.01$). There was no difference between the groups on alcohol, cigarette, and caffeine consumption. Demographically, PN reported significantly less educational attainment compared to NN ($p<.05$) and greater BMI ($p<.05$). However, the magnitude of the difference on the latter was marginal.
Conclusion: Participants endorsing experiences of certain narcoleptic symptoms are not functioning as well as those not having these symptoms in terms of sleep and daytime functioning. Maladaptive health behaviors do not differ between these groups.
Support (optional): Research supported by National Institute on Aging grants AG12136 and AG14738

0633

A STUDY OF THE DIAGNOSTIC UTILITY OF HLA TYPING, CSF HYPOCRETIN-1 MEASUREMENTS, AND MSLT TESTING FOR THE DIAGNOSIS OF NARCOLEPSY IN 163 KOREAN PATIENTS WITH UNEXPLAINED EXCESSIVE DAYTIME SLEEPINESS

Hong S,[1] Lin L,[2] Jeong J,[3] Shin Y,[3] Han J,[3] Lee J,[3] Lee S,[3] Mignot E[4]
(1) St. Vincent´s Hospital, Catholic University of Korea, Suwon, Gyunggi-do, South Korea, (2) Center for Narcolepsy, Stanford University, CA, palo Alto, CA, USA, (3) St. Vincent Hospital, Catholic University of Korea, Suwon, Gyunggi-do, South Korea, (4) Stanford University, Palo Alto, CA, USA

Introduction: To study DQB1*0602 status and hypocretin-1 levels in the cerebrospinal fluid (CSF) in a cohort of patients with hypersomnolence and to test International Classification of Sleep Disorders-2 (ICSD-2) criteria for hypersomnia of central origin.
Methods: Retrospective case series of 163 consecutive patients with unexplained sleepiness and 282 controls recruited at St. Vincent´s Hospital, Korea. The gold standard for diagnosis was ICSD-2 criteria. Patients and controls completed the Stanford Sleep Inventory (SSI) and agreed to HLA typing. Polysomnography (87%), MSLT (96%), and CSF hypocretin-1 measurements (53%) were conducted in patients.
Results: Most (80%) patients could be classified using the ICSD-2. The 33 patients who could not be classified were without cataplexy (4 with low CSF hypocretin-1). These could not be included because of sleep apnea (AHI ≥ 5/hr, 84%) and/or because sleep prior to MSLT was less than 6 hrs (27%). Narcolepsy with cataplexy cases were 92% HLA positive with low hypocretin-1. Cataplexy at interview was predicted by validated SSI questions regarding cataplexy triggers. In contrast, cataplexy-like events were frequently reported in all groups including controls. Cases with narcolepsy without cataplexy were frequently male (73%) and heterogeneous biologically (36% HLA positive, 40% with low CSF hypocretin-1). None of the controls had low CSF hypocretin-1 while 13% were HLA positive.
Conclusion: The ICSD-2 was easily applicable in cases with typical cataplexy.
In these cases, the MSLT and further evaluations were almost always positive and may thus not always be needed. Many patients without cataplexy were difficult to classify because of difficulties in interpreting the MSLT in the presence of sleep apnea or reduced sleep.
Support (optional): This was not an industry supported study

0634

SOREMS IN SLEEP DISORDER PATIENTS: ASSOCIATION WITH SLEEPINESS AND ALERTNESS

Kim C,[1] Ong A,[2] Chung S,[1] Shapiro C[2]
(1) University Health Network, Toronto, Ontario, Canada, (2) University Health Network, Ontario, Canada

Introduction: Sleep-onset rapid eye movement (SOREM) episodes during daytime naps is recognized as a main diagnostic feature of narcolepsy. However, SOREMs have been reported to occur in other disorders. This study set out to answer three questions: 1) whether patients with SOREMs are sleepier and less alert than patients without SOREMs; 2) if the number of SOREMs is linked with the degree of daytime sleepiness; and, 3) whether the majority of patients with SOREMs are found to have narcolepsy.
Methods: 223 charts of sleep clinic patients with SOREMs on the Multiple Sleep Latency Test (MSLT) or Maintenance of Wakefulness Test (MWT) were collected. Further, 223 charts from clinic patients without SOREMs were collected as a control group. Information was collected from the initial sleep study.
Results: The mean ages of the study groups at the time of their sleep studies were: SOREM: 38.8 ± 14.1 years (range 13-76 years) and controls: 45.9 ± 15.4 years (range 15-98 years). Scores on scales of subjective sleepiness (ESS, SSS) and alertness (THAT, ZOGIM-A) were not different between the SOREM and control group. However, the SOREM group had significantly shorter mean sleep onset latency on the MSLT and MWT. Subjective sleepiness or alertness was not correlated with the number of SOREMs on the MSLT or MWT. Patients with SOREMs were almost equally as frequently diagnosed with narcolepsy, sleep apnea and depression/anxiety.
Conclusion: Based on objective measures, patients with SOREMs are sleepier than those without SOREMs, but they are not subjectively aware of their degree of sleepiness and impaired alertness. The number of SOREMs is not associated with the level of objective sleepiness or patients´ subjective sleepiness and alertness. Lastly, SOREMs are found across a wide variety of sleep and psychiatric disorders.

0635

INCREASED CSF TRANSFERRIN AND IRON LEVELS IN HYPOCRETIN DEFICIENT NARCOLEPSY

Kanbayashi T,[1] Sagawa Y,[1] Kanayama H,[1] Hayashi-Ogawa Y,[1] Kondo H,[2] Takemura T,[3] Kaneko Y,[2] Shimizu T,[1] Nishino S[4]
(1) Akita University, Akita, Japan, (2) Akita University, AA, (3) Akita University, Akia, Japan, (4) Stanford University, CA, USA

Introduction: Periodic leg movements during sleep (PLMS) are often associated with restless legs syndrome (RLS). Reduced ferritin and elevated transferrin levels (with normal or low iron levels) in CSF (as indicators of low brain iron) are reported in PLMS/RLS subjects. A much higher incidence (25-50% vs. ~5% in general population) of PLMS is reported in narcoleptic patients. Since altered dopaminergic neurotransmissions are suggested in both diseases and since iron is a co-factor for dopamine synthesis (thyrosine hydoroxylase), we evaluated CSF ferritin, transferrin and iron in patients with hypocretin deficient narcolepsy in the study.
Methods: We enrolled 16 patients with hypocretin deficient narcolepsy and age, gender-matched 20 control subjects. The lumbar puncture was performed between 10:30 AM and 15:30 PM on an outpatient basis. Three milliliters of CSF were stored at -80 C until assayed for iron, transferrin and ferritin using routine laboratory techniques by the Special Reference Laboratories (SRL), Tokyo, Japan. Differences between patients with hypocretin deficient narcolepsy and control subjects were tested using the standard two-tailed t-test.
Results: Patients with hypocretin deficient narcolepsy had higher CSF transferrin (21.8 +/- 8.0 mg/L vs 17.1 +/- 3.9 mg/L; mean +/- SD, p=0.03) and iron levels (25.0 +/- 15.9 mcg/L vs 16.5 +/- 6.7 mcg/L; p=0.04) when compared to control subjects. There was no difference in CSF ferritin levels (2.9 +/- 1.5 mcg/L vs 2.8 +/- 1.7 mcg/L) between the two groups.
Conclusion: As seen in RLS subjects, an increase in transferrin was observed in narcoleptic subjects. However, normal ferritin and increased iron levels in these subjects may possibly suggest a higher utilization of iron in narcolepsy. It is not known if these findings are direct or indirect (such as a compensatory increase in dopaminergic synthesis) to hypocretin deficiency, and whether or not this contributes to the high incidence of PLMS in narcolepsy. As a result of these findings, further studies are warranted.

0636

IMMUNOREACTIVE OREXIN-A IN HUMAN URINE : A STUDY TO COMPARE THE NARCOLEPTIC PATIENTS WITH IDIOPATHIC HYPERSOMNIA PATIENTS

Kanayama H,[1] Kanbayashi T,[2] Kondou H,[1] Kaneko Y,[1] Takemura T,[1] Sagawa Y,[1] Tokunaga J,[1] Shimizu T[2]
(1) Akita University School of Medicine, Akita, Japan, (2) Akita University, Akita, Japan

Introduction: It has been found that orexin system is disappeared in narcoleptic patients, and orexin level in CSF is extensively decreased. The measurement of orexin in CSF is one of the criteria for definite diagnosis of narcolepsy in ICSD-2. However, lumbar puncture test is invasive for the patients.
While, there is evidence to indicate the presence of orexin in peripheral region. Although the possibility to determine orexin in blood has been reported, it has been difficult to use it as definite diagnosis because it was present only in slight quantity. Takahashi (2005) reported that orexin was detected in urine at a concentration about three times as high as in blood. For establishing a diagnostic method using urine, we measured urinary orexin in the patients with narcolepsy and idiopathic hypersomnia.
Methods: Urine samples were collected from 8 patients with narcolepsy and 8 patients with idiopathic hypersomnia. Written informed consent was obtained from each patient. In both patients, it has been confirmed that the orexin levels were very low in narcolepsy, while the values were normal (about 300pg/ml) in idiopathic hypersomnia. This study was permitted by the Ethics Committee of Akita University.
50 ml urine samples were extracted using Sep-Pak C18 column. Thereafter, orexin was determined by RIA method. Data of urinary orexin was corrected by urinary creatinine value of each patient for comparison.
Results: Orexin immune reactivity was detected in all of urine samples. No significant difference was noted between the patients with narcolepsy and idiopathic hypersomnia before (64.7+/-28.4pg/ml, 51.8+/-18.7pg/ml, respectively)and after (0.033+/-0.015,0.045+/-0.012)the adjustment.
Conclusion: It is known that orexin is primarily synthesized in hypothalamus, and it passes through BBB by simple diffusion. It was expected that urinary orexin values in the patients with narcolepsy might be significantly lower compared with those with idiopathic hypersomnia, but the results were on the contrary. It is known that orexin receptors are distributed in digestive system and adrenal gland. Also, there have been reports that a slight quantity of orexin itself was present in renal tubule and testis. The results of the present experiment may reveal the possibility that orexin may be present at the sites other

than brain. It would be difficult to use the value of urinary orexin instead of CSF for definite diagnosis of narcolepsy.

0637

A STUDY ON SUBJECTIVE SLEEPINESS IN MEDICAL STUDENTS BY USING EPWORTH SLEEPINESS SCALE

Takemura T, Kondoh H, Takemura F, Ohnuma S, Suzuki M, Kanbayashi T, Shimizu T
Akita University, Akita, Japan

Introduction: We performed a study on the relation between subjective sleepiness and sleep time in medical students by using Epworth Sleepiness Scale ("ESS"). The results of our study are reported.
Methods: The study was performed on 335 students in the School of Medicine of three universities in different regions in Japan. Questions were asked on age, sex, and sleep time on weekdays and weekends through questionnaire, and the study was conducted by using ESS. The survey of the study was performed from 2003 to 2004.

In the results of the study, 313 students (157 male students and 156 female students) gave consent on the survey and presented effective replies.
Results: Sleep time of the subjects on weekdays was 6.34 +/- 1.01 hours (mean +/- SD). On the other hand, sleep time on weekends was 8.37 +/- 1.46 hours. The difference of sleep time between weekdays and weekends ("sleep time difference") was -2.03 +/- 1.49 hours. Significant correlation was noted between the duration of sleep time on weekends and the sleep time difference.

Mean value of ESS scores was 7.30 +/- 2.79. No significant correlation was found between the sleep time and ESS scores.
Conclusion: There were 37 students who had ESS scores of 11 points or more. This accounted for 11.8% of the total subjects under study. The results of our present study reveal that most of the medical students have a difference of 2 hours or more between the sleep time on weekends and that of weekdays. This may mean that the students are in the state of insufficient sleep on weekdays and they are trying to compensate this by taking longer sleep time on weekends.

0638

THE SLEEP LABORATORY FINDINGS IN KLEINE-LEVIN SYNDROME

Lin Y,[1] Huang Y,[2] Chen N,[3] Guilleminault C[4]
(1) Chang Gung Memorial Hospital, Taoyaung, Taiwan, (2) Chang Gung Memorial Hospital, Taiwan, (3) Taiwan, (4) AE (Africa)

Introduction: Kleine-Levin syndrome (KLS) is a rare disorder affecting mainly male adolescents .The etiopathogenesis remains unknown . There is only scant information on sleep characteristics in KLS patients. This study described the findings of polysomnography (PSG) and Multiple Sleep Latency Test (MSLT) and the correlation obtained with different episodes between clinical and PSG findings in the largest group of patients followed at a single place.
Methods: 18 patients (16 males and 2 females) with KLS were investigated with PSG and MSLT. 9 patients had complete data during the symptomatic episode and the asymptomatic interval. We took into consideration in the analyses the day of onset of symptoms and the relationship between this time of onset and the day of recording during the symptomatic period.
Results: When PSG were performed very early, and always during the 1st half of the symptomatic period there was always an important reduction in slow wave sleep (SWS) with a progressive return to normal during the second half, despite persistence of clinical symptoms: in the second half of the symptomatic period percentages of SWS were very similar to those monitored during the asymptomatic period. In opposition, rapid eye movement (REM) sleep remained normal in the1st half of the episode but decreases in the second part, with significant difference (Mann-Whitney test) for SWS (p= 0.014) and REM (p= 0.027) between first and 2nd half of episodes. Overall sleep efficiency is poor (<75%) during the symptomatic episodes, but it is worse during the 2nd half. MSLT showed that 3 (37.5%) out 16 patients had sleep onset in REM >=2 and the overall mean sleep latency was 9.37(+/-)4.83 minutes.
Conclusion: It is important to systematically precise the day when PSG studies are performed compared to onset of clinical symptoms, as findings vary overtime during that period, with a clear impairment of SWS close from onset of symptoms. MSLT is of little help and findings appears to be not related to time of onset of symptoms.

0639

THE EFFICACY OF VARIOUS DOSES OF MODAFINIL IN NARCOLEPSY AS REFLECTED BY SUBJECTIVE AND OBJECTIVE TESTS

Szternak N, Szakacs Z
Central Hospital of the Hungarian Home Defence Force, Budapest, Hungary

Introduction: Modafinil is an effective remedy for somnolence associated with narcolepsy. Nevertheless, appropriate determination of drug dose and dosage route is important.
Methods: Patients receiving modafinil for narcolepsy were stratified into four groups according to drug dose and dosage route. Baseline parameters of subjects were compared to test results obtained during 6-month follow-up. Testing started by administering Epworth´s subjective somnolence test, this was followed by polysomnography during the night, and multiple sleep latency test (MSLT) on the next day.
Results: Patients (n=17, 12 females and 5 males, mean age 39 years [range 18 to 56 years]) in Group I received 200 mg modafinil in the morning. Treatment reduced mean Epworth score from 17.94 to 6.82 and increased mean sleep latency (determined by MSLT) from 4.5 to 17.5 minutes. Group II (n=19, 10 females and 9 males, mean age 53 years [range 24 to 79 years] – 6 patients had cataplexy) was treated with 2≥100 mg/day modafinil administered in the morning and at midday. In this group, mean Epworth score decreased from 19.73 to 6.5, mean sleep latency (MSLT) increased from 4.0 to 17.5 minutes. In Group III, patients (n=26, 9 females and 17 males, mean age 45 years [range 18 to 72 years], cataplexy was diagnosed in 10 subjects) received 400 mg modafinil in the morning, which reduced mean Epworth score from 20.46 to 6.07 and increased mean sleep latency from 4.75 to 16.05 minutes. Modafinil 2≥200 mg/day was administered (in the morning and at midday) to patients in Group IV (n=21, 8 females and 13 males, mean age 51 years [range 20 to 81 years], cataplexy in 8 patients). Modafinil reduced mean Epworth score from 20.19 to 5.66, and prolonged mean sleep latency from 4.0 to 19.15 minutes.
Conclusion: Modafinil proved effective and it was well-tolerated by patients. Subjective testing revealed similar improvement in all four groups. MSLT showed longer sleep latency in patients taking 2≥200 mg modafinil daily. It seems therefore that larger daily modafinil doses are best divided to accomplish greater efficacy.

0640

PSYCHODERMATOLOGIC COMPLICATIONS OF STIMULANT THERAPY FOR HYPERSOMNIAS OF CENTRAL ORIGIN

Teman P, Olson E, Silber M
Mayo Foundation for Medical Education and Research, Rochester, MN, USA

Introduction: Stimulant therapy for narcolepsy or idiopathic hypersomnia is generally safe and effective. However, there are some psychiatric complications, including psychosis, anxiety, irritability, depression, and insomnia. Obsessive-compulsive behavior associated with stimulant therapy for attention-deficit hyperactivity disorder has been reported. We describe psychodermatologic manifestations in four patients treated with stimulants for hypersomnia.
Methods: Patients seen at our Sleep Center with narcolepsy or idiopathic hypersomnia and psychodermatologic symptoms were identified. Charts were reviewed for demographic and clinical features, type, dosage and duration of stimulants, and response to drug withdrawal.
Results: Four patients were identified; three women. Age at evaluation was 21-54 years (median 24.5). One had idiopathic hypersomnia, two narcolepsy with cataplexy and one narcolepsy without cataplexy. One had obsessive-compulsive disorder and two obsessive-compulsive personality traits. Dermatologic symptoms commenced 1 month to 7 years (median 12.5 months) after commencing stimulant therapy (dextroamphetamine/amphetamine (Adderall) in 3; SR methylphenidate in one). Doses ranged between 60-160 mg daily (median 80 mg). All patients picked skin off their faces and two plucked eyebrow hair. Two believed parasites were growing under the skin, one obsessed with perceived skin blemishes and one denied that the lesions were self-induced. One also reported paranoid ideation, believing someone was breaking into her home. Skin picking behavior ceased in all cases within a month of discontinuing stimulants (3) or reducing the dose (1). Symptoms recurred in two patients; one with SR methylphenidate and another with pemoline.
Conclusion: Psychodermatologic manifestations were similar in all 4 patients, consisting predominantly of skin picking behaviors involving the face accompanied by delusional parasitosis in two. The relationship to stimulants was demonstrated by the time course. Underlying obsessive-compulsive traits may have predisposed. Three of the four patients were using the drug at less than the recommended maximum dose. Sleep physicians should be aware of this rare complication of stimulant treatment.

0641

PEDIATRIC NARCOLEPSY: A SINGLE CENTER CLINICAL EXPERIENCE

Havaligi N,[1] Matadeen-Ali C,[2] Adams R,[3] Kothare S[3]
(1) Drexel University, Philadelphia, PA, USA, (2) Drexel University College of Medicine, PA, USA, (3) St. Christopher's Hospital for Children, PA, USA

Introduction: There are few studies which describe narcolepsy in the pediatric population, even though it can present itself in early childhood. The purpose of this study is to describe the characteristics of narcolepsy in a cohort of children.
Methods: Retrospective chart analysis of patients with hypersomnia seen in the sleep clinic between 01/2005 to 11/2006 was performed, with special attention given to identifying patients with narcolepsy (MSLT, HLA typing and CSF hypocretin-1 measurements were performed in appropriate cases, after a complete history and physical examination).
Results: There were 125 patients identified with hypersomnia. The various diagnoses of hypersomnia based on ICSD-2 criteria included Sleep Disordered Breathing (72%), PLMD(14.4%), DSPS(17.6%), narcolepsy(16%) and parasomnias(2.4%). Mean age of all patients was 12.6 years.The mean age of the narcoleptics was 11.6 years (range 5-19). 20% had history indicative of cataplexy. On MSLT, the mean sleep latency was 6.14 minutes (range 1.0- 16.5) with SOREMPs (mean 2.8, range 0-5). PSG amongst narcoleptics showed that 85% had SDB, 25% had PLMD and 5% had confusional arousals. Both HLA DR15 and HLA DQB1*0602 were positive in 8 of 14 (57%) narcoleptics and 1 had only HLA DR15 positive. 100% of the narcoleptics with cataplexy had both alleles positive and had the lowest MSL (mean 3.1minutes). Forty three percent of the non-narcoleptics also had HLA positivity. CSF hypocretin level was 22pg/ml in 1 patient. Treatment of narcolepsy included Modafinil (12), SSRI´s (10), and GHB(2). One third had follow up and good response to treatment. One third had intermittent follow-up and another third were lost to follow-up.
Conclusion: Narcolepsy was present in 16% of patients who presented with excessive sleepiness. Pediatric patients had similar profile to adults with narcolepsy regarding PSG, MSLT, HLA typing and treatment. DSPS is a common masquerader of narcolepsy in teenagers.

0642

HLA-DQB1 GENOTYPING IN A FAMILY WITH NARCOLEPSY-CATAPLEXY

Pedrazzoli M,[1] Pontes J,[2] Peirano P,[3] Tufik S[4]
(1) Universidade Federal de Sao Paulo, Sao Paulo, Brazil, (2) Universidade Federal de Sao Paulo, Brazil, (3) Universidad de Chile, Chile, (4) Univ Fed Sao Paulo, Sao Paulo, Brazil

Introduction: Narcolepsy is a unique model for dysfunction in mechanisms that regulate wakefulness and the transition between NREM, wake, and REM sleep. The narcolepsy syndrome is characterized by narcolepsy tetrad: excessive daytime sleepiness with recurrent episodes of irresistible sleep, cataplexy, hypnagogic and/or hypnopompic hallucinations, and sleep paralysis. The current hypothesis regarding the etiology of narcolepsy is that it is an autoimmune disorder because of its strong association with the human leukocyte antigen (HLA) system. HLA-DQ alleles are not particularly mutated in narcoleptic patients but influence directly the susceptibility to develop the disease. DQB1*0602 homozygotes have a two to four times higher risk of developing the disease than heterozygotes. The objective of the present was to investigate the HLA-DQB1 alleles present in a familial case of Narcolepsy-Cataplexy and try to correlate them with cataplexy severity.
Methods: In this study we report a familial case of narcolepsy-cataplexy and show the strong effect of the allele HLA-DQB1*0602 on the disease phenotype in the family. DNA was extracted from blood lymphocytes and the HLA-DQB1 high resolution genotyping was performed using PCR- based allele specific assay with the Micro SSPTM Allele Specific HLA Class II DNA Typing Tray – DQB1 kit (One Lambda, Inc. CA, USA).
Results: In the family studied here both brothers are DQB1*0602 homozygous and are severely affected, on the other hand, their sister did not carry the allele and is not affected at all. These data confirm data suggesting that subjects homozygous DQB1*0602 are much more susceptible to develop narcolepsy. The individuals in the paternal branch of the family who carry at least a copy DQB1*0602 are symptomatic to narcolepsy while in the maternal branch there is no sign of the disease in the individuals who carry a copy, suggesting disease heterogeneity.
Conclusion: We have reported here, for the first time in South America,

a familial case of narcolepsy-cataplexy associated with the gene HLA-DQB1*0602. Familial cases positive to this allele are not common and suggest that these patients are very likely to have hypocretins abnormal neurotransmission.
Support (optional): Fapesp (grant # 98/143003-3) and AFIP

0643

MODAFINIL REDUCES SYMPTOMS OF EXCESSIVE SLEEPINESS IN CHILDREN AND ADOLESCENTS WITH OBSTRUCTIVE SLEEP APNEA OR NARCOLEPSY FOLLOWING 6 MONTHS OF OPEN-LABEL THERAPY

Dauvilliers Y,[1] Nevšímalová S,[2] Lecendreux M,[3] Bruni O[4]
(1) Hôpital Gui de Chauliac, CHU Montpellier, Montpellier, France, (2) Charles University, Prague, Czech Republic, (3) Hôpital Robert Debré, Paris, France, (4) University of Rome La Sapienza, Rome, Italy

Introduction: Excessive sleepiness (ES) commonly interferes with functioning and contributes to psychosocial and academic difficulties in children and adolescents with obstructive sleep apnea (OSA) or narcolepsy. This study assessed the efficacy and safety of modafinil, a wake-promoting agent, in children and adolescents with ES associated with OSA (despite nCPAP therapy) or narcolepsy.
Methods: Patients aged 6–16 years with ES associated with OSA or narcolepsy were evaluated in a 6-month, multicenter, open-label, flexible-dosage study. Patients received modafinil 100–400 mg/day based on efficacy and tolerability. Efficacy parameters included the Clinical Global Impression of Change and the Pediatric Daytime Sleepiness Scale (PDSS). Safety and tolerability were monitored.
Results: The study included 91 evaluable patients (OSA, n=45; narcolepsy, n=46). The mean±SD age was 12.2±3.1 years, and 58% were boys. At final visit, modafinil improved overall clinical condition in 91% of patients. The mean±SD change from baseline at final visit in PDSS total score was –7.5±5.8 and –5.6±5.9 in patients with OSA and narcolepsy, respectively. Common treatment-related AEs in the OSA group were decreased appetite (16%), weight loss (13%), and headache (11%); for the narcolepsy group, headache (20%), decreased appetite (15%), and insomnia (7%). Over the course of the study, mean height increased (OSA, +2.5±2.4 cm; narcolepsy, +2.4±3.7 cm); there were minimal effects on mean weight (OSA, –0.4±4.1 kg; narcolepsy, +0.8±3.0 kg). No clinically meaningful change in blood pressure or clinical laboratory parameters was observed. Competencies and behavioral problems, as assessed by Child Behavior Checklist for Ages 6–18, improved with modafinil.
Conclusion: Modafinil improves overall clinical condition, wakefulness, and patient competencies and behavior in children and adolescents with ES associated with OSA or narcolepsy. Modafinil is well tolerated. Modafinil is only needed in OSA patients awaiting surgery or for residual ES despite nCPAP, but is necessary for children affected with narcolepsy.
Support (optional): Cephalon, Inc.

0644

A NOVEL CANDIDATE GENE FOR NARCOLEPSY CO-LOCALIZED IN HUMAN AND MOUSE HYPOCRETIN/OREXIN NEURONS

Honda M,[1] Eriksson K,[2] Lin L,[2] Salehi A,[3] Tanaka S,[1] Gaus S,[2] Honda Y,[4] Mignot E[2]
(1) Tokyo Institute of Psychiatry, Tokyo, Japan, (2) Center for Narcolepsy, Stanford University, Palo Alto, CA, USA, (3) Department of Neurology, Stanford University, Palo Alto, CA, USA, (4) Seiwa hospital, Neuropsychiatric Institute, Tokyo, Japan

Introduction: The sleep disorder narcolepsy is caused by a vast reduction in neurons producing the hypocretin (orexin) neuropeptides. Although there are no confirmed immunological abnormalities in narcolepsy, it is believed to result from an autoimmune attack on hypocretin neurons, based on the tight association with HLA-DQB1*0602.
Methods: Eight controls and 6 narcolepsy postmortem posterior hypothalamic samples were selected after verification of brain tissue quality, and used for microarray experiments (Affymetrix U133A and B chips, covering approximately 40,000 transcripts) to compare the transcriptome of narcoleptic versus control hypothalamus. Data were statistically analyzed and verified by quantitative RT-PCR using Taqman probes. Distributions of selected candidate genes were studied by in situ hybridization on C57BL/6J mice. Human brain tissues were used to study the distribution of confirmed protein by immunohistochemistry.
Results: Out of 11 upregulated and 35 downregulated genes in narcolepsy, 9 down-regulated genes were verified with quantitative RT-PCR. Hypocretin was the most down-regulated gene. One of these 9 genes, an insulin-like growth factor binding protein, was confirmed to be highly expressed in hypocretin neurons but in only a few other brain areas, including the pedunculopontine nucleus region and the cerebellum. Circulating levels in the blood or CSF did not differ in patients versus controls; neither did we detect antibodies against the protein in serum or CSF.
Conclusion: We found a novel candidate narcolepsy related gene using gene expression profiling of postmortem human brain samples. Although we did not find a difference in serum or CSF levels and did not detect autoantibodies against the protein, insulin growth factor protein pathway proteins are known to have cell growth regulatory properties and may thus be involved in hypocretin cell death.
Support (optional): Supported by NIH-NS23724 to E. Mignot and by the Ministry of Education, Science, Sports and Culture, Grant-in-Aid for Scientific Research 16659308, 1739034 to M Honda.

0645

CHANGES IN CIRCULATING PLASMA GHRELIN AND OBESTATIN IN NARCOLEPSY-CATAPLEXY

Huda M,[1] Mani H,[2] Durham B,[3] Dovey T,[2] Halford J,[2] Aditya S,[2] Pinkney J,[2] Wilding J,[2] Hart I[4]
(1) University of Liverpool, Liverpool, England, United Kingdom, (2) University of Liverpool, England, United Kingdom, (3) Royal Liverpool University Hospital, england, United Kingdom, (4) Walton Centre of Neurology and Neurosurgery, england, United Kingdom

Introduction: Narcolepsy-cataplexy is characterised by orexin deficiency and various neuro-endocrine abnormalities. Ghrelin acts partially via hypothalamic orexin neurones, and also promotes wakefulness. Obestatin, a newly discovered peptide that is also produced from the ghrelin gene, has opposing effects to ghrelin on appetite, and also affects NREM sleep in rodents. We explored whether ghrelin and obestatin profiles were altered in narcolepsy-cataplexy.
Methods: Eight subjects with clinically diagnosed narcolepsy-cataplexy and eight sex, age and BMI matched controls were given a fixed energy meal (1550kJ) and samples taken regularly. Seven subjects consented to estimation of cerebrospinal fluid (CSF) orexin, which was assayed with control CSF.
Results: Control CSF showed significantly higher orexin-A levels (control 246.2±4 pg/ml v narcolepsy 42.8±12 pg/ml p=0.01) within the same assay, confirming that our subject group was markedly orexin deficient. Fasting ghrelin was similar in both groups (narcolepsy 589.5±88 pg/ml v control 686.9±81 pg/ml p=0.5) and there was no difference in area under the curve (AUC) (narcolepsy

161.3±22ng/ml/min v control 188.6±62ng/ml/min p=0.4). Only the narcolepsy group showed a significant suppression of ghrelin release after the meal (ANOVA p=0.004). Obestatin however was significantly higher in narcolepsy subjects in both the fasted state (narcolepsy 89.6±16 pg/ml v control 24.9±3 pg/ml p<0.001) and AUC (narcolepsy 155.2±2 ng/ml/min v control 5.6±0.6 ng/ml/min p<0.001). Obestatin did not significantly vary with time or in response to the meal in either group.
Conclusion: This is the first study to characterise ghrelin and obestatin meal-related profiles in narcolepsy-cataplexy. Circulating ghrelin is unaltered in narcolepsy-cataplexy and the typical pattern of suppression after a meal is preserved. Circulating obestatin levels are 3-4 fold increased in narcolepsy-cataplexy, although the mechanism underlying this is unclear. Obestatin affects NREM sleep in rodents and it is possible that abnormally high plasma levels contribute to the disruption in sleep microstructure observed in narcolepsy-cataplexy subjects.

0646

CHARACTERISTICS OF PATIENTS WITH EARLY AND LATE ONSET NARCOLEPSY IN GERMANY

Mayer G,[1] Neumann H,[1] Ploch T,[2] Kesper K[2]
(1) Hephata Klinik Schwalmstadt-Treysa, Schwalmstadt-Treysa, Hessen, Germany, (2) Philipps-University Marburg, Marburg, Hessen, Germany

Introduction: Recent studies in European and Canadian narcoleptics confirmed two peaks in the age of onset. We were interested to investigate the differences between the two groups.
Methods: A prospective study in 136 consecutive patients (63 males, 73 females, age 13-78) was performed using a German narcolepsy questionnaire (51 questions on demographics, symptoms, co-morbidity), nocturnal polysomnography (NPSG), Mutiple Sleep latency Test (MSLT, both n=90) and Epworth Sleepiness Scale (ESS, n=84). Statistical analysis was performed with the Mann-Whitney-U-Test.
Results: Age at symptom onset has a major peak at 16.6 years (group1, n=105), a second peak at 40.1 years (group2, n=31). The age separating both groups is 30 years. Women have first symptoms significantly earlier than men (p=0.015). In the majority of both groups excessive daytime sleepiness is the first symptom. Mean latency between the first symptom and sleep attacks is 1.5 years in group1, 0.6 years in group2. The latency between the first symptom and cataplexy is 6.3 years in group1, 1.7 years in group2. Men in group2 suffer significantly more often from sleep apnea, diabetes and hypertension. Mean sleep latency in the MSLT is shorter in group1 (p=0.007) and number of sleep onset REM periods is higher (p=0.043) than in group2. In the NPSG wake after sleep onset in group1 is shorter (p=0.045) than in group2. No significant differences were found for ESS scores, total sleep time, sleep latency, sleep efficiency and REM latency.
Conclusion: Patients with early and a late onset of narcolepsy are distinctly different in clinical and polysomnographic features. The results evidence the existence of two different narcolepsy phenotypes. The whole array of narcoleptic symptoms starts much earlier in patients with late onset, whereas their NREM and REM sleep propensity seems to be higher. Future studies will focus on pathophysiological differences of the two groups.

0647

MODAFINIL IMPROVES WAKEFULNESS AND IS WELL TOLERATED IN CHILDREN AND ADOLESCENTS WITH EXCESSIVE SLEEPINESS ASSOCIATED WITH NARCOLEPSY

Owens J,[1] Harsh J,[2] Rosen C[3]
(1) Rhode Island Hospital, Providence, RI, USA, (2) University of Southern Mississippi, Hattiesburg, MS, USA, (3) Case University School of Medicine, Rainbow Babies and Children´s Hospital, Cleveland, OH, USA

Introduction: In children and adolescents, excessive sleepiness (ES) associated with narcolepsy contributes to poor daytime functioning, reduced academic performance, intense psychosocial distress, and behavioral problems. The efficacy, safety, and tolerability of modafinil, a wake-promoting agent, was evaluated in this patient population.
Methods: In a double-blind, multicenter study, patients aged 6–16 years with ES and narcolepsy were randomized to receive modafinil 100, 200, or 400 mg/day or placebo for 6 weeks. Efficacy evaluations included scores on the Multiple Sleep Latency Test (MSLT), Clinical Global Impression of Change (CGI-C), and Pediatric Daytime Sleepiness Scale (PDSS). Safety evaluations included scores on the Child Behavior Checklist for Ages 6–18 (CBCL/6–18), Kaufman Brief Intelligence Test, Second Edition (KBIT-2), adverse events (AEs), and vital signs.
Results: Of 165 patients randomized (modafinil, n=123; placebo, n=42), mean±SD age was 12.5±2.8 years and 57% were boys. Mean baseline MSLT scores were 6.5±4.5 and 6.7±4.4 min for the modafinil and placebo groups, respectively. Modafinil increased mean sleep latency on the MSLT by 3.9±4.5 vs 0.6±3.9 min for placebo (P<.0001). At final visit, modafinil improved overall clinical condition (CGI-C) in 81% of patients vs 66% in the placebo group (P=.052). PDSS total score was not statistically different between groups (P=.319). At final visit, mean change from baseline in CBCL/6–18 total score was –7.9±18.9 vs –4.3±13.1 for the modafinil and placebo groups, respectively. For the IQ composite score of the KBIT-2, the mean change was 7.2±10.7 vs 3.8±6.4, respectively. The most common AE for modafinil vs placebo was headache (18% vs 17%). In both groups, there were small mean changes in heart rate and systolic and diastolic blood pressure. Mean change in weight was minimal (modafinil, 0.4±2.8 kg; placebo, 1.6±3.0 kg).
Conclusion: Modafinil improves wakefulness and is well tolerated in children and adolescents with ES associated with narcolepsy.
Support (optional): Cephalon, Inc.

0648

PHARMACOLOGICAL EVALUATION OF DIRECT TRANSITION FROM WAKE TO REM SLEEP (DREM) IN OREXIN/ATAXIN-3 NARCOLEPTIC MICE

Fujiki N,[1] Cheng T,[2] Yoshino F,[2] Nishino S[3]
(1) Stanford University, Palo Alto, CA, USA, (2) Stanford University, CA, USA, (3) Stanford University, Stanford, CA, USA

Introduction: Hypocretin/orexin KO or hypocretin/orexin neuron ablated mice (orexin/ataxin-3 mice) have been reported to exhibit sleep fragmentation, cataplexy-like behavior and direct transitions from wake to REM sleep (DREM). However, there is no consistent way to elicit cataplexy in these animals, and spontaneous occurrence of cataplexy has been visually monitored for most experiments. In contrast, DREM can be more objectively evaluated, and the specificity of DREM in narcolepsy can be improved by applying a rule for defining the DREM (in our definition, the proceeding epochs should be wake and ≥40 sec). In the current study, we evaluated the effects of desipramine (a tricyclic), amphetamine and modafnil on DREM in orexin/ataxin-3 mice

in order to further validate the DREM assessments.
Methods: Orexin/ataxin-3 TG mice (N9, backcrossed to C57BL/6) (n=8 for each drug session) were used. The mice were surgically prepared for EEG and EMG recordings and they were maintained in a 24-hr light–dark cycle (LD12:12) within separate compartments with a running wheel in a sound-attenuated stainless steel recording chamber. Two or three doses of each compound (plus vehicle) was administered at ZT 14:00, and sleep data for 6 hours after injections for each animal were scored visually, and each 10-second epoch is classified as wake, NREM sleep, REM sleep or DREM. Effects of these compounds on sleep during light periods were also evaluated and drug administrations were done at ZT2.
Results: We observed that desipramine does dependently suppress the occurrence of DREM, and 60% of the reduction was observed at the high dose (20 mg/kg, i.p.). Amphetamine also moderately reduced DREM (40 % of reduction at 4 mg/kg i.p.), while modafinil had no effects (50 and 200 mg/kg, p.o.) on DREM. Sleep recordings at the light period demonstrated that amphetamine and modafinil significantly enhanced wakefulness, while desipramine had no effect on alerting.
Conclusion: Desipramine, a trycyclic and an anti-cataplectic, potently reduced DREM, while the two wake-promoting compounds had moderate (amphetamine) and no effect (modafinil) on DREM in the mice model of narcolepsy. These effects mirror the anticataplectic effects of the same compounds previously reported in canine and human narcolepsy, suggesting that the DREM evaluations in narcoleptic mice may also be useful to screen the anti-cataplectic properties of pharmacological compounds.
Support (optional): This research was supported by NIH Grant MH072525.

0649

EVALUATIONS OF FRAGMENTED REST/ACTIVITY PATTERNS IN OREXIN/ATAXIN-3 NARCOLEPTIC MICE

Del Cid-Pellitero E,[1] Fujiki N,[2] Yoshino F,[3] Nishino S[4]
(1) Autonoma University of Madrid, Madrid, Spain, (2) Stanford University, Palo Alto, CA, USA, (3) Stanford University, CA, USA, (4) Stanford University, Stanford, CA, USA

Introduction: Sleep fragmentation and cataplexy (behavioral arrest or direct transitions from wake to REM sleep in rodents) are two primary symptoms of narcolepsy. Although sleep/wake fragmentation is an interesting phenotype to analyze in various animal models of the human disease and/or in genetically engineered animal models, the analysis is mostly done in sleep laboratories. This is mostly due to the limitation that sleep fragmentation can only be evaluated with polygraph recordings with headstage implantations. Furthermore, sleep scoring is labor intensive, and the inter-rater variation is another concern. In the current study, we attempted to develop a standardized method to detect rest/activity fragmentation as an alternative, by locomotor monitoring using orexin/ataixn-3 narcoleptic mice as a standard.
Methods: Orexin/ataxin-3 TG mice (N9, backcrossed to C57BL/6) (n=8 for each drug session) and their littermate wild-type (WT) mice were used. With standard sleep implant surgery, the telemetry transmitter for activity and core body temperature (G2 E-Mitter; MiniMitter, OR) was implanted in the abdominal cavity of each mouse. They were maintained in a 24-hr light–dark cycle (LD12:12) in separate compartments within a sound-attenuated stainless steel recording chamber. After a two-week accommodation, activity data was collected with a 10 sec time bin for 24 hours. The original 10 sec data was summed to calculate the activity for 30s, 1min, 2 min, 5 min, 10 min and 30 min time. Each time bin was then defined as an "active" or "inactive" period using the activity threshold set with the mean activity count of each animal during light, dark and 24-hour period, respectively. The mean duration of active and inactive periods as well as the state change frequency was computed for the respective time bins for WT and narcoleptic mice.
Results: We found that narcoleptic mice frequently changed their activity states over 24 hours, and their mean duration of active periods during the dark, and that of inactive periods during both light and dark periods are significantly shorter than those of WT mice. These differences were however, best detected between a 30 sec to 5 min time bin (there was no significant difference with a longer time bin). These time bins correspond to the mean wake and sleep bout of these animals, suggesting that sleep fragmentation can be evaluated by high time resolution locomotor monitoring.
Conclusion: Our results suggest that sleep fragmentation can be assessed by locomotor monitoring with a high time resolution (30 sec to 5 min time bin). This method does not require headstage implant surgeries and sleep recording systems. The evaluation method is fast, fully objective and normalized for each animal. Further evaluations in various disease models and pharmacological experiments are warranted.
Support (optional): This research was supported by NIH Grant MH072525.

0650

DEVELOPMENTAL DIVERGENCE OF SLEEP-WAKE PATTERNS IN OREXIN KNOCKOUT AND WILD-TYPE MICE

Blumberg M, Coleman C, Johnson E, Shaw C
University of Iowa, Iowa City, IA, USA

Introduction: Narcolepsy, a disorder characterized in part by fragmented bouts of sleep and wakefulness, has been linked in humans and non-human animals to the functional integrity of the orexinergic system. As with narcolepsy, infant sleep-wake cycles in humans and rats are highly fragmented, with consolidated bouts of sleep and wakefulness developing gradually. Based on these common features of narcoleptics and infants, we hypothesized that the development of sleep-wake fragmentation in orexin knockout mice would be expressed as a developmental divergence between knockouts and wild-types, with the knockouts lagging behind the wild-types.
Methods: The sleep-wake patterns of infant orexin knockout and wild-type mice were examined across the first three postnatal weeks (at P4, P12, and P21). Using well-established procedures, on the day of testing pups were implanted nuchal EMG electrodes for the discrimination of sleep and wakefulness. Pups were tested during the day and night in chambers maintained at thermoneutrality.
Results: Both knockout and wild-type mice exhibited decreasing fragmentation of sleep and wake bouts between P4 and P21. Moreover, mice of both strains exhibited orderly changes in the statistical distributions of sleep and wake bouts. Against this backdrop of orderly, orexin-independent developmental change, by P21 the knockouts were lagging behind the wild-types with regard to the developmental consolidation of sleep and wake bouts. These knockouts also appeared to lag behind the wild-types in the onset of circadian rhythmicity, exhibiting similar mean sleep bout durations during the light and dark periods as the wild-types exhibited increased sleep bout durations during the light period.
Conclusion: We conclude that narcolepsy in orexin knockout mice entails retention of the more fragmented patterns of sleep and wakefulness normally exhibited by infants. Accordingly, we hypothesize that adult-onset human narcolepsy entails reversion back toward the infantile pattern of fragmented sleep and wakefulness.
Support (optional): NIH grants MH50701 and MH66424.

0651

KLEINE-LEVIN SYNDROME IN ISRAEL, PATIENTS CHARACTERISTICS

Sivan Y
Tel-Aviv University, Tel Aviv, Israel

Introduction: Kleine-Levin syndrome (KLS) is a rare disease characterized by recurrent episodes of hypersomnia, behavioral disturbances, compulsive eating and hypersexuality. A significant increased Jewish predisposition was observed in the US. While KLS affects approximately one in a million people in the US, a 6-7 per million rate has been reported from Israel . The aim of study was to investigate the frequency of KLS in Israel, characterize the clinical spectrum and identify environmental variables that may affect KLS in Israel.
Methods: Thirty-four patients were recruited from the databases of the 3 Medical Centers. All patients and their parents completed a detailed questionnaire. Ethnic origin was defined by grandparents' origin.
Results: Twenty-four KLS patients were contacted (71%). Demographic data: 20/24 (83%) were male, mean age of onset was 16 (8-22) years, mean diagnosis delay = 2.8+3.9 years, mean attack duration = 17 (3-49) days and mean number of attacks/patient = 5.6+5.9. All patients were Jewish: 17 (71%) of Ashkenazi origin, 4 Sepharadic and 3 of mixed origin. In 12 patients (50%) a mild illness or fever preceded the 1st attack. Mean sleep duration during an attack was 17 (12-24) hours/24 hours. 79% reported eating disorders and 58% reported hypersexuality. The mean number of KLS episodes per patient was 15 (1-50). Mean time from onset to recovery was 4.2 years (1-8).
Conclusion: KLS characteristics of Israeli patients is similar to the worldwide KLS population. All cases occurred in Jewish people. Although KLS is more common in Ashkenazi Jews, KLS is not an Ashkenazi disease. KLS in this population usually starts during adolescence and male gender is much more frequent. Due to the rarity of the disease, diagnosis is frequently delayed, hence a high index of suspicion should be applied in cases of hypersomnia especially in adolescents and young adults.
Support (optional): None

0652

LOW-RESOLUTION BRAIN ELECTROMAGNETIC TOMOGRAPHY (LORETA) APPLIED TO EVENT-RELATED POTENTIALS REVEALS IMPAIRED EVENT-ENCODING IN UNTREATED NARCOLEPTICS

Saletu M,[1] Anderer P,[2] Saletu-Zyhlarz G,[3] Mandl M,[3] Zeitlhofer J,[4] Saletu B[4]
(1) Medical University of Vienna, Austria, Vienna, Austria, (2) Medical University of Vienna, Vienna, AE (Europe), Austria, (3) Medical University of Vienna, Vienna, Austria, (4) Vienna, Austria

Introduction: Event-related potentials (ERPs) are sensitive measures of both perceptual and cognitive processes. ERP components can be described in latencies, amplitudes and current source density distribution. The aim of the present study was to identify brain regions involved in the disease process of narcoleptic patients by means of ERP tomography.
Methods: In 17 drug-free narcoleptics (criteria of the International Classification of Sleep Disorders ICSD; 8 males and 9 females; aged 39 ± 90 years) and 17 age- and sex-matched normal controls, ERPs were recorded in an auditory odd-ball paradigm and latencies, amplitudes and LORETA sources were determined for standard (N1 and P2) and target ERP (N2 and P300) components.
Results: Narcoleptics did not differ from normal controls in N1 and P2 components. N2 and P300 components, however, were delayed (+31.7 and +32.4ms; $p<0.01$) and showed reduced amplitudes ($p<0.01$) as well asdecreased source strength ($p<0.01$). In detail, reduced P300 sources were observed bilaterally in the precuneus, in the anterior and posterior cingulate, in the ventrolateral prefrontal cortex and in the parahippocampal gyrus.
Conclusion: Narcoleptics showed a prolonged information processing speed, as indexed by N2 and P300 latencies and decreased energetic resources for cognitive processing, specifically in brain regions associated with event-encoding during an oddball task.

0653

DEVELOPMENT OF AN EX VIVO OREXIN RECEPTOR OCCUPANCY ASSAY USING TRANSGENIC RATS

Murphy K
Merck & Co., West Point, PA, USA

Introduction: The orexin signaling pathway plays a critical role in arousal state control. Limited orexin receptor expression in the brain makes characterization of this pathway with pharmacologic agents challenging. To increase signal detection for orexin receptor occupancy we developed a transgenic line of rats over-expressing the human orexin receptor-2. This has enabled the establishment of a sensitive method to measure orexin receptor occupancy in vivo.
Methods: Transgenic rats expressing the human orexin 2 receptor were generated. Brain homogenates were prepared from these animals following compound or vehicle treatment. Competition assays were conducted using radiolabeled compounds followed by filter binding and quantitation.
Results: Scatchard analyses were performed to determine the density of human orexin receptor-2 in transgenic rat lines. This also enabled calculation of Kd values. High levels of the receptor were detected in the transgenic rats. Further characterization confirmed that this assay was suitable for evaluating small molecule interactions in the brain.
Conclusion: This approach has enabled us to develop a robust binding assay which can measure in vivo receptor occupancy for the human orexin receptor-2. The development of this ex vivo assay has proven to be successful for evaluating the in vivo brain occupancy of small molecules.

0654

HYPERSOMNOLENCE ASSOCIATED WITH DOPAMINE RELEASE IS ANTAGONIZED BY DAT INHIBITION

Gruner J, Marcy V, Clas D, Lin Y, Bozyczko-Coyne D, Marino M
Cephalon, Inc., West Chester, PA, USA

Introduction: Amphetamine, a dopamine (DA) transport (DAT) inhibitor and DA releasing agent, produces waking followed by pronounced hypersomnia, which has been suggested to be due to DA release. These studies examined the in vitro effect of several DAT inhibitors on amphetamine-induced DA release, and their in vivo wake promoting efficacy and propensity for sleep rebound, and the in vivo interaction of amphetamine and the DAT inhibitor nomifensine.
Methods: (^{3}H)-DA release was evaluated in (^{3}H)-DA prelabeled rat striatal synaptosomes. Sleep/wake activity was evaluated using EEG/EMG scoring criteria. After 24 h habituation in an isolated chamber, rats were dosed i.p. at 1 PM (CT-5; 12 h light cycle) and recorded for 22 h.
Results: EC_{50} values (μM) (95% C.I.) obtained for DA release were as follows: methamphetamine, 0.054 (0.04-0.07); amphetamine, 0.092 (0.06-0.14), phentermine, 0.31 (0.12-0.75), GBR-12909, 1.66 (0.49-5.6); GBR-12935, 11.8 (5.4-26). The following compounds had EC_{50} values

>100 μM and at 100 μM shifted the amphetamine EC_{50} value consistent with published DAT Ki values (fold shift): mazindol (448), nomifensine (272), methylphenidate (123), cocaine (41), and bupropion (25). In the EEG wake model, DA releasing agents induced greater sleep rebound than other DAT inhibitors. Amphetamine (1 mg/kg) and nomifensine (3 mg/kg) produced similar maximal cumulative wake surplus (CWS) at 3-4 h (89 and 100 min respectively). The CWS for amphetamine decreased to 2±15 min at 22 h ($p< 0.001$) vs. 58±20 min for nomifensine. Co-administration of nomifensine and amphetamine resulted in a greater maximal CWS (216±8 min at ~7 h) than the summed individual CWS values, with maintained CWS of 110±11 min at 22 h.
Conclusion: Nomifensine co-administered with amphetamine produced an additive wake-enhancing effect while blunting amphetamine-induced hypersomnia. We conclude that hypersomnolence is exacerbated by DA release, and that DAT inhibitor-induced decreases in DA release can reduce excess rebound and maintain CWS.
Support (optional): Research supported by Cephalon, Inc.

0655

MODAFINIL IMPROVES INFORMATION PROCESSING SPEED AND INCREASES ENERGETIC RESOURCES FOR ORIENTATION OF ATTENTION IN NARCOLEPTICS: DOUBLE-BLIND, PLACEBO-CONTROLLED ERP STUDIES WITH LOW-RESOLUTION BRAIN ELECTROMAGNETIC TOMOGRAPHY (LORETA)

Saletu B,[1] Anderer P,[1] Saletu-Zyhlarz G,[1] Mandl M,[2] Saletu M,[3] Zeitlhofer J[1]
(1) Medical University of Vienna, Vienna, Austria, (2) Vienna, Austria, (3) Medical University of Vienna, Austria, Vienna, Austria

Introduction: Low-resolution brain electromagnetic tomography (LORETA) recently objectified a functional deterioration of the fronto-temporo-parietal network of the right-hemispheric vigilance system in narcolepsy and a therapeutic effect of modafinil on the left hemisphere, which is less affected by the disease. In the present study event-related potential components (ERPs) were applied to investigate the therapeutic efficacy of modafinil as compared with placebo in perceptual and cognitive processes.
Methods: In a double-blind, placebo-controlled cross-over design, 15 patients (7 males and 8 females; aged 38 ± 18 years) were treated with a 3-week fixed titration of modafinil (200, 300, 400 mg) and placebo. Auditory ERPs recorded in an odd-ball paradigm, Epworth Sleepiness Scale (ESS) and Maintenance of Wakefulness Test (MWT) measures were obtained before and after three weeks of therapy.
Results: The ESS was significantly improved with modafinil as compared with placebo ($p = 0.004$). In the MWT latency to sleep was not significantly altered by modafinil treatment. While modafinil had only minor effects on ERP amplitudes, N2 ($p<0.05$) and P300 latencies ($p<0.01$) were reduced and LORETA revealed increased source strength: for N1 in the left auditory cortex and for P300 in the medial and right dorsolateral prefrontal cortex.
Conclusion: Modafinil reduced subjective sleepiness in narcoleptics. It further improved information processing speed and energetic resources in brain regions shown to be altered in narcoleptics in previous neuroimaging studies.

0656

MARKOV ANALYSIS OF EYE MOVEMENT DENSITY IN NORMAL CONTROLS AND NARCOLEPTICS.

Biard K,[1] Douglass A,[1] Orr L[2]
(1) University of Ottawa, Ottawa, Ontario, Canada, (2) Royal Ottawa Hospital, Ottawa, Ontario, Canada

Introduction: Lack of orexin has been found to be the major pathology of narcolepsy. Normal orexin tone suppresses REM sleep onset, likely by acting at several monoamine nuclei simultaneously. It is not clear whether the cholinergic eye-movement (EM) generating neurons of the LDT / PPT are similarly affected, or whether they are only indirectly controlled via monoamine inhibition. We compared the phasic EMs of narcoleptics and normals by a novel Markov method. If similar, this would suggest that the LDT / PPT does not receive direct orexin control.
Methods: Sleep was measured during a full night of sleep in 10 normal subjects and 10 narcoleptic patients. The latter were also measured during a 4-nap MSLT. Markov analysis (Douglass 1992, Biol. Psychiatry) was done on the time intervals between successive EMs. Markov states were defined as: "Burst" (< 4.2 s), and "Isolated" (> 4.2 s). A 2 x 2 Markov transition probability matrix was calculated from EMs in all REM periods by subject by condition, then analyzed using a categorical log-linear model.
Results: The Markov "Isolated-to-Isolated" transition probability did not differ significantly between the 3 conditions (+S.E.): Normal = 0.384 (0.023); Narc Night = 0.377 (0.027); Narc Nap = 0.380 (0.029). Markov "Burst-to-Burst" transition probability also did not differ significantly between the 3 conditions: Normal = 0.777 (0.011); Narc Night = 0.755 (0.025); Narc Nap = 0.704 (0.025).
Conclusion: While the narcoleptic subjects (only) displayed typical REM intrusions during daytime naps, their phasic REM events did not differ significantly from normal controls in either the day or night samples. Therefore, while narcoleptics have intrusions of REM sleep at unusual times due to lack of orexin, their EM generating system does not differ from normals in this Markov analysis; this suggests that there is no direct effect of orexin on the LDT / PPT.
Support (optional): Royal Ottawa Foundation, and University of Ottawa Medical Research Fund

0657

SLEEPINESS AND NARCOLEPTIC-LIKE SYMPTOMS IN ADULTS WITH ADHD

Konofal E,[1] Brion A,[2] Lecendreux M,[2] Arnulf I[3]
(1) University Pierre et Marie Curie Paris 6, Paris, France, (2) France, (3) Paris, France

Introduction: Adults with attention-deficit/hyperactivity disorder (ADHD) often complain of altered night sleep,sometimes associated with daytime sleepiness. Recent findings suggest a possible overlap between symptoms of hypersomnia and ADHD. The aim of this study is to compare night-time and daytime polysomnographic measures in adults with ADHD and narcoleptic subjects.
Methods: Fourteen adults with ADHD (mean age: 40 years) and 14 (8 males, 6 females) sex- and age- matched patients with narcolepsy completed the Epworth Sleepiness Scale and the Adult ADHD-Rating Scale (ADHD-RS). They underwent night-time sleep monitoring and daytime multiple sleep latency tests (MSLT) after withdrawal of stimulants.
Results: As a mean, the score at the Epworth sleepiness scale were 12±4 in ADHD group vs. 17±4 in narcolepsy group. The score at the ADHD-RS were 42±3 in ADHD patients vs. 27±15 in narcoleptic subjects. Nighttime sleep measures were not different between groups,

except for increased duration of wake after sleep onset in adults with ADHD (97±48 min) compared to narcoleptic subjects (44±25 min; p<.001). During MSLT, the mean sleep latency was subnormal in adults with ADHD (10±5 min), but higher than in narcoleptic subjects (7±3 min; p<.001).
Conclusion: In this first study comparing night-time and daytime sleep measures in adults with ADHD and with narcolepsy, we found evidence for subnormal sleepiness and altered sleep continuity in ADHD patients, and moderately increased ADHD symptoms in patients with narcolepsy. These results should now be compared to normal subjects. Symptoms of ADHD in adult may hide an excessive sleepiness, possibly caused by sleep deprivation. Conversely, subjects with narcolepsy may develop symptoms of ADHD (impulsivity, overactivity) as a strategy to fight sleepiness. Symptoms of ADHD should be systematically assessed in subjects with narcolepsy when confusion between both pathologies is possible.
Support (optional): N/A

0658

IDENTIFICATION OF NOVEL TRANSCRIPTS EXPRESSED IN HYPOCRETIN-CONTAINING NEURONS

Bourgin P,[1] Lin L,[2] Priest M,[3] Renier C,[4] Sakurai T,[5] De Lecea L,[6] Mignot E[4]
(1) Department of Biological Sciences and Center for Narcolepsy Research, Stanford University, Stanford, CA, USA, (2) Center for Narcolepsy research, Stanford University, CA, Palo Alto, CA, USA, (3) Department of Biological sciences and Center for Narcolepsy Research, Stanford University, CA, USA, (4) Center for Narcolepsy Research, Stanford University, CA, USA, (5) Institute of Basic Medical Science, University of Tsukuba, Japan, (6) Department of Psychiatry and Behavioral Sciences, Stanford University, CA, USA

Introduction: Identifying novel molecular markers for hypocretin-containing cells is critical to further understand the functioning of these neurons as well as the pathogenesis of human narcolepsy. To reach this goal, we used subtractive hybridization between wild type (WT) and hypocretin neuron-ablated mice (Tg) (orexin/ataxin3 transgenic mice).
Methods: Multiple (different time points) directional tag libraries were constructed from fresh cytoplasmic polyA+ mRNAs isolated from posterior hypothalami (WT, Tg, n=25/groups, mean age 50 weeks, littermates). Several optimized Tag PCR subtraction were performed (1 µg of WT target tracer cDNA hybridized with an excess of 40 µg Tg driver cRNA). The generated subtracted libraries (SL) were sequenced (150 clones/library) and hybridized on cDNAs microarrays in comparison to a universal reference.
Results: SL were validated by real time PCR and by applying the following criteria: (1) enrichment in hypocretin (250 fold as compared to WT libraries) (2) complete removal of endogenous control genes (beta actin) (3) complete removal of genes expressed in cells located in the vicinity of hypocretinergic neurons (e.g. MCH). Clones represented several times (hypocretin: 1.75% of clones) per SL were considered as potential candidate as well as genes over-expressed more than four fold in SL-cDNA microarrays (as compared with universal reference), leading to 50 candidates including transcription factors, genes related to apoptosis, immunological processes, cell trafficking regulatory proteins and unknowns. Real time PCR confirmed that 90 % of these genes were overexpressed in WT versus hypocretin cell ablated Tg mice (>1,5 fold). Several of them show strong dorsolateral hypothalamic expression (In situ hybridization, ISH). Finally, the candidate genes with highest selective expression in hypocretinergic neurons (ISH combined with immunocytochemistry) will be selected for further studies.
Conclusion: Several candidate genes were identified. Further experiments including anatomical analysis in post-mortem human brain tissue, genetic polymorphisms association studies in narcolepsy and functional analysis is under way.
Support (optional): ASMF Faculty Career Advancement Award# 31-CA-05 and NIH 23724

0659

VOXEL-BASED MORPHOMETRY AND MAGNETIC RESONANCE SPECTROSCOPY IN HYPOTHALAMUS OF NARCOLEPSY PATIENTS

Poryazova R,[1] Schnepf B,[2] Crelier G,[3] Werth E,[4] Boesiger P,[5] Bassetti C[6]
(1) University Hospital Zurich, Switzerland, Zurich, Switzerland, (2) Institute for Biomedical Engineering, University and ETH Zurich, Switzerland, Zurich, Switzerland, (3) Institute for Biomedical Engineering, University and ETH Zurich, Switzerland, (4) University Hospital Zurich, Switzerland, Switzerland, (5) Institute for Biomedical Engineering, University and ETH Zürich, Switzerland, (6) University Hospital Zürich, Zürich, Switzerland

Introduction: Different brain matters contain metabolites in different concentrations. In order to account for these variations, the content of grey (GM), white matter (WM) and cerebrospinal fluid (CSF) of a single voxel of interest and the anatomy of the whole brain have to be assessed. Morphometric studies in narcolepsy show conflicting results. One magnetic resonance spectroscopy (MRS) study demonstrated reduction in N-acetylaspartate (NAA)/creatine-phosphocreatine (Cr) in the hypothalamus of narcolepsy patients with cataplexy.
Methods: In 14 narcolepsy patients with clear-cut cataplexy, CSF hypocretin deficiency (10/10) and HLA-DQB1*0602 positivity (13/13, 1/1 DR2 positive) and 8 age, gender and body mass index matched controls MRS and a 120 slice T1/3D/TFE measurement with a slice thickness of 1.25 mm (no gap) were performed. Patients were treatment naive or off therapy for at least 14 days before scanning. The data were collected using a 3T Philips Achieva whole body MR scanner. Single-voxel proton MR spectra were acquired from hypothalamus and processed with LCModel to determine metabolite concentration ratios. A fully automatic algorithm was used for the image segmentation analysis. The tissue types in the whole brain and in the region of interest of the single voxel MRS were determined.
Results: No metabolic differences were observed in hypothalamus of patients and controls, especially no differences in the (total NAA)/Cr ratio (patients 1.2 ± 0.2, controls 1.1 ± 0.3, mean ± SD). The distribution of GM, WM and CSF showed no differences between the patient and the control group in the whole brain as well as in the hypothalamic voxel of interest.
Conclusion: Despite the inclusion of homogenous hypocretin deficient group of patients and the use of combined approach no metabolic or GM changes were found in the hypothalamus of narcolepsy patients

0660

SUSTAINED VIGILANT ATTENTION DURING SLEEP DEPRIVATION IN PATIENTS WITH NARCOLEPSY-CATAPLEXY AND IDIOPATHIC HYPERSOMNIA

Khatami R,[1] Landolt H,[2] Nadig U,[2] Adam M,[2] Retey J,[3] Schmid D,[1] Bassetti C[4]
(1) Dept of Neurology, University Hospital Zurich, Zurich, Switzerland, (2) Institute of Pharmacology and Toxicology, University of Zürich, Zurich, Switzerland, (3) Institute of Pharmacology and Toxicology, University of Zürich, Switzerland, (4) Dept of Neurology, University Hospital Zurich, Zürich, Switzerland

Introduction: To examine whether the impairment of sustained vigilant

attention during sleep deprivation (SD) differs among patients with narcolepsy-cataplexy (NC), idiopathic hypersomnia (IH) and matched healthy controls (C).
Methods: Five NC-patients (mean age: 30.4±7.2 years; ESS 15.6±3.5), four IH-patients (32.8±4.8 years; ESS 14±5.1), and nine age- and sex-matched controls (30.4±7.2 years; ESS 6.3±4.1) completed a 40-hour prolonged waking protocol under continuous supervision. Patients and controls performed 10-min sessions of the psychomotor vigilance task (PVT) at 3-hour intervals. The effect of prolonged waking on PVT performance was quantified by comparing the mean values of three test sessions at analogous times of day (at 11, 14 and 17h) before and after one night without sleep. To examine the effect of recovery sleep on PVT variables, the first test after the baseline night was compared to the test after the recovery night. The data were analyzed with repeated-measures ANOVA (GLM) and post-hoc Tukey tests.
Results: Performance variability (10th - 90th inter-percentile range) and slowest 10th percentile of PVT speed (1/reaction time) tended to differ among NC, IH and C (factor `group´: p=.07 and p=.08). In contrast, median and fastest 10th percentile of response speed, and response lapses (reaction time > 500 ms) were similar in all groups. All PVT variables deteriorated with sleep deprivation (factor `day´: p<.02) similarly in all groups (`group´ x `day´ interaction: p>.18). In the morning following the recovery night, performance in all PVT variables was similar to baseline in all groups.
Conclusion: Our preliminary data suggest that sustained vigilant attention as assessed by PVT is similarly impaired in NC and HS when compared to C.
Support (optional): Swiss National Science Foundation

0661

HUMOR PROCESSING IN NARCOLEPTIC PATIENTS ASSESSED BY FUNCTIONAL MRI

Schwartz S,[1] Ponz A,[1] Poryazova R,[2] Werth E,[3] Khatami R,[4] Boesiger P,[5] Bassetti C[6]
(1) University of Geneva, Switzerland, Geneva, Switzerland, (2) Zurich University Hospital, Zurich, Switzerland, (3) University Hospital Zurich, Switzerland, Zurich, Switzerland, (4) University of Zurich, Zurich, Switzerland, (5) University and ETH Zurich, Zürich, Switzerland, (6) University Hospital Zürich, Zürich, Switzerland

Introduction: Narcoleptic patients have cataplexy attacks when they experience positive emotions, in particular when they hear or tell jokes. Narcolepsy with cataplexy (NC) is linked to a hypothalamic hypocretin/orexin deficiency, but the neurophysiological mechanisms underlying such dramatic reaction to positive emotion remain unknown.
Methods: Here we used functional magnetic resonance imaging (fMRI) to assess regional brain responses to humorous stimuli in 12 drug-free narcoleptic patients with clear-cut cataplexy and 12 healthy matched volunteers. While they were scanned, subjects performed a humor judgment task on "mini-action scenes" composed of a succession of two almost identical pictures. The first picture always depicted a neutral scene while the second picture could reveal either a humorous or a neutral new element. MRI data were acquired on a 3-T scanner and analyzed using the general linear model for event-related designs (SPM2).
Results: Behaviorally, NC patients had slower reaction times than controls, as expected. Importantly, there was no group difference in humor rating. The fMRI results revealed that patients and controls share a common neural network for humor processing including associative visual areas, fronto-insula and amygdala, bilaterally. However, when compared to the controls, NC patients showed reduced hypothalamic but enhanced amygdala response to humorous stimuli.
Conclusion: These data provide a first neurophysiological evidence for an exaggerated limbic response to positive emotions in NC patients. Our findings also suggest that hypothalamic hypocretin/orexin activity, which is deficient in narcolepsy, might exert a crucial modulatory influence on emotional processing within the amygdala, gating emotional signals to afford appropriate autonomic reactions.
Support (optional): This work is supported by the Swiss National Science Foundation (grant # 3200B0-104100)

0662

PREVALENCE AND CLINICAL RELEVANCE OF SLEEP APNEA IN NARCOLEPSY

Santamaria J,[1] Sansa G,[2] Iranzo A[1]
(1) Hospital Clinic of Barcelona, Barcelona, Spain, (2) University of Barcelona, 08036, Spain

Introduction: Narcolepsy and obstructive sleep apnea (OSA) are commonly associated with sleepiness and may occur together in some patients. The presence of sleep apnea may difficult considerably the diagnosis of narcolepsy. The actual prevalence of sleep apnea in narcolepsy, however, is unknown.
Methods: All the patients (n:152) diagnosed with narcolepsy (ICSD II criteria) and studied polysomnographically (PSG) at our center were included. The apnea/hypopnea index (AHI), number of patients initially diagnosed only with OSA and clinical response of sleepiness to CPAP treatment when used were assessed.
Results: Thirty two (21%) patients (27 men, 5 women) had an AHI>10, with a mean AHI of 32 (SD:19). Ten of these 32 patients (31%) were initially diagnosed with OSA in other centers and nine of them treated with CPAP (mean CPAP pressure: 8 cm) without clear changes in sleepiness. The diagnosis of narcolepsy was only made when reevaluated for residual sleepiness after CPAP, a mean of 3.5 years later. In the other 22 narcolepsy and sleep apnea were diagnosed simultaneously and in 6 CPAP was started due to an AHI >30. There was no change in sleepiness, although patients referred an improvement in nocturnal sleep quality. The prevalence of cataplexy in the 10 patients initially not diagnosed of narcolepsy was similar to the rest (80% vs. 75%). Patients with an AHI>10 were more likely men (88% vs. 55%), older (48 vs 38yo) and with a higher body mass index (25.1 vs 23.1).
Conclusion: Twenty percent of narcoleptic patients have an AHI>10 and in a third of them the diagnosis of narcolepsy was delayed several years because their physicians did not ask for cataplexy and initially attributed to OSA the sleepiness of the patients, which did not improve with CPAP. Cataplexy should be actively looked for in patients initially suspected to have OSA.

0663

MODAFINIL TREATMENT STARTED WITH LOW INDIVIDUALLY TITRATED DOSE PREVENTS SIDE EFFECTS.

Stefadu Y
Great Lakes Sleep Medicine Institute, Sterling Heights, MI, USA

Introduction: Prevention of side effects is critical for the successful use of any medication. By literature 8% to 15% of patients may develop headache after initiating treatment with Modafinil in standard dose of 200/400 mg, which for some patients became a reason for disconnecting the medication.
Methods: 104 consecutive patients with excessive daytime sleepiness (which have been confirmed by MSLT with mean sleep latency of less than 8 min or ESS of more then 12) secondary to narcolepsy, obstructive sleep apnea (on treatment with CPAP but still continued to have excessive daytime sleepiness), and shift work sleep disorders have been

started on treatment with Modafinil. Modafinil was given once a day after awakening. Patients were instructed to stop medication in the case of a headache or other side effects and increase dose up to minimal dose which prevents somnolence. They titrated the dose from 50 mg a day for four days, to 100 mg for two days, then increase, if necessary, to 200 mg for two days, then increase, if necessary, to 300 mg for 2 days (total 7 tablets of Modafinil 200 mg as a sample), then if necessary the dose increased to 400 mg.
Results: With this regimen none of the patients developed a headache. The Modafinil was stopped only for one patient who developed chest pain which was most likely coincidental. All other patients did not have any side effects. Effective dose was in the range from 100 mg to 400 mg. For example, for one patient a dose of 100 mg was not effective and 200 mg created symptoms of jitters, 150 mg was effective without side effects. All patients improved their alertness on treatment.
Conclusion: 1. Individual titrating dose of Modafinil permits to find effective dose and prevents the development of side effects, which could be related to two factors:

1) Patients were on the minimal effective dose which was on one hand clinically effective, but on the other hand it did not produce side effects.

2) Very small doses of Modafinil at the beginning of the treatment self-induce metabolism of Modafinil in the liver and this way they prevent, hypothetically, high levels of Modafinil and side effects.
2. The alerting effect of Modafinil is dose depending.

0664

MOOD, QUALITY OF LIFE AND CATAPLEXY IN CENTRAL HYPERSOMNIAS

Dauvilliers Y,[1] Paquereau J,[2] Bastuji H,[3] Drouot X,[4] Weil J,[5] Baconnet B,[5] Viot-Blanc V[6]
(1) Hôpital Gui de Chauliac, CHU Montpellier, Montpellier, France, (2) CHU la Milètrie, POITIERS, France, (3) CHU Lyon, France, (4) CHU Henri Mondor, CRETEIL, France, (5) CEPHALON FRANCE, France, (6) Hôpital Lariboisière, CEPHALON FRANCE, Paris, France

Introduction: An important population of French central hypersomnia patients (narcolepsy with cataplexy (C+), narcolepsy without cataplexy and idiopathic hypersomnia (C-)) were studied in order to clarify clinical and therapeutic aspects.
Methods: 577 (53% female, 47% male) patients over 15y were included from 70 French sleep specialists. Clinical, polysomnographical and immunogenetic data were collected retrospectively over a period of 6 months in 2004. A standardized clinical interview plus questionnaires including the Epworth Sleepiness Scale (ESS) and the Beck Depression Inventory (BDI) and 36-item Short Form Health survey (SF-36) were systematically performed.
Results: At the time of the study, 44.9% of patients had no depressive symptoms (BDI score<4), while 26.3% had mild depression (score 4-7), 23.2% moderate (score 8-15) and 5.6% severe (score >16). Cataplexy was present in 73.5% (generalised 45, 8% and partial 45%) with > 1 attack /day in 21.6%. Patients with cataplexy had a higher BMI (26.2 ± 5.4 vs.23.3 ± 3.4, p=0.023) 21.3% of them being obese (BMI>30) and none in the C- group. There was no difference according to mean sleep latency at MSLT. C+ patients had higher scores on BDI, (5.8 ±5.5 vs. 4.4 ± 4.1, p<0.068) as well on both scores of mental and physical health of SF-36 (p=0.003). At the time of study, mean ESS was still 13.1 ± 5.3 with 29% of patients with a score above 16 in the whole group. 80.8% of the patients were treated with modafinil (<200 mg/day: 43.8 %, 300-400mg in 50.4%, > 400mg in 5.8%). Among C+ patients only 37.5% received an anticataplectic drug, mainly SSRIs. Patients treated with anticataplectics had higher BDI scores than patients treated with stimulants only (6.8 ± 6.0 vs 5.1 ± 5.0, p= 0.016). The treatment effect was considered as important/certain by 88.5% for EDS and 79.3% for cataplexy.
Conclusion: Our data further illustrate the large frequency of depressive symptoms and the major impact of central hypersomnias on health-related quality of life. We also reported higher depressive symptoms and psychosocial consequences in patients with cataplexy despite their anticataplectic medication.
Support (optional): CEPHALON FRANCE

0665

INCREASED FEMALE OBESITY IN HYPOCRETIN DEFICIENT NARCOLEPSY SUBJECTS

Khaja A,[1] Mignot E,[2] Chin Soo W,[3] Mali E,[4] Faizy R[5]
(1) Stanford University, Department of Psychiatry and Behavioral Sciences, Stanford, CA, USA, (2) Stanford University, Narcolepsy Center, Stanford Sleep Disorders Clinic, Department of Psychiatry and Behavioral Sciences, Palo Alto, CA, USA, (3) Stanford University, San Juan, Trinidad and Tobago, (4) Stanford University, Narcolepsy Center, Stanford, CA, USA, (5) University of California Riverside, Redlands, CA, USA

Introduction: Increased Body mass Index has been reported in patients with narcolepsy. A study in Hypocretin knockout mice has suggested increased obesity and leptin in female versus male animal models (knockout and ataxin/transgenic). This study was designed to investigate sex differences in BMI distribution in hypocretin deficient narcoleptic patients.
Methods: Subjects (n=168) with narcolepsy and hypocretin deficiency were selected from our database. Mean age ± SEM was 43.5 ± 1.88, 57% were male. Demographics, ethnicity, symptom occurrence and MSLT results were first compared across sex. We next looked at the % of subjects with obesity (BMI ≥30) in both groups and compared symptomatology and treatment across obese and non-obese male and female subgroups.
Results: Male and female did not differ statistically in term of age, BMI, ethnicity, symptom occurrence and age of onset. Interestingly, however, the risk of obesity was OR=2.4 (Odds ratio) higher in female versus men (p=0.02). A comparison of obese and non obese subjects across sex did not reveal any difference in narcolepsy symptomatology, % treated or MSLT results.
Conclusion: In agreement with the mouse data, these preliminary results suggest that a subgroup of female patients with hypocretin deficiency may be at increased risk of developing obesity. Further studies in larger samples will be needed to expand on this finding.
Support (optional): None.

0666

EFFECT OF MODAFINIL ON CEREBRAL BLOOD FLOW IN NORMAL VOLUNTEERS: PLACEBO-CONTROLLED, CROSS-OVER STUDY

Joo E,[1] Tae W,[2] Han S,[2] Cho J,[2] Hong S[3]
(1) Ewha Woman University Hospital, Seoul, South Korea, (2) Samsung Medical Center, Sungkyunkwan University School of Medicine, South Korea, (3) Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

Introduction: To investigate the changes of regional cerebral blood flow (rCBF) after modafinil administration, we performed 99mTc-ethylcysteinate dimer single photon emission computed tomography (SPECT) before and after modafinil administration.

Methods: In a randomized, double-blind, crossover study, 21 right-handed subjects (13 male, mean age 23 years old) received 400 mg single dose of either modafinil or a placebo separated by a 2 week wash-out period. Brain SPECT were performed before and 3 hours after modafinil or placebo administration in healthy subjects. For SPM analysis, all SPECT images were spatially normalized to the standard SPECT template and then smoothed using a 14-mm full width at half-maximum Gaussian kernel. The paired t-test was used to compare pre- and post-modafinil or placebo SPECT images.
Results: Epworth sleepiness scale scores decreased from 3.4 to 2.7 ($p=0.036$, paired t-test) after modafinil administration whereas it did not decrease significantly after placebo administration (from 3.7 to 3.1, $p > 0.05$). In SPM analysis, the on-Modafinil condition was associated with increased rCBF in bilateral thalami and brainstem (uncorrected $p < 0.001$) compared to off-modafinil state, whereas the on-placebo condition increased rCBF in smaller area of dorsal brainstem compared to the off-placebo condition (uncorrected $p < 0.001$). There was no brain area showing hypoperfusion after modafinil or placebo administration. rCBF was significantly increased in bilateral orbitofrontal and prefrontal cortices, right cingulate cortex, left lateral and basal temporal areas, and left brainstem in the on-modafinil condition compared to the on-placebo condition (uncorrected $p < 0.001$).
Conclusion: Our study demonstrated that single dose of modaifnil significantly increased rCBF of arousal-related brain structures and decreased the sleepiness scale in healthy volunteers without sleep deprivation.

0667

CEREBRAL BLOOD FLOW CHANGES BY METHYLPHENIDATE ADMINISTRATION IN NARCOLEPSY PATIENTS

Cho J,[1] Joo E,[2] Tae W,[1] Hong S[1]
(1) Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, (2) Ewha Woman University Hospital, Seoul, South Korea

Introduction: To investigate the effects of methylphenidate (MPHE) on rCBF in narcolepsy, we performed 99mTc-ethylcysteinate dimer single photon emission computed tomography (SPECT) before and after MPHE administration.
Methods: Brain SPECT was performed twice during the awake state before and after MPHE administration for 4 weeks in 18 drug naïve narcolepsy patients (M/F=10/8, 33.7 ± 14.2 years). Nine of them (50%) had cataplexy. For SPM analysis, all SPECT images were spatially normalized to the standard SPECT template and then smoothed using a 14-mm full width at half-maximum Gaussian kernel. The paired t-test was used to compare pre- and post-MPHE SPECT images.
Results: The mean MPHE dose used was 21.5 ± 5.8 mg/day (ranged 10-30). After MPHE administration, Epworth sleepiness scale scores decreased from 15.1± 4.9 to 7.8 ± 4.3 ($p<0.01$, paired t-test). In SPM analysis, the on-MPHE condition decreased rCBF in bilateral amygdala and hippocampi, nuclei accumbens, cingulate gyri, and superior frontal gyri (uncorrected $p < 0.001$), whereas increased rCBF in left supramaginal gyrus compared to the off-MPHE condition (uncorrected $p < 0.001$).
Conclusion: Our study demonstrates first the effect of MPHE on rCBF in narcolepsy patients. MPHE reduced rCBF in cortico-limbic areas, but increased rCBF in the right parietal cortex.

0668

DOES MODAFINIL CHANGE THE CORTICAL EXCITABILITY OF NARCOLEPTIC BRAIN?

Han S,[1] Joo E,[2] Cho J,[1] Hong S[1]
(1) Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, (2) Ewha Woman University Hospital, Seoul, South Korea

Introduction: To evaluate the changes of cortical excitability after modafinil administration, we tested various parameters of cortical excitability using transcranial magnetic stimulation (TMS) in the patients with narcolepsy.
Methods: We consecutively recruited 11 drug naïve narcolepsy patients. TMS was applied on motor cortex using two Magstim 200 stimulators connected via a Bistim module (Magstim Company, UK) and a figure of 8-shaped coil (7 cm wing diameter). Surface EMG was recorded from the first dorsal interosseus muscle (FDI) of the hand. TMS indices obtained in the study were resting motor threshold (rMT), motor evoked potential (MEP) amplitudes, cortical silent period (CSP), intracortical inhibition (ICI) and facilitation (ICF).
Results: Eleven patients received modafinil and performed TMS studies three times (baseline, 3 hours after modafinil single dose of 200mg administration and after 14 days of 200mg/day of modafinil administration). Epworth sleepiness scale was significantly decreased after 14 days-modafinil treatments (15.0±5.8 to 12.2±5.8, ANOVA, $p=0.002$). Resting motor thresholds was also significantly reduced from 49.2 ± 5.9 to 44.8 ± 6.5 after 14 days of modafinil treatment in right hemisphere (ANOVA, $p<0.002$). The durations of the cortical silent period and paired pulse results (ICI, ICF) were not changed after single dose or 14 days of modafinil administrations (repeated ANOVA, $p>0.05$). The ANOVA for stimulus-response curves revealed a significant difference for the factor Intensity (120, 140, 150%) but no significance for the factor Time. All tested values were not different between right and left hemispheres.
Conclusion: Modafinil administration decreased resting motor threshold of right hemisphere but not in left hemisphere and reduced the daytime sleepiness significantly after 14 days treatment in the patients with narcolepsy. However, other parameters of cortical excitability were not changed by modafinil treatment.

0669

NARCOLEPSY SPECTRUM IN PROBANDS´ FAMILIES AND THE GENERAL POPULATION

Ohayon M,[1] Guilleminault C,[2] Black J,[3] Wells C[4]
(1) Stanford University, Palo Alto, CA, USA, (2) Stanford University, CA, USA, (3) Stanford University, Stanford, CA, USA, (4) Sleepmed, inc., GA, USA

Introduction: Previous genetic studies have shown there is a genetic etiology in narcolepsy-cataplexy. However, multiple cases of narcolepsy-cataplexy can be found in only 8%-10% of the families of narcoleptic individuals. The risk for a first-degree relative of developing excessive daytime sleepiness or other symptoms of REM anomalies is uncertain. This study aims to document the risk of developing such anomalies among first-degree relatives of narcoleptic subjects.
Methods: Information on 1,383 individuals was collected: 186 subjects with narcolepsy and 1,197 family members (51 grandfathers/grandmothers; 215 fathers/mothers; 217 uncles/aunts; 272 brothers/sisters; 99 sons/daughters; 150 first-degree cousins; and 23 great-uncles/aunts). Participants were also asked to give a blood sample in other to perform genetic testing. Data of the general population (GP) came from a sample of 6,694 subjects aged 18 and older living in the

states of New York and California. In both studies, interviews were conducted by telephone with the Sleep-EVAL system.
Results: A total of 32 cases of narcolepsy were identified among the family members: 3 uncles, 6 aunts, 6 mothers,5 fathers, 3 daughter, 3 brothers, 4 sisters and 1 niece. Four of them were confirmed with HLA typing (HLA-DQb1*0602). Excessive daytime sleepiness was common among the family members (36.2% vs. 28.1% in the GP). Sleepiness in situations that require moderate to high attention was at least two times more frequent among family members than in the GP. Sleep paralysis occurring at least once per month was reported by 15.1% of family members (vs. 3.5% in the GP). Hypnagogic hallucinations were also 3 times more frequent in family members compared to the GP (13.7%).Weekly episodes of cataplexy were reported by 3.4% of the family members and 0.7% of the GP.
Conclusion: Risks for narcolepsy and narcolepsy symptoms are high in family members of narcoleptic individuals and show a genetic vulnerability to REM anomalies.
Support (optional): NIH grant # NS44199

0670

IS CHRONIC INSOMNIA A RISK FACTOR FOR HIPPOCAMPAL VOLUME LOSS?

Riemann D,[1] Voderholzer U,[2] Spiegelhalder K,[1] Hornyak M,[1] Nissen C,[1] Hennig J,[1] Tebartz Van Elst L,[1] Feige B[1]
(1) Freiburg University Medical center, Freiburg, Baden-Württemberg, Germany, (2) Freiburg University Medical Center, Freiburg, Germany

Introduction: Sleep is important for brain function and development with respect to gene expression, protein translation and learning and memory. It has been shown that sleep restriction or sleep deprivation has a detrimental impact on neuro-neogenesis in the rat hippocampus. These data raise the possibility that chronically disturbed sleep in humans, as in primary insomnia (PI) may affect the morphology of hippocampal structures, known to play a role in learning and memory processes. To test this hypothesis, patients with chronic primary insomnia were investigated with magnetic resonance imaging (MRI) and their data were compared to good sleepers.
Methods: MRI images (1.5 Tesla) of the brain were obtained from insomniac patients and good sleepers. MRI scans were analyzed bilaterally by manual morphometry for different brain areas including hippocampus, amygdala, anterior cingulate, orbitofrontal and dorsolateral prefrontal cortex. Subjects were 8 unmedicated physician-referred patients (three males, five females; 48.4 +/- 16.3 yrs.) with chronic primary insomnia (according to DSM-IV criteria) and 8 good sleepers matched for age, sex, body mass index and education.
Results: Patients with primary insomnia demonstrated significantly reduced hippocampal volumes bilaterally. Hippocampal volumes correlated significantly negative with the Pittsburgh sleep quality index.
Conclusion: Similar findings have been described in other neuropsychiatric conditions, for example depression or borderline personaility disorder. We speculate that insomnia may be the common underlying pathway leading to hippocampal volume reductions. The results may also explain why conditions like primary insomnia or those associated with insomnia are frequently coupled with neuropsychological impairments.

0671

ETHNIC DIFFERENCES IN SLEEP BETWEEN MIDDLE-AGED AFRICAN-AMERICAN AND CAUCASIAN-AMERICAN INSOMNIACS

Ruiter M,[1] Lichstein K,[2] Durrence H,[3] Taylor D,[4] Riedel B,[5] Bush A[6]
(1) University of Alabama, Tuscaloosa, AL, USA, (2) The University of Alabama, AL, USA, (3) Somaxon Pharmaceuticals, CA, USA, (4) University of North Texas, TX, USA, (5) University of Memphis, TN, USA, (6) University of Tennessee, TN, USA

Introduction: Previous research has revealed significant differences in the prevalence distribution of insomnia across age groups between African-Americans (AA) and Caucasian-Americans (CA). In particular, the prevalence of insomnia in AA peaks amid ages 30 to 59 while the prevalence of insomnia in CA gradually increases with age. The goal of this paper is to compare middle-aged AA and CA quantitatively classified as insomniacs on demographic, health behavior, subjective sleep, and daytime functioning variables.
Methods: We identified 25 AA and 28 CA, aged 30-59, out of 772 participants in an epidemiological survey. All participants completed the following questionnaires: two weeks of sleep diaries, a general health questionnaire, and daytime functioning questionnaires including sleepiness, fatigue, insomnia impact, depression, and anxiety.
Results: t-tests between AA and CA insomniacs were conducted. Results on the sleep variables indicate that AA report longer SOL (p=.001), more naptime (p<.01), and less sleep efficiency (p=.01) compared to CA. AA with insomnia also reported significantly less educational attainment than CA with insomnia (p=.001). There were no differences between the groups in daytime functioning or any other health-related problem.
Conclusion: Middle-aged AA with insomnia are reporting a more severe presentation of insomnia than CA with insomnia. There are no differences in reported health or daytime functioning that can account for these differences.
Support (optional): Research supported by National Institute on Aging grants AG12136 and AG14738

0672

IMPULSIVITY AS A RISK FACTOR FOR INSOMNIA: EVIDENCE FROM AN EXPLORATORY STUDY

Schmidt R, Gay P, Van Der Linden M
University of Geneva, Geneva, CH, Switzerland

Introduction: Despite its prominent status in psychopathology, impulsivity has rarely been considered as a potential risk factor for insomnia in previous research, and the few studies that have done so produced equivocal evidence. Meanwhile, indirect evidence continues to hint at a possible link between impulsivity and insomnia, for example, well-documented sleep disturbances in impulsivity-related disorders such as borderline personality disorder. The purpose of the present study was to investigate the relationship between impulsivity and insomnia based on the comprehensive approach to impulsivity proposed by Whiteside and Lynam (2001). According to these authors, four facets of impulsivity can be distinguished: urgency, lack of premeditation, lack of perseverance, and sensation seeking.
Methods: A sample of undergraduate students (N=233) completed three questionnaires: the UPPS Impulsive Behavior Scale, the Sleep Impairment Index (Morin, 1993), and a short questionnaire on hypnagogic and dreamlike mentation.
Results: The main findings were as follows: (a) urgency was related to insomnia (r=.33, p<.01); (b) lack of perseverance was related to insomnia (r=.24, p<.01); (c) urgency was related to frequency of upsetting thoughts at sleep onset (r=.32, p<.01), upsetting images at sleep onset (r=.37, p<.01), upsetting dreams (r=.28, p<.01), and nightmares (r=.21, p<.01); (d) the effect of urgency on difficulty in falling asleep was partially mediated by frequency of upsetting thoughts and images at sleep onset (Sobel test: Z=4.04, p<.001).
Conclusion: To our knowledge, the present study is the first to provide clear evidence for a link between two facets of impulsivity (urgency, lack of perseverance) and insomnia, and for a link between urgency and sleep-interfering cognitive activity. The specific relations between facets of impulsivity and aspects of insomnia might open up new avenues for modeling the development and maintenance of insomnia and for clinical interventions.

0673

DO SLEEP PROBLEMS AFFECT WHAT WE EAT?

Engle-Friedman M,[1] Hayrapetyan L,[1] Orodel O,[2] Loshak M[2]
(1) Baruch College, City University of New York, New York, NY, USA, (2) Baruch College, City University of New York, NY, USA

Introduction: Individuals who consume fast food two or more times a week may gain approximately 10 more pounds and have twice as much insulin resistance in a 15-year period than those who consume fast food less than once per week (Pereira, 2004). Sleep loss has also been associated with insulin resistance (VanHelder, *et al.*, 1993). This study assessed eating patterns in persons who described themselves as having

sleep problems.
Methods: 9 female (mean age 20 yrs; range = 18-25) and 12 male (mean age 21 yrs; range = 18-34) undergraduates completed sleep and eating habits questionnaires. For 7 days, participants completed Sleep and Activities Diaries every morning and an Evening Diary concerning the largest meal of the day and called data into an answering machine twice per day.
Results: Preliminary finding show individuals reporting problems with total sleep time, sleep latency and awakenings were more likely to eat restaurant-prepared or fast food rather than food made at home on day 2 than were individuals with no reported sleep problems ($p<.05$). Individuals with sleep problems were also less likely to eat food prepared at home on days 4 (sleep latency problems) ($p<.05$) and 7 (awakening problems) ($p<.05$).
Conclusion: Persons with sleep complaints are less likely to eat at home. These meals may require less effort and may be less healthful than meals prepared at home. Over time, persons with sleep complaints may have weight or health problems related to their nutrition.

0674

SLEEP PROBLEMS AND HEALTH CARE UTILIZATION IN COLLEGE STUDENTS

Bramoweth A, Taylor D, Grieser E, Roane B, Gardner C, Williams J, Zimmerman M
University of North Texas, Denton, TX, USA

Introduction: Little data exists evaluating the role of sleep problems in health care utilization (HCU). The present study compares HCU of students with and without self-reported sleep problems as well as HCU of students with chronic insomnia, transient insomnia, and normal sleepers.
Methods: An undergraduate student sample completed an online delivered survey. Students were asked questions to determine the presence, frequency, and duration of sleep problems (e.g. insomnia, apnea, periodic limb movements). Students were also asked questions regarding HCU in the past 6 months (e.g. physician, hospital, mental health) and medication use for the past week (e.g. prescription, over-the-counter, natural supplements).
Results: To date, 854 students have volunteered for the study and we expect over 1800 by June 2007 (i.e. in time for the APSS Conference). At present, we have analyzed pilot data of 387 students who completed similar measures in spring 2006, and their results follow. We distributed 515 packets with a 75% return rate. Sleep problems were reported in 28% of the sample. Analyses found students with a sleep problem reported more physician visits than students without a sleep problem ($p < .001$). Students with a sleep problem also reported significantly higher medication use than students without a sleep problem ($p < .001$). Students with chronic insomnia reported significantly higher physician visits than normal sleepers ($p < .05$). Students with chronic insomnia also reported significantly higher medication use than normal sleepers ($p < 01$). Analyses found no significant differences for emergency rooms visits, hospital admissions, or total nights in a hospital.
Conclusion: These data suggest that significant differences exist in HCU for students with a sleep problem. It is impossible to determine a causal relationship between sleep problems and HCU, but these results indicate that more research is needed to examine the role of sleep disorders in HCU.

0675

INSOMNIA AS A PRESENTING MANIFESTATION OF AUTISM IN CHILDREN

Cruz M,[1] Kaleyias J,[2] Adams R,[2] Legido A,[2] Kothare S[2]
(1) St. Christopher's Hospital for Children, Philadelphia, PA, USA, (2) St. Christopher's Hospital for Children, PA, USA

Introduction: Children with autistic spectrum disorders (ASD) frequently experience sleep disorders and exhibit atypical sleep architecture. The aim of this study was to evaluate the occurrence of ASD in children who have insomnia (difficulty in initiating and maintaining sleep).
Methods: We retrospectively reviewed the medical records of 48 patients (age range 1.5-18 years), who were referred in 2005 to our sleep –disorder clinic for evaluation of insomnia, out of 246 patients seen for diverse sleep problems.
Results: The vast majority of children (92%) had secondary insomnia. Among them, nine children (19%) were found to have ASD non-previously diagnosed. The insomniac patients with ASD were younger (median age 3 years old; range 2-15) as compared with the non-ASD insomniac patients (median age 10 years, range 1.5-18) ($p=0.002$). The mean childhood autism rating scale (CARS) score in the ASD subgroup was 44 and in non-ASD subgroup was 14 ($p=0.001$). Six patients with ASD associated insomnia had polysomnographic studies, of which three had periodic leg movement disorders, two with obstructive sleep apnea syndrome, and one being normal.
Conclusion: Careful assessment of sleep quality should be an integral part of the treatment plan in children with autism. Conversely, when assessing children with insomnia, the possibility of undiagnosed ASD as a presenting manifestation, needs to be considered.

0676

EFFICACY AND NEXT-DAY RESIDUAL EFFECTS OF RAMELTEON 8 MG IN ADULTS WITH CHRONIC INSOMNIA: A COMBINED ANALYSIS OF 2 DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSSOVER TRIALS

Mini L,[1] Maloney P,[1] Wang-Weigand S,[2] Zhang J,[2] Kasten K[2]
(1) Takeda Pharmaceuticals North America, Deerfield, IL, USA, (2) Takeda Global Research and Development Center, Deerfield, IL, USA

Introduction: The chronohypnotic RozeremTM (ramelteon) is a selective MT1/MT2-receptor agonist approved for the treatment of insomnia.
Methods: This analysis evaluated the efficacy and safety of ramelteon 8 mg compared to placebo using data from 2 double-blind, placebo-controlled, crossover trials of adults (ages 18 to 83 years) with chronic insomnia. A reduction in latency to persistent sleep (LPS) of > 50% from baseline (as measured by polysomnography) was the primary endpoint for this analysis. Level of alertness and ability to concentrate (post-sleep questionnaire), immediate and delayed recall (Word List Memory Test), visual analog scales for mood and feelings, and psychomotor effects (Digit Symbol Substitution Test) were used to assess next-day residual effects. Data on adverse events were recorded for each group.
Results: This analysis included 203 subjects. With ramelteon 8 mg, 63.1% of subjects demonstrated an LPS reduction of at least 50% compared to 44.8% of subjects taking placebo ($P<0.001$). No statistically significant difference on any next-day performance measures was observed between the ramelteon and placebo groups. Headache was the only adverse event occurring in at least 3% of subjects. Overall, the incidences of adverse events were similar between the ramelteon and placebo groups.

Conclusion: In adults with chronic insomnia, a significantly higher percentage of subjects in the ramelteon 8 mg group experienced a >50% reduction in LPS than those in the placebo group. Ramelteon was well tolerated, did not result in significant adverse events, and did not impair cognition, memory, mood, or psychomotor function compared to placebo.
Support (optional): This research was supported by Takeda Pharmaceutical Company.

0677

DAYTIME CONSEQUENCES OF INSOMNIA: A FACTOR ANALYSIS

Beaulieu-Bonneau S, Fortier-Brochu E, Ivers H, Morin C
Universite Laval, Quebec, Canada

Introduction: Although insomnia is frequently associated with complaints of significant daytime impairment, little is known regarding the nature of these consequences. This study aimed at defining the nature of self-reported daytime consequences of insomnia and at identifying predictors of these complaints.
Methods: Participants were 160 adults (aged 30-72, mean = 50.3; 60.6% women) meeting criteria for chronic insomnia recruited in the context of a larger treatment study. For the present study, only baseline data were used. Daytime consequences were measured by 14 indicators: five Multidimensional Fatigue Inventory (MFI) subscales, eight SF-36 Health Survey subscales, and the Insomnia Severity Index item asking to what extent sleep difficulties interfere with daily functioning. Potential predictors of daytime consequences were socio-demographic, sleep (continuity and architecture), health (number of medical conditions, frequency of physical activity), and clinical (psychiatric co-morbidities, depressive and anxiety symptoms assessed by the BDI and BAI) variables.
Results: A factor analysis using the promax oblique rotation method was performed on the 14 indicators. A three-factor structure was selected based on parsimony and interpretability. Variables included in each factor were: F1) all MFI subscales, SF-36 vitality subscale, and ISI interference item; F2) SF-36 physical functioning, role physical, bodily pain, and general health subscales; and F3) SF-36 social functioning, role emotional, and mental health subscales. Correlations between factors ranged from r = .22 (F2 vs. F3) to .55 (F1 vs. F2). Stepwise logistic regressions were then performed on the aggregate standardized score of each factor. Significant predictors were: for F1 (R2 = .473): higher BDI, younger age, longer wake after sleep onset (diary), and higher BAI; for F2 (R2 = .406): younger age, higher number of medical conditions, being unemployed, higher BDI, lower sleep efficiency (PSG), higher BAI, presence of past psychiatric diagnosis, and longer time in bed (diary); for F3 (R2 = .450): higher BDI, younger age, higher number of medical conditions, more frequent physical activity, and lower sleep efficiency (PSG).
Conclusion: These results suggest that daytime impairment in individuals with insomnia can be classified as related to fatigue, physical health, and mental health. Furthermore, these different subtypes of daytime consequences are explained by distinct sets of variables. Confirmation of these findings with more objective data of daytime impairment is needed.
Support (optional): Research supported by the National Institute of Mental Health (MH60413).
The first author is supported by the Fonds de la recherche en sante du Quebec.

0678

SLEEP AND FATIGUE IN INDIVIDUALS WITH INSOMNIA

Fortier-Brochu E,[1] Beaulieu-Bonneau S,[1] Ivers H,[1] Morin C[2]
(1) Laval University, Quebec, Canada, (2) Laval University, Ste-Foy, Quebec, Canada

Introduction: Although fatigue is the most consistent complaint among individuals with insomnia, its relation to sleep impairment remains poorly understood. The aim of this study was to describe different patterns of relations between sleep and fatigue among individuals with insomnia.
Methods: The current analysis used baseline data collected in the context of a larger treatment study. Participants were 160 adults who met the diagnostic criteria for chronic insomnia (aged 30-72, mean = 50.3; 60.6% women). All underwent three nights of polysomnographic (PSG) recordings and completed the Multidimensional Fatigue Inventory (MFI). Sleep variables and scores obtained on the MFI were standardized into z-scores. For each participant, a composite score of sleep impairment averaging z-scores for PSG-defined sleep onset latency, wake after sleep onset and total sleep time was then derived. Similarly, a composite score of fatigue averaging z-scores for the five sub-scales of the MFI was computed. Participants also completed the Beck Depression Inventory (BDI), the Beck Anxiety Inventory (BAI) and the SF-36 Health Survey.
Results: Composite sleep impairment and fatigue scores were submitted to a hierarchical cluster analysis using Ward´s method. A 4-cluster solution was selected based on parsimony, interpretability and cluster sizes (R2 = 0.68). Individuals were thus classified as having either 1) both severe insomnia and severe fatigue (SI-SF; n = 15); 2) severe insomnia but mild fatigue (SI-MF; n = 15); 3) mild insomnia but severe fatigue (MI-SF; n = 68) or 4) both mild insomnia and mild fatigue (MI-MF; n = 61). Those with SI-SF had greater self-reported sleep problems compared to all other clusters, while those with SI-MF had significantly more impaired PSG-defined sleep. While general and mental fatigue were higher in both SF clusters compared to MF clusters, physical fatigue and decrease in activities were different across all 4 clusters, those with SI-SF being the most impaired, followed by those with MI-SF, those with SI-MF and finally those with MI-MF. Compared to both clusters with MF, those with SF had significantly higher BDI ($p < .01$) and lower SF-36 scores ($p < .01$).
Conclusion: Results suggest different patterns of sleep-fatigue relations among individuals with insomnia, such that fatigue seems to occur independently of PSG-defined sleep difficulties and appears paralleled by more depressive symptoms and a greater decrease in quality of life.
Support (optional): Research supported by the National Institute of Mental Health (MH60413). The first author is supported by the Canadian Institutes of Health Research.

0679

POLYSOMNOGRAPHIC EVALUATIONS OF THE EFFECT OF NYTEX (NATURAL SUPPLEMENTS) IN INSOMNIAC PATIENTS

Cvetanovic I, Golbin D
Sleep and Behavior Medicine Institute, Vernon Hills, IL, USA

Introduction: The aim of this study was to evaluate the effect of combination of natural supplements in patients with insomnia using the polysomnographic technique (PSG).
Melatonin, a pineal hormone supplement that regulates circadian rhythm can be helpful to readjust the timing of internal biological rhythm and reduce insomnia. Valerian (herbal product) and blueberry extract (antioxidants) might be beneficial for the treatment of insomnia and

anxiety disorder. However, little is known about the effect of the combination of these three compounds on improving a sleep pattern in insomniac patients. Nytex, a new over-the counter supplement for sleep which contains a combination of melatonin, valerian, and blueberries extract, is used in this study.
Methods: This open-label study included overnight polysomnographic recordings of five female adults with primary insomnia, before and after thirty days of using nytex a half hour before bed time. Participants were not allowed to take any CNS stimulants, sedative medications or other herbs during the duration of the study. Data from the PSG recordings are expressed as percentage change from the baseline to the completion of the thirty days of taking nytex.
Results: Total time in bed (TTB), total sleep time (TST), non REM stage I and REM stage were obtained respectively. Compared to baseline measurements, it showed increased total time in bed by 10%, CI 95% 3.4 – 16.6%; total sleep time by 18 %, CI 95% 8.6 – 27.4%, non REM stage I by 43% CI 95% -76.2 – 162.2; REM stage by 99 %, CI 95% 3.7 – 194.3.
Conclusion: Results showed significantly improved quality of sleep with increased the TTB, TST, REM stage, but non-REM stage I was not different. Further study with a larger population and control is necessary.
Support (optional): The Research was partially supported by unrestricted grants from the Tharos Laboratories.

0680

PATIENT-REPORTED OUTCOMES (PROS) IN INSOMNIA: AN ENDPOINT MODEL

Kleinman L,[1] Roth T,[2] Buysse D,[3] Kalsekar A,[4] Harding G,[1] Lichstein K,[5] Revicki D[1]
(1) United BioSource, Bethesda, MD, USA, (2) Henry Ford Hospital, Detroit, MI, USA, (3) University of Pittsburgh, Pittsburgh, PA, USA, (4) Eli Lilly, Carmel, IN, USA, (5) University of Memphis, Tuscaloosa, AL, USA

Introduction: Insomnia is a disorder determined clinically by the patient´s subjective reports on sleep experience rather than by physiologic markers of sleep-wake function. The aim of this study was to identify key aspects of insomnia and its daytime impact using qualitative research to develop an endpoint model of outcomes in insomnia.
Methods: A literature review was conducted to identify endpoints in insomnia and questionnaires used in insomnia research. In order to identify how patients describe concepts included in the identified endpoints, three focus group discussions were conducted in persons (n=28) with insomnia, recruited from three clinical sites in the United States using Research Diagnostic Criteria for insomnia. The combination of literature, patient input and clinical expert input was used to construct a conceptual endpoint model of PRO endpoints in insomnia.
Results: Endpoints identified in literature review included sleep latency, sleep maintenance, sleep quality and various daytime impact measures. Apart from desire to fall asleep quickly and stay asleep longer, sleep experience was described by focus group participants more qualitatively as “adequate”, “uninterrupted”, “restful”, “deep”, and “sound”. Participants additionally desired a wake time experience in which they felt “well rested,” “refreshed,” and “energized, feeling ready to take on the day.” Good sleep quality was defined by a combination of sleep experience and waking experience. Daytime experience of insomnia included complaints that were physical (e.g., feeling tired), emotional (e.g., feeling inpatient or irritable), and cognitive (e.g., not able to concentrate). Participants also reported interference with daily activities, although the impact was minimized due to coping mechanisms. Draft item pools for the measurement of sleep, wake time and daytime experience are proposed.
Conclusion: An endpoint model of outcomes in insomnia should include PROs that patient´s value: sleep experience, wake time experience and daytime experience. Further research in insomnia requires the systematic development of psychometrically sound measures of these outcomes.
Support (optional): Eli Lilly

0681

THE EFFECT OF INTERPERSONAL THERAPY FOR DEPRESSION ON INSOMNIA SYMPTOMS IN A COHORT OF WOMEN WITH SEXUAL ABUSE HISTORIES

Pigeon W,[1] Talbot N,[2] Perlis M[3]
(1) University of Rochester, Rochester, NY, USA, (2) University of Rochester, NY, USA, (3) University of Rochester, Pittsford, NY, USA

Introduction: Insomnia is highly prevalent in patients with depression and often persists following successful antidepressant treatment with CBT or pharmacotherapy. This suggests that insomnia and depression may be comorbid disorders, each requiring targeted treatment. To further explore this proposition, we evaluated whether Interpersonal Psychotherapy (IPT) for depression in women with childhood sexual abuse histories might yield sleep related benefits.
Methods: Data were gathered from a published clinical trial of IPT for depression in women with childhood sexual abuse histories. Thirty-six subjects met criteria for Major Depressive Disorder as assessed by the Structured Clinical Interview for DSM IV (SCID). A 16 session treatment was delivered in a community mental health center. Ten subjects were excluded for having no data beyond baseline or for completing <5 sessions. The remaining 26 women completed 14+/-5 sessions and 85% received >8 sessions. Assessments were made at baseline, Wk 10, Wk 24 and Wk 36 and included the Beck Depression Inventory II (BDI) and the Hamilton Rating Scale for Depression (HAMD). Three sleep items from the HAMD (difficulty falling asleep, waking in the night, waking too early), which range from 0-2, were summed to derive a total insomnia score. The baseline insomnia was compared to scores at weeks 10, 24 and 36 by two-tailed, paired samples t-tests. Missing items were imputed using the last observation carried forward approach. Exploratory analyses were conducted to ascertain what variables might be related to either total insomnia at Wk 36 or total change in insomnia.
Results: At baseline 30 of 36 women (83%) met SCID criteria for insomnia. In the analyzed sample, BDI scores were significantly improved at all time points (all p<.01). In contrast, total insomnia scores did not improve significantly over time (p = .12, .18, and .09 respectively), although an obvious trend was present. At baseline, 54% of the sample endorsed at least one of the sleep items as severe and an additional 23% as moderate. By Wk 36, these percentages were 35% and 23% respectively. Interestingly, early morning awakening was the least frequently endorsed sleep item in this depressed sample. Finally, neither total insomnia at Wk 36 nor the insomnia change score were related to the BDI change score, BDI at any time point, baseline comorbidities, or the two HAMD anxiety items.
Conclusion: These results suggest that IPT which is effective for depression in a childhood sexual abuse sample also tends to exert positive clinical effects on sleep continuity disturbance (though not at a statistically significant level with this sample size). The trend cannot be accounted for by sleep specific interventions (as IPT does not include such components) or by changes in overall severity of depression. One possible moderator, which may be unique to this population, is that

sleep continuity gains are achieved through real or perceived gains regarding personal safety.
Support (optional): NIH NS049789 (WRP) & MH064528 (NLT)

0682

COMPARISON OF SLEEP DIARIES, ACTIGRAPHY AND AMBULATORY POLYSOMNOGRAPHY IN COLLEGE STUDENTS WITH INSOMNIA

Williams J, Taylor D, Gardner C
University of North Texas, Denton, TX, USA

Introduction: Accurately and cost effectively measuring sleep in insomnia patients can be particularly difficult. Actigraphy, a wrist worn activity sensor, is an inexpensive and objective way of measuring sleep. Actigraphy use has been previously validated for older adults with insomnia for measuring the number of awakenings in a night (NWAK), wake after sleep onset (WASO), total sleep time (TST), and sleep efficiency percentage (SE). However actigraphy has not been studied in the college population suffering from insomnia and has not been validated against ambulatory polysomnography. This study sought to validate actigraphy for college students with insomnia.
Methods: Participants were recruited from the general college population and screened for insomnia (n = 3). A single night of data from actigraphy recordings at three sensitivity levels and self-report sleep diaries were compared to data from an ambulatory polysomnograph (PSG) recording, the gold standard of sleep measurement.
Results: Dependent variables included sleep onset latency (SOL), NWAK, WASO, TST, and SE. PSG was significantly correlated with actigraphy on WASO at all sensitivity levels (all $p < .05$). PSG was significantly correlated with actigraphy on SE at the high sensitivity level ($p < .05$). No significant correlations were found between PSG and any sensitivity level of actigraphy for SOL or TST. Sleep diaries were significantly correlated with PSG on NWAK and SE ($p < .05$) but were not correlated for SOL, WASO or TST.
Conclusion: These results concur with previous studies showing actigraphy is effective in measuring WASO and SE. Because the power was low in the current study negative results should be discounted at this point. We are in the process of collecting data on 50 more subjects, which should improve the power and generalizability of the study, and expect to have this completed by the conference.

0683

COMBINING ESCITALOPRAM OXALATE (ESCIT) AND INDIVIDUAL COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA (CBTI) TO IMPROVE DEPRESSION OUTCOME

Manber R,[1] Edinger J,[2] San Pedro M,[3] Kuo T[3]
(1) Stanford University, Stanford, CA, USA, (2) VA and Duke University Medical Centers, Durham, NC, USA, (3) Stanford University, CA, USA

Introduction: Insomnia contributes to the severity of major depressive disorder (MDD), hinders response to antidepressant therapies, and, when unresolved, increases the risk for relapse of MDD. Therefore when MDD and insomnia co-occur treating both disorders concomitantly could improve outcome.
Methods: This controlled pilot study compared the responses of patients randomized to receive EsCIT+CBTI with those receiving EsCIT+CTRL (Pseudo-desensitization, a control psychotherapy for insomnia). Participants had to meet DSM-IV-TR criteria for MDD, score ≥ 14 on the HRSD17, have sleep onset latency ≥ 30 minutes and/or wake after sleep onset ≥ 30 minutes ≥ 3 nights / week; and sleep ≤ 6.5 hours ≥ 3 times/week. Excluded were those with a respiratory disturbance with arousal index ≥ 10 per hour, PLMS index ≥10, co-morbid psychiatric and uncontrolled medical conditions, and concomitant treatment for depression or insomnia.
All participants received 12 weeks of EsCIT and 7 individual sessions of CBTI or CTRL. The main outcome was remission of depression (HRSD < 8). Additional measures were sleep diary, actigraphy and the Insomnia Severity Index (ISI).
Results: 9 men and 16 women were randomized (13 to CBTI and 12 to CTRL). EsCIT+CBTI resulted in higher rate of remission (64%) than EsCIT+CTRL (41%). Mean end-of-treatment HRSD scores were 8.0±7.2 for CBTI and 12.0 ± 9.1 for CTRL (Cohen´s d=.44). Participants in the EsCIT+CBTI had larger improvement in all sleep measures, except for TST, with a large effect size for the ISI (d=.95) and moderate effect sizes for sleep quality, total wake time (TWT), and sleep efficiency (average d=.51). The correlations between the change in HRSD (sleep items removed) and changes in sleep were statistically significant (.56, p<.01 for TWT and .78, p<.001 for ISI).
Conclusion: This pilot study provides indications that the strategy of combining antidepressant medications with CBTI is promising for patients with co-morbid depression and insomnia.
Support (optional): This research was supported by NIMH grant number MH66131. Medications were provided by Forest Laboratories.

0684

THE INTERRELATIONSHIP OF INSOMNIA AND MENTAL HEALTH CROSS-SECTIONALLY AND LONGITUDINALLY

Gardner C,[1] Taylor D,[1] Tatum J,[1] Bramoweth A,[2] Grieser E,[1] Roane B,[1] Williams J,[1] Zimmerman M[1]
(1) University of North Texas, Denton, TX, USA, (2) University of North Texas, TX, USA

Introduction: Insomnia and mental health problems are highly interrelated, but the relationships do not follow a traditional cause-and-effect pattern where one disorder always precedes another. The National Institutes of Health called for more longitudinal studies of insomnia and mental health to help us untangle this relationship. We performed the current study to answer this call by examining the relationships between insomnia and mental health problems in college students both cross-sectionally and longitudinally.
Methods: To date, 365 undergraduate students have been assessed cross-sectionally in the spring of 2006 and will be assessed again at 1-year follow-up in the spring of 2007. Insomnia was assessed with self-report and one-week sleep diaries. Mental health problems were assessed with the Symptom Check List (SCL-90), which measures 9 symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism, and a global severity index.
Results: Using a one-way multivariate analysis of variance (MANOVA) we determined that people with insomnia had significantly more mental health problems than those without insomnia Wilk's Ü = .90, $F(1, 364) = 3.80$, $p < .001$. Follow-up univariate analyses found significant differences in all nine symptom dimensions and global severity (all ps < .05).
Conclusion: This study confirms that college students with insomnia have significantly more mental health problems than college students without insomnia. Further analyses will allow us to assess if insomnia is a risk factor for the development of these mental health problems over the course of one year.

0685

GABAPENTIN AS A TREATMENT FOR MENOPAUSE RELATED SLEEP DISTURBANCE

Yurcheshen M,[1] Guttuso T,[2] Perles M,[1] Sarah M,[1] McDermott M[1]
(1) University of Rochester, Rochester, NY, USA, (2) University of Buffalo, Buffalo, NY, USA

Introduction: Nearly two million women in the United States enter menopause every year and approximately 40% of these women experience sleep difficulties. Traditionally, treatment for menopausal symptoms, including hot flashes and sleep disturbances, has relied on hormone replacement therapy (HRT). Recent data suggests increased risk of breast cancer and cardiovascular complications in post-menopausal women using HRT, necessitating explorations into alternate therapies. The present analysis, based on data from a randomized clinical trial of gabapentin for treatment of hot flashes, evaluates this agent´s effects on menopausal sleep disruption.
Methods: As part of the parent study, 59 postmenopausal women with hotflashes were randomized to treatment with gabapentin (dose upwardly titrated to 300mg TID) or to placebo for a period of 12 weeks. For the present analysis, sleep was assessed at baseline, 4 weeks and 12 weeks using a recently developed 3 factor scoring model for the Pittsburgh Sleep Quality Index (Sleep Efficiency, Sleep Quality, and Daily Disturbance).
Results: After 12 weeks of treatment, patients randomized to 300mg TID gabapentin demonstrated a 35% improvement in their sleep quality factor score, compared to 8% in placebo-treated subjects (p=0.05). No significant improvement was observed for the two other factors (sleep efficiency and daily disturbance).
Conclusion: Gabapentin subjectively improves sleep quality in menopausal women with hot flashes. Future investigations (using sleep diary measures, assessment with actigraphy, and polysomnographic measures) should be undertaken to determine 1) if the effect is limited to sleep quality only 2) if the sleep quality effects are related to the potential of this compound to augment slow wave sleep and 3) the extent to which any of the sleep effects are related to decreased nocturnal hot flashes. When completed, such studies may serve as a foundation for an evidence based approach using gabapentin for management of menopausal sleep disturbances.
Support (optional): None

0686

EFFICACY OF COGNITIVE BEHAVIOR THERAPY FOR PRIMARY AND CO-MORBID INSOMNIA: FINAL REPORT

Edinger J,[1] Means M,[2] Lineberger M,[3] Stechuchak K,[4] Olsen M,[5] Goodin A,[4] Carney C[3]
(1) VA and Duke University Medical Centers, Durham, NC, USA, (2) VA & Duke University Medical Centers, NC, USA, (3) Duke University Medical Center, NC, USA, (4) VA Medical Center, NC, USA, (5) VA and Duke University Medical Centers, NC, USA

Introduction: Cognitive-Behavioral Therapy (CBT) has proven efficacious for primary insomnia (PI) and for insomnia co-morbid to a sleep-disruptive medical or psychiatric condition (CMI). This study compared CBT to a control therapy in both PI and CMI patients.
Methods: VA outpatients with insomnia were screened via structured interviews, a sleep diary, and polysomnography. Those enrolled met Research Diagnostic Criteria for insomnia disorder and had an average diary total wake time (TWT) > 60 minutes. Forty PI and 41 CMI patients enrolled and completed pre-therapy sleep diaries (2 weeks), actigraphy (2 weeks), and questionnaires to assess insomnia symptoms, dysfunctional beliefs about sleep, mood, and quality of life. They then were randomized and underwent either 4 biweekly sessions of CBT (20 PI; 21 CMI) or a generic sleep hygiene (SH) therapy (20 PI and 20 CMI). All pre-therapy assessment procedures were re-administered during 2-week periods immediately after treatment and again 6 months later. Linear mixed models were used to test the relative efficacy of CBT for PI and CMI patients.
Results: Pre-to-post-therapy changes showed benefits of CBT over SH in both PI and CMI groups. For PI patients, CBT produced greater improvements than did SH in objective (actigraphy) TWT, wakefulness after sleep onset (WASO) and sleep efficiency (SE), as well as in measures of global insomnia symptoms (ISQ) and confidence about sleep. CBT-treated CMI patients showed greater improvements in subjective (diary) TWT and sleep onset latency as well their dysfunctional sleep-related beliefs than did SH-treated patients. At follow-up, CBT continued to show benefits over SH in the PI group on the ISQ and both TWT and WASO taken from actigraphy. In contrast, none of the comparisons showed benefits of CBT over SH at the 6-month follow-up within the CMI group.
Conclusion: Results suggest only PI patients have a relatively better long-term response to CBT than they do to SH. Findings imply that modifications to CBT may be needed to improve its relative efficacy for CMI.
Support (optional): Department of Veterans Affairs Health Services Research and Development Grant # IIR 00-091.

0687

EFFECTS OF BRIEF BEHAVIORAL TREATMENT FOR INSOMNIA (BBTI) PERSIST FOR SIX MONTHS IN OLDER ADULTS

Buysse D,[1] Germain A,[1] Laurie B,[1] Moul D,[2] Franzen P,[1] Miewald J,[1] Reynolds C,[1] Monk T[1]
(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) Pittsburgh, PA, USA

Introduction: Preliminary findings show that a two-session Brief Behavioral Treatment for Insomnia (BBTI) has good efficacy on self-report outcomes compared to an Information-only Control (IC) among older adults with insomnia. We present additional self-report data on short-term outcomes in a larger sample (including participants switched from IC to BBTI) and preliminary six-month outcomes.
Methods: Participants were adults >60y.o. meeting ICSD-2 and DSM-IV criteria for insomnia disorder. Exclusion criteria were unstable medical illness, dementia, and untreated sleep or major psychiatric disorders; stable, treated disorders and all medications were permitted. Baseline (T1) and follow-up evaluations at 4 weeks (T2) and 6 months (T3) included questionnaires and sleep diaries. Participants were randomly assigned to BBTI, consisting of two 30-60 minute treatment sessions, or IC, consisting of 3 patient information pamphlets from the AASM. After initial treatment, participants in IC were offered BBTI, and assessed again after 4 weeks. “Response” was defined as an increase >10% sleep efficiency on the sleep diary OR >3 point decrease on PSQI score; “remission” was defined as sleep efficiency >85% AND PSQI score <5. BBTI responders and remitters were re-evaluated at T3.
Results: At T2, 7/21 BBTI subjects were classified as responders, and 8/21 as remitters (71% total); 8/25 IC subjects were responders and 1/25 remitters (36% total) (X2=5.74, p=.02). Seven subjects assigned to IC subsequently completed BBTI; 3/7 were responders and 2/7 remitters (71% total). At T3, 5/11 subjects previously treated with BBTI were responders and 5/11 remitters (91% total). One initial BBTI responder became a non-responder, 3 initial remitters became responders, and the other 7 subjects maintained or improved their response status at T3.
Conclusion: BBTI appears to be an efficacious intervention for late-life

insomnia over four weeks, with good preservation of self-reported improvement at 6-months. Polysomnography and actigraphy outcomes will be examined in future reports.
Support (optional): AG20677, MH24652, RR023506

0688

COGNITIVE AROUSAL SUBTYPES AND THEIR RELATIONSHIP TO ICSD-2 INSOMNIA DIAGNOSES

Carney C,[1] Edinger J,[2] Wyatt J,[3] Stepanski E,[4] Kirby A[5]
(1) Duke University Medical Center, Durham, NC, USA, (2) VA and Duke University Medical Centers, Durham, NC, USA, (3) Rush University Medical Center, Chicago, IL, USA, (4) Accelerated Community Oncology Research Network, Memphis, TN, USA, (5) Duke University Medical Center, NC, USA

Introduction: Hyper-arousal is a widely used construct in the insomnia literature. However, arousal has both physiologic and cognitive components as well as state and trait manifestations. The current study was conducted to identify distinctive cognitive arousal subtypes and to compare these subtypes in terms of their ICSD-2 insomnia diagnoses.
Methods: One hundred eleven adults with insomnia completed the Response Styles Questionnaire, Beck Depression Inventory II, Beck Anxiety Inventory, Dysfunctional Attitudes about the Self scale, Dysfunctional Beliefs and Attitudes about Sleep Worry (DBAS-W) subscale, Penn State Worry Questionnaire (PSWQ), Pre-Sleep Arousal Scale, Fatigue Severity Scale, and State-Trait Anger Expression Inventory. They were also assigned ICSD-2 insomnia diagnoses by teams of sleep specialists based on structured and unstructured sleep and psychiatric interviews, sleep diary data, and PSG findings. Participants´ scores on the various questionnaires were subjected to a statistical cluster analysis to identify cognitive arousal subtypes, and then a cross-tabs analysis was used to compare these groups´ ICSD-2 diagnoses.
Results: The cluster analysis identified four cognitive arousal subgroups that accounted for 73% of the variance. Based on questionnaire and psychiatric data, these subgroups seemed best characterized as the High-Arousal, Tired/Anxious, Negative-Cognitions, and Low-Arousal groups. Chi Square analysis showed a significant relationship ($p = .03$) between cluster group and ICSD-2 diagnostic assignments. Insomnia due to a Mental Disorder was relatively prevalent about the High-Arousal group, whereas the Tired/Anxious group accounted for the most inadequate hygiene and psychophysiological insomnia diagnoses. Despite being among the smallest groups, the Low Arousal group accounted for most (67%) paradoxical insomnia diagnoses.
Conclusion: Findings support the multidimensional nature of cognitive arousal in insomnia and suggest that the distinctive patterns of arousal identified differentiate ICSD-2 insomnia diagnostic subtypes.
Support (optional): This research was supported by a Pickwick Fellowship Award from the National Sleep Foundation and by the National Institute of Mental Health Grant # R01, MH067057.

0689

EFFICACY AND TOLERABILITY OF GABOXADOL IN ADULTS WITH PRIMARY INSOMNIA: A 3-MONTH, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Anderson D,[1] Roth T,[2] Zheng Y,[3] Vandormael K,[4] Smith A,[3] Li M,[3] Digravio D[3]
(1) Anderson Clinical Research, Redlands, CA, USA, (2) Henry Ford Hospital, Detroit, MI, USA, (3) Merck Research Laboratories, North Wales, PA, USA, (4) Merck Sharp and Dohme, Brussels, Belgium

Introduction: Gaboxadol is a selective extrasynaptic $GABA_A$ agonist (SEGA) that has demonstrated improvements in both sleep maintenance and onset measures in short-duration preliminary studies in patients with insomnia. This study evaluated the efficacy and tolerability of 2 doses of gaboxadol over 3 months of treatment in adults with primary insomnia.
Methods: Adults 18-64 years of age with DSM-IV primary insomnia entered a randomized, double-blind, parallel-group, patient report study in which they were randomized to receive gaboxadol 15mg (N=308), gaboxadol 10mg (N=310), or placebo (N=309) every night for 3 months. Efficacy measures were recorded daily by patients using electronic diaries. Tolerability was assessed by adverse event reports and other safety measures.
Results: Gaboxadol 15mg improved patient-reported total sleep time (sTST) and time to sleep onset (sTSO) versus placebo over 3 months. The estimated mean change from baseline improvement in sTST at month 3 was 87.6min for gaboxadol 15mg and 67.2min for placebo; the estimated difference between gaboxadol 15mg and placebo was approximately 20min ($p<0.01$). The estimated mean change from baseline reduction in sTSO at month 3 was 44.2min for gaboxadol 15 mg and 34.4min for placebo; the estimated difference between gaboxadol 15mg and placebo was approximately 10min ($p<0.01$) Gaboxadol 10mg did not differ significantly from placebo on these measures at month 3. Gaboxadol was generally well-tolerated over 3 months.
Conclusion: Gaboxadol 15mg, but not 10mg, was effective at improving sleep maintenance and onset over 3 months in adults with primary insomnia. Both gaboxadol doses were generally well-tolerated.
Support (optional): Merck Research Laboratories

0690

GABOXADOL IMPROVES SLEEP MAINTENANCE AND ONSET IN A MODEL OF TRANSIENT INSOMNIA: RESULTS FROM A RANDOMIZED CLINICAL TRIAL

Walsh J,[1] Mayleben D,[2] Guico-Pabia C,[3] Vandormael K,[4] Martinez R,[3] Deacon S[5]
(1) St. Luke´s Hospital, Sleep Medicine and Research Center, Chesterfield, MO, USA, (2) Community Research & Sleep Management, Crestview Hills, KY, USA, (3) Merck Research Laboratories, North Wales, PA, USA, (4) Merck Sharp and Dohme, Brussels, Belgium, (5) Lundbeck Ltd., Milton Keynes, United Kingdom

Introduction: Gaboxadol is a selective-extrasynaptic-$GABA_A$-agonist (SEGA) with demonstrated improvements in sleep maintenance and onset measures in preliminary studies in insomnia patients. This study evaluated gaboxadol in a model of transient insomnia.
Methods: Healthy subjects (18-64y) completed a randomized, double-blind, parallel-group study in which the sleep period was advanced 4h from habitual sleep time. Polysomnographic (PSG) and self-reported sleep measures were used to compare gaboxadol 10mg (N=271) and 15mg (N=274) versus placebo (N=277).
Results: In the placebo group, the phase-advance procedure significantly disrupted sleep maintenance as measured by PSG wakefulness-after-sleep-onset (WASO) and self-reported WASO (sWASO), and also significantly disrupted sleep onset as measured by PSG latency-to persistent-sleep (LPS) and self-reported time-to-sleep-onset (sTSO) (all $p<0.01$). Both doses of gaboxadol decreased mean WASO (46.1 and 39.0min for 10mg and 15mg, respectively, versus 54.2min for placebo) and mean sWASO (20.0 and 13.6min versus 31.2min) compared to placebo ($p<0.05$). Gaboxadol 15mg also reduced mean LPS compared to placebo (15.7min versus 19.4min, $p<0.01$) and both 10mg and 15mg reduced mean sTSO (19.0 and 17.0min versus 23.0min) compared to placebo ($p \leq 0.01$). PSG and self-reported total sleep time as well as ratings of sleep quality were improved with both

gaboxadol doses relative to placebo (all p<0.01). The amount of slow-wave-sleep was greater with both doses of gaboxadol than with placebo (p<0.001). No group differences in the amount of rapid-eye-movement sleep were found. Most PSG and self-report measures suggested a possible dose-response. The percentage of subjects with ≥1 adverse event was low (<10% in any treatment group); events were mild/moderate, none were serious, and gaboxadol did not impact morning gait or coordination.
Conclusion: Gaboxadol 10mg and 15mg were efficacious in reducing the sleep maintenance and onset disruption produced by this model of transient insomnia, with beneficial effects generally being most pronounced for the 15mg dose.
Support (optional): Merck Research Laboratories

0691

COMPARISONS OF COGNITIVE AROUSAL SUBTYPES ON SLEEP DIARIES, PSG AND AROUSAL RATINGS

Carney C,[1] Edinger J,[2] Wyatt J,[3] Stepanski E,[4] Kirby A[5]
(1) Duke University Medical Center, Durham, NC, USA, (2) VA and Duke University Medical Centers, Durham, NC, USA, (3) Rush University Medical Center, Chicago, IL, USA, (4) Accelerated Community Oncology Research Network, Memphis, TN, USA, (5) Duke University Medical Center, NC, USA

Introduction: Physiologic and cognitive components as well as state and trait manifestations all define the hyperarousal presumed to sustain insomnia. This study identified distinctive cognitive arousal subtypes and compared them on ratings of pre-sleepl arousal and on subjective (diary) and objective (PSG) sleep measures.
Methods: Adults (N=111) with insomnia completed the Response Styles Questionnaire, Beck Depression Inventory II, Beck Anxiety Inventory, Dysfunctional Attitudes Scale, Dysfunctional Beliefs and Attitudes about Sleep Worry (DBAS-W) subscale, Penn State Worry Questionnaire (PSWQ), Pre-Sleep Arousal Scale, Fatigue Severity Scale, and State-Trait Anger Inventory. They also completed PSG (2 nights) monitoring and two weeks of nightly sleep diaries and concurrent prospective pre-sleep Visual Analog Scale (VAS) ratings of physical tension, active mind, anxious mood, worry, and frustration. Questionnaire scores were subjected to a statistical cluster analysis to identify cognitive arousal subtypes. ANOVAs were then used to compare these subtypes in regard to their VAS and sleep (PSG/diary)measures.
Results: The cluster analysis identified four arousal subgroups we labeled the High-Arousal, Tired/Anxious, Negative-Cognitions, and Low-Arousal groups. VAS comparisons showed distinctive pre-sleep arousal patterns across groups. Low- and High-Arousal subjects differed across all VAS dimensions. The Tired/Anxious group reported less arousal than did the High Arousal group across all but one VAS dimensions, whereas only lower ratings of worry distinguished the Negative Cognitions group from the High-Arousal group. PSG comparisons showed no subgroup differences, but diaries suggested the High Arousal group had significantly lower TST and felt significantly less rested upon awakening than did the Tired/Anxious and Negative-Cognitions groups. Post-hoc tests showed diary TST was correlated with global negative beliefs (r = .223), and restfulness ratings were correlated with symptom-focused rumination (r = -.220).
Conclusion: These findings confirm the existence of distinctive cognitive arousal insomnia subtypes that differ across dimensions of pre-sleep arousal and sleep perceptions.
Support (optional): This research was supported by a Pickwick Fellowship Award from the National Sleep Foundation and by the National Institute of Mental Health Grant # R01, MH067057.

0692

FREQUENCY AND TIME DOMAIN ANALYSIS OF EEG POWER DURING NREM SLEEP IN WOMEN WITH PRIMARY INSOMNIA

Buysse D,[1] Germain A,[1] Moul D,[2] Franzen P,[1] Hall M,[2] Nofzinger E,[1] Miewald J,[1] Begley A,[1] Thompson W[1]
(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) Pittsburgh, PA, USA

Introduction: Individuals with primary insomnia (PI) have increased high-frequency EEG power during NREM sleep compared to good sleeper controls (GSC). This study examined NREM EEG power across the entire 1-32 Hz frequency range in successive NREM periods. Because of sex differences in EEG power, only women were included.
Methods: Participants included 17 women with DSM-IV PI (mean 28.1 years; PSQI 10.5), diagnosed by structured interview, and 17 age-matched GSC women (mean 27.8 years; PSQI 1.9). No quantitative sleep criteria were used, but all participants had AHI and PLMAI <15. EEG signals were sampled at 128 Hz from the C4-(A1+A2) channel during NREM sleep, and analyzed in 4-second epochs with Fast-Fourier Transformations. Four-second epochs contaminated with high-frequency artifact were excluded. Power-frequency curves were generated for all-night NREM sleep and each NREM period, and modeled with fixed-knot cubic splines. Fitted 1 Hz log power values were compared between groups using F statistics. We also compared spectral power for standard bandwidths across NREM periods using repeated-measures ANOVA.
Results: Groups did not differ on visually-scored PSG measures. Whole-night NREM and NREM1 data showed higher power in PI than GSC for 8-10 Hz and 16-32 Hz ranges (F values >4.1). In NREM 2, significant differences were observed at 10 Hz and between 20-32 Hz; in NREM 3, between 28-32 Hz; and in NREM 4 no differences were observed. Analysis of standard EEG frequency bands showed a 3-way interaction of group, band, and NREM period, confirming group differences in beta during NREM 1 and 2.
Conclusion: Women with PI had higher alpha and beta power during NREM sleep than GSC, particularly in the first two NREM periods. Time of night may be an important variable in understanding sleep differences between PI and GSC. EEG power may show PI-GSC differences in the absence of visually-scored PSG differences.
Support (optional): MH24652, RR023506

0693

WHO IS AT RISK FOR EARLY TERMINATION FROM COGNITIVE-BEHAVIOR THERAPY FOR INSOMNIA?

Ong J,[1] Kuo T,[2] Manber R[2]
(1) Stanford, CA, USA, (2) Stanford University, Stanford, CA, USA

Introduction: Despite the strong evidence supporting the efficacy of cognitive-behavior therapy for insomnia (CBT-I), little is known about risk factors for early termination (ET) from treatment. The aim of the present study was to identify characteristics of patients who are at risk for ET from CBT-I in a clinic setting using the receiver operating characteristics curve (ROC) approach.
Methods: ROC analysis was conducted on a series of 528 patients who attended a 7-session CBT-I group at the Stanford Sleep Disorders Clinic between 1999-2004. Predictor variables were taken from questionnaire packets and sleep diaries collected at baseline and included age, gender, Beck Depression Inventory (BDI), Morningness-Eveningness Questionnaire, Beliefs and Attitudes about Sleep, sleep medication usage, sleep onset latency (SOL), wake time after sleep onset (WASO),

and total sleep time (TST). The outcome measure was ET, defined as withdrawal from treatment prior to the fourth session.
Results: The ROC analysis revealed that patients who reported an average baseline TST < 3.65 hours were at greatest risk for ET. Forty percent of patients in this group terminated early compared to 3.4% of patients with TST ≥ 3.65 hours. Among patients with TST ≥ 3.65 hours, 20% of those with SOL ≥ 1.97 hours terminated early compared to 3% of those with SOL < 1.97 hours. Among the remaining patients (TST ≥ 3.65 and SOL < 1.97), 7.8% of those with BDI scores ≥ 16 terminated early compared to 1.2% of those with BDI scores < 16.
Conclusion: These findings indicate that self-reported severity of sleep disturbance (i.e., TST and SOL) and severity of depressive symptoms are two potential risk factors for early termination from CBT-I in a clinic setting. Future studies should seek to test these preliminary guidelines in other samples and conditions (e.g., different number of sessions, individual therapy).
Support (optional): None

0694

DAYTIME PERFORMANCE DEFICITS AND THEIR RELATION TO SLEEP AMONG INSOMNIA SUFFERERS

Edinger J,[1] Means M,[2] Carney C[3]
(1) VA and Duke University Medical Centers, Durham, NC, USA, (2) VA & Duke University Medical Centers, NC, USA, (3) Duke University Medical Center, Durham, NC, USA

Introduction: Insomnia sufferers complain about daytime dysfunction, but many investigations of these complaints have failed to document diurnal deficits. Small samples and use of insensitive performance tests may have hampered previous investigations. This investigation enrolled a large sample and employed a range of performance tests to determine if primary insomnia (PI) sufferers show daytime deficits.
Methods: Through structured interviews, medical examinations, and PSG screenings, we obtained a sample of 95 (51 women) PI sufferers (MAge = 49.1±17.1 yrs.) and 100 (51 women) well-screened normal sleepers (NS: MAge = 47.0±16.9 yrs.). Participants underwent three nights of polysomnograpy-PSG followed by daytime testing with a four-trial Multiple Sleep Latency Test (MSLT). Before each MSLT nap, they rated their sleepiness and completed a performance battery that included simple reaction time (SRT), continuous performance (CPT) and four switching attention (SAT) tests. Performance measures included the mean response latency and the standard deviation of each subject´s within-test response latencies. Linear mixed models (LMM) were used to compare the PI and NS groups on these measures.
Results: The PI group rated themselves as significantly (p = .02) sleepier throughout the day than did the NS group. The NS group was slightly, albeit not significantly (p = .06), sleepier than was the PI group on the MSLT. The groups did not differ on the SRT or CPT, but the PI group had significantly longer response latencies and greater response variability (i.e., more attention lapses) across all SAT subtests. Mean values of objective (PSG) and subjective (diary) sleep efficiency (SE) for the nights preceding daytime testing correlated with the SAT measures. However, only PSG values of SE eliminated most significant group effects when entered as covariates into our LMM analyses.
Conclusion: Findings support the diurnal complaints of PI sufferers and suggest these complaints relate to objective nocturnal sleep disturbance.
Support (optional): This research was supported by Grants for the Department of Veterans Affairs Merit Review Program (Grant # 0009) and The National Heart, Lung and Blood Institute (Grant # R01-HL-073259-01).

0695

USE OF ACTIGRAPHY FOR PREDICTING INSOMNIA THERAPY RESPONSE

Means M,[1] Edinger J,[2] Carney C[3]
(1) VA & Duke University Medical Centers, Durham, NC, USA, (2) VA and Duke University Medical Centers, Durham, NC, USA, (3) Duke University Medical Center, NC, USA

Introduction: Actigraphy has a well-established role in circadian rhythm research and increasingly is being used in insomnia studies to track treatment outcomes. The usefulness of actigraphy for predicting the eventual treatment response of insomnia sufferers has yet to be tested. The current exploratory study was conducted to determine whether pre-treatment actigraphic indices might discriminate subsequent treatment responders from non-responders.
Methods: VA outpatients with insomnia were screened via structured interviews, a sleep diary, and polysomnography. Those enrolled met Research Diagnostic Criteria for insomnia disorder and had an average diary total wake time (TWT) > 60 minutes. Forty Primary (PI) and 41 Comorbid (CMI) insomnia patients enrolled and completed actigraphy (1 week) and the Pittsburgh Sleep Quality Index (PSQI) before beginning treatment. They then were randomized and underwent 4 biweekly sessions of CBT (20 PI; 21 CMI) or a generic sleep hygiene (SH) therapy (20 PI and 20 CMI). The PSQI and other outcome measures were repeated immediately following therapy and again six months later. Patients who showed a > 50% reduction in their PSQI scores from pre-therapy to their study endpoint were labeled responders; the remainder were labeled non-responders. Sensitivity/specificity analyses then were conducted using common cut-offs to determine if measures derived from pre-therapy actigraphy discriminated responders from non-responders.
Results: Twenty-three responders and 44 non-responders were identified using PSQI criteria. Patients who had a baseline mean actigraphic TST > 390 minutes per night were significantly more likely to be labeled responders than those who did not (p = .0012; Sensitivity = 77%, Specificity = 65%). Likewise, those who showed a pre-therapy actigraphic TST > 390 minutes 6-7 nights per week were prone to be responders (p = .0041; Sensitivity = 74%, Specificity = 66%).
Conclusion: Results suggest that actigraphy may prove useful for screening candidates for insomnia therapy.
Support (optional): Department of Veterans Affairs Health Services Research and Development Grant # IIR 00-091 and Respironics Corporation.

0696

CHRONICITY OF ADOLESCENT INSOMNIA

Roane B, Taylor D
University of North Texas, Denton, TX, USA

Introduction: Approximately 10.7% of adolescents experience insomnia during their lifetime, with roughly 9.4% experiencing chronic insomnia (Johnson, 2006). Little is know about the natural course of insomnia in adolescents.
Methods: The current study utilized data from a national longitudinal study that evaluated health behaviors (Urdy, 2003). Six thousand and four adolescents participated and a sub-sample of 3510 adolescents (M=14.48, SD=1.52, 53.3% female) completed both baseline and 2-year follow-up in-home interviews. Participants were excluded from analyses if no ethnicity, gender, or insomnia data were given. Adolescents were classified into one of three groups: (a) good sleepers (n=2705), (b) transient insomnia (n=482), and (c) chronic insomnia (n=323). Transient insomnia was operationally defined as a report of insomnia "Sometimes" during the past year at the adolescent interview. Chronic

insomnia was operationally defined as a report of insomnia "Almost everyday" or "Everyday."
Results: At baseline, 13.7% reported transient and 9.2% reported chronic insomnia. At 2-year follow-up, 15.6% reported transient and 7.4% reported chronic insomnia. Of the adolescents with chronic insomnia at baseline, 32.8% continued to have chronic insomnia, 29.1% downgraded to transient insomnia, and 38.1% no longer reported insomnia at 2-year follow-up. Of the adolescents with transient insomnia at baseline, 9.8% developed chronic insomnia, 32.4% continued to report transient insomnia, and 57.9% downgraded to no insomnia. For the adolescents with no insomnia at baseline, 3.9% developed chronic insomnia, 11.1% developed transient, and 85% stayed good sleepers. Significantly more females than males experienced transient or chronic insomnia at baseline (25.4% vs. 20.2%) and at follow-up (25.7% vs. 19.9%).
Conclusion: Preliminary results indicate variability exists in the course of adolescent insomnia. However, approximately 23% of adolescents reported chronic or transient insomnia at either baseline or follow-up, indicating that a treatment study in this population is warranted. Further analyses plan to control for possible confounds (e.g., gender).

0697

EPIDEMIOLOGY OF INSOMNIA IN KOREAN ADULTS

Cho Y,[1] Yun C,[2] Shin W,[3] Hong S,[4] Kim J,[5] Earley C[6]
(1) Keimyung University Dongsan medical center, Taegu, KyungBuk, South Korea, (2) Inha University Hospital, Incheon, KyungGy, South Korea, (3) Kyunghee University East-West Neo Medical Center, Seoul, South Korea, (4) Sungkyunkwan University, Samsung Medical Center, Seoul, South Korea, (5) Hanyang University Hospital, Seoul, South Korea, (6) Johns Hopkins University, Hopkins Bayview Medical Center, Baltimore, MD, USA

Introduction: Insomnia is a common sleep disorder in adults and it is associated with various psychological, medical, and neurological problems. The prevalence of insomnia was reported around 20-30% in western countries. However, epidemiologic studies of insomnia in Asian countries were rarely performed. We performed an epidemiologic study of insomnia in a large Korean adult population.
Methods: A total of 5000 subjects completed our interview using a computer aided telephone interview method. A representative sample with subjects aged 20 to 69 was constituted according to a stratified, multistage random sampling method. For our interview we defined insomnia as either difficulty initiating or maintaining sleep. This survey was conducted by trained interviewers from Taylor Nelson Sofres (TNS). Sampling error is ±1.39 point for 95% confidence interval.
Results: Of the total of 5000 persons, 1382 (27.6%) complained of insomnia. The prevalence of insomnia was higher in women than in men (30.3% versus 24.9%) and increased with aging. Twelve point six percent (men 9.4% and women 15.6%) complained of difficulty initiating sleep and 22.7% (men 21.1% and women 24.2%) complained of difficulty maintaining sleep. The groups with house wives and lower monthly incomes suffered higher sleep problems compared with the other groups. In the severity of sleep disturbance, overall 14.9% (men 12.8% and women 17.0%) complained of insomnia at least two nights per week, which included 8.6% who complained of difficulty initiating sleep and 11.2% who complained of difficulty maintaining sleep.
Conclusion: The prevalence of insomnia is similar to those of western countries and a common complaint in Korean adults. However, it is not likely that most insomniacs have help-seeking behaviors to improve their sleep problems. We need to announce the importance of healthy sleep to the public and further studies for clarifying causative factors for insomnia are required in Korea.

0698

SLEEP EEG SPECTRAL MEASURES IN OBJECTIVE AND SUBJECTIVE INSOMNIA SUBTYPES

Krystal A,[1] Edinger J,[2] Kirby A,[3] Carney C[4]
(1) Duke University, Durham, NC, USA, (2) VA and Duke University Medical Centers, Durham, NC, USA, (3) Duke University Medical Center, NC, USA, (4) Duke University Medical Center, NE, USA

Introduction: Many, but not all primary insomnia sufferers show significant sleep disturbance during PSG monitoring. Perhaps conventional PSG measures misrepresent the sleep experiences of some PI sufferers. This study tested sleep EEG spectral measures for differentiating objective and subjective PI sufferers and predicting their respective sleep perceptions.
Methods: We used archival data taken from thoroughly screened primary insomnia sufferers and normal controls. All participants completed home and in-lab PSGs as well as concomitant sleep diary monitoring. These PSGs were reviewed, and only technically acceptable records with sufficient artifact-free epochs were selected. Each recording was subjected to a fast Fourier transformation (FFT) analysis in 2-sec epochs yielding measures of EEG amplitude in the Delta, Theta, Alpha, Sigma, Beta, and Gamma bands during non-REM sleep. Additionally, participants were dichotomized into good and poor sleepers using conventional PSG measures. Those with a mean TST > 360 minutes, a mean SE > 85% and mean SOL or WASO < 31 minutes were labeled good sleepers (GS); the remaining individuals were labeled poor sleepers (PS).
Results: Sixty-one (25 GS, 36 PS) PI and 62 (34 GS, 28 PS) controls comprised the final sample. GS and PS subgroups had comparable gender compositions, but GS were significantly younger than PS. A multivariate statistical profile analysis that controlled for age showed the spectral profiles of the four subgroups differed ($p < .01$) in their shapes and elevations. The two insomnia subgroups´ profiles were non-flat and differed significantly in their relative delta, theta, and alpha spectral measures. Regression analyses showed that spectral measures predicted subjective (diary) estimates of nocturnal wakefulness in the PI-GS group, but conventional PSG measures (TST, SE%) predicted subjective wakefulness with the PI-PS and normal groups.
Conclusion: Sleep EEG spectral measures appear useful for identifying so-called subjective PI sufferers and predicting their experiences of nocturnal wakefulness.
Support (optional): This research was supported by Grants from the Department of Veterans Affairs Merit Review Program (Grant # 0009) and The National Heart, Lung and Blood Institute (Grant # R01-HL-073259-01).

0699

ADULTS WITH MIDDLE-OF-THE-NIGHT (MOTN) INSOMNIA ARE ABLE TO ACCURATELY SELF-IDENTIFY THEIR CONDITION

Scharf M
Tri-State Sleep Disorders Center, Cincinnati, OH, USA

Introduction: Middle-of-the-night (MOTN) awakenings with difficulty returning to sleep is a well recognized manifestation of insomnia. However insufficient attention has been paid to this form of insomnia, in part due to the absence of rapidly effective, prn therapies that can be taken during the night without next-day residual sedation. The present study evaluated the reporting accuracy of subjects in self-identification and characterization of MOTN insomnia relative to PSG screening.
Methods: Adults (N=113) with a diagnosis of DSM IV primary

insomnia and a history of prolonged MOTN awakenings. Subjects completed a 10-day sleep diary to confirm MOTN insomnia before undergoing 2 nights of polysomnography (PSG) screening. In order to pass the sleep diary screen, individuals had to indicate that they experienced at least 3 MOTN awakenings per week with Latency to Sleep Onset (LSO) of >30 minutes per awakening. PSG entry criteria required a mean of >20 minutes Latency to Persistent Sleep (LPS) for two successive nights. Using sleep diary data in conjunction with subsequent single-blind placebo PSG assessments of sleep, the relationship between subjective self-reporting and objective PSG assessments was explored.
Results: A total of 113 subjects identified themselves as having MOTN insomnia that met the study LSO entry criteria. This self-diagnosis was subsequently confirmed for 83 (73%) subjects who during 2-nights of PSG evaluation had mean LPS values of 54.6 minutes (SE 3.7).
Conclusion: MOTN insomnia can be diagnosed with a relatively high degree of accuracy using subject sleep diaries. This study indicates that individuals can correctly self-identify their MOTN insomnia, and sleep diaries can be reliable tools to assist clinicians with the diagnosis of MOTN insomnia.
Support (optional): This study was fully funded and supported by TransOral Pharmaceuticals Inc. San Francisco, CA, USA

0700

HYPERAROUSAL DURING REM SLEEP IN PRIMARY INSOMNIA: PRELIMINARY PET FINDINGS

Germain A,[1] Nofzinger E,[1] Hall M,[2] Miewald J,[1] Kupfer D,[1] Buysse D[1]
(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) Pittsburgh, PA, USA

Introduction: Primary insomnia (PI) is characterized by EEG and functional alterations in NREM sleep, but the functional neurobiological correlates of PI during REM remain unknown. We explored changes in patterns of absolute and relative regional cerebral metabolic rate of glucose (rCMRglc) during REM vs. wakefulness in PI and healthy subjects.
Methods: Methods. Nine PI subjects (M age = 42, SD = 7), and 8 age-matched healthy subjects (M age 38.5, SD = 9.5) were analyzed. All subjects were medication-free, right-handed, and completed 3 nights of polysomnographic recordings, and [18F]-fluoro-2-deoxy-D-glucose positron emission tomography scans during wakefulness and the second REM sleep episode. Regression analyses were conducted to evaluate Group (PI vs. healthy) by State (REM vs. wakefulness) differences.
Results: PI subjects showed higher absolute rCMRglc during both REM sleep and wakefulness compared to healthy subjects, and both groups showed reduced absolute rCMRglc during REM sleep vs. wakefulness. Relative to wakefulness, PI subjects showed a greater increase in relative rCMRglc during REM sleep in the right middle occipital, lingual, fusiform, and parahippocampal cortices ($p = 0.005$) compared to healthy subjects. Trends were also observed for greater increases in the right orbitofrontal and anterior cingulate cortex ($p = .05$). Healthy subjects showed greater increase of rCMRglc in REM relative to wakefulness compared to PI subjects in the left middle and inferior frontal gyri ($p = .02$), pre- and post-central gyri ($p < .05$) , and cerebellum.
Conclusion: These findings suggest that hyperarousal in sleep may not be confined to NREM in PI. PI subjects showed higher absolute rCMRglc in both wakefulness and REM sleep compared to healthy subjects, and patterns of relative rCMRglc during REM sleep relative to wakefulness differed in the two groups. Increased activity in right ventral regions in PI subjects may indicate heightened activity of the stress response system.
Support (optional): This study was supported by the National Institute of Mental Health (MH24652, MH66227, MH061566, AG020677, MH01414, MH60473), the National Institutes of Health (RR00056 and RR023506), and by the US Department of Defense Medical Research Program (PR054093).

0701

NIGHTTIME INSOMNIA SYMPTOMS PREDICT DAYTIME CONSEQUENCES IN MOOD AND ALERTNESS

Franzen P,[1] Thompson W,[2] Moul D,[2] Hall M,[2] Germain A,[2] Buysse D[2]
(1) University of Pittsburgh School of Medicine, Pittsburgh, PA, USA, (2) University of Pittsburgh, Pittsburgh, PA, USA

Introduction: Although it is widely accepted that sleep and daytime symptoms are related to each other in Primary Insomnia (PI), there is little evidence to indicate a particular directionality in this relationship. To address this question, we analyzed the relationship between four daytime symptom scales and concurrent sleep diary measures in adults with PI (n=56) and Good Sleeper Controls (GSC, n=21).
Methods: Daytime symptoms were assessed with 19 visual analog scale items that were completed 4 times/day for one week using ecological momentary assessment methods. Functional principal components analysis of the 19 items derived four scales: Positive Affect, Negative Affect, Alert Cognition, and Sleepiness-Fatigue. Sleep quality and sleep efficiency were collected from daily sleep diaries. Mixed model regressions with subject as a random factor were used to model the data in two ways: First, with the nighttime sleep variable as the dependent variable and daytime scales as covariates (independent variables); and second, with daytime scales as dependent variables and sleep as the covariate.
Results: We observed a bidirectional influence between daytime symptoms and sleep quality in PI, with larger relationships in the direction of sleep quality influencing daytime symptoms. Sleep efficiency was significantly related to subsequent daytime symptoms, but daytime symptoms were not related to subsequent sleep efficiency. Among GSC, significant bidirectional relationships were again evident between sleep quality and daytime symptoms, although weaker than among PI. There was no relationship between sleep efficiency and daytime symptoms in either direction.
Conclusion: These data suggest that PI have a fundamentally different relationship between sleep and daytime mood than GSC; that the direction of relationship is stronger for sleep to daytime symptoms than vice versa; and that this relationship varies for different self-report sleep measures. These findings demonstrate the importance of studying sleep and waking symptoms and their relationships in PI.
Support (optional): MH24652, RR023506

0702

LONG-TERM SAFETY OF GABOXADOL IN THE TREATMENT OF ELDERLY PATIENTS WITH PRIMARY INSOMNIA: A 12-MONTH, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL

Bodkin J,[1] Anderson D,[2] Zheng Y,[3] Golm G,[3] Gottwald R,[3] Kametz K[3]
(1) McLean Hospital, Belmont, MA, USA, (2) Anderson Clinical Research, Redlands, CA, USA, (3) Merck Research Laboratories, North Wales, PA, USA

Introduction: Gaboxadol is a selective extrasynaptic $GABA_A$ agonist (SEGA) that is being investigated for the treatment of insomnia. The present study evaluated the long-term safety of gaboxadol in elderly patients with primary insomnia.
Methods: Patients ≥65 years of age with DSM IV primary insomnia

completed a randomized, double-blind, parallel-group study in which they were allocated to receive gaboxadol 10 mg (N=246) or placebo (N=80) every night for 12 months. This treatment period was followed by a 1-week double blind run-out period in which half the gaboxadol patients were switched to placebo while the remaining patients continued their previous treatment. Safety was assessed by adverse events (AEs) as well as laboratory tests and physical exams. In addition, withdrawal (using the Tyrer withdrawal symptoms scale) and rebound (worsening of insomnia relative to baseline) effects were assessed during the double-blind run-out period.
Results: During the treatment period, no significant differences (p-values ≤0.05) were seen between treatments with regard to the percentages of patients with ≥1 AE (78.0% for gaboxadol 10 mg versus 77.5% for placebo), with a serious AE (12.6% versus 8.8%), or who discontinued due to an AE (14.6% versus 8.8%). The most common AE following gaboxadol 10 mg was dizziness (9.3% versus 8.8%). No clinically meaningful differences were seen between treatment groups with regard to laboratory tests or physical exams. During the double-blind run-out period, there was no evidence that patients previously assigned to gaboxadol who were switched to placebo experienced withdrawal symptoms or manifested rebound insomnia.
Conclusion: Long-term use of gaboxadol 10 mg in elderly patients with primary insomnia was generally safe and well tolerated. Abrupt discontinuation of gaboxadol 10 mg after long-term use did not cause significant withdrawal symptoms or rebound insomnia.
Support (optional): Merck Research Laboratories

0703

SINGLE DOSE PHARMACOKINETICS OF ZOLPIDEM IN CHILDREN 2-18 YEARS OLD WITH SLEEP DIFFICULTIES

Blumer J,[1] Reed M,[1] Steinberg F,[2] O´Riordan M,[1] Rosen C,[1] Springer M,[3] Christensen M,[4] Glaze D[5]
(1) Case Western Reserve University, Cleveland, OH, USA, (2) Evanston, Illinois, Evanston, IL, USA, (3) Louisiana State University Health Sciences Center, Shreveport, LA, USA, (4) University of Tennessee, Memphis, TN, USA, (5) Baylor College of Medicine, Houston, TX, USA

Introduction: Due to the limited study of hypnotic use in children, the present study evaluated the pharmacokinetics and safety of three different doses of zolpidem following single dose administration in children aged 2-18 years with insomnia.
Methods: Multicenter, open-label, dose-escalation study in children within three age groups (2-6, >6-12, >12-18 years) with insomnia. Zolpidem administered in liquid oral formulation to twenty-one subjects, seven from each age group, within each dose level [0.125 mg/kg, 0.25 mg/kg, or 0.50 mg/kg (20mg max dose allowed)], with 7 patients/age group completing lowest dose before initiation of the next dose level. Single-night sleep laboratory evaluation with blood sampled at 9 intervals (0.5-12 hours post-dose). Pharmacokinetic parameters included: maximum concentration (Cmax), time to peak plasma concentration (Tmax), half-life (T1/2), area under the plasma-concentration time curve (AUC), mean residence time (MRT), oral total body clearance (CI/F), and oral steady-state volume of distribution (Vdss/F). Interactions of dose and age on pharmacokinetic parameters were assessed by 2-way ANOVA (P≤.05 significance level).
Results: 62/67 subjects completed the study with 65 providing sufficient data (0.125 mg/kg, n=21; 0.25 mg/kg, n=21; 0.5 mg/kg, n=22). By dose, significant, linear increases were observed for Cmax (P<.001) and AUC (P<.001), with no effect on Tmax, T1/2, MRT, CI/F, and Vdss/F. By age groups, AUC (P=.02), T1/2 (P=.04) and MRT (P=.01) increased with age; CI/F (P=.01) declined, and Vdss/F (P=.02) was variable, with no effect for Tmax and Cmax. Fourteen subjects experienced 22 treatment-emergent adverse events with no observed pattern by dose.
Conclusion: Zolpidem pharmacokinetic parameters in children were similar to those previously observed for adults. Zolpidem was well-tolerated and safe in this pharmacokinetic study´s population, providing a foundation for a future efficacy study.
Support (optional): Supported by sanofi-aventis

0704

THE NOCTURNAL SLEEP LATENCY PROFILE (NSLP): PRELIMINARY DATA FROM PATIENTS WITH PRIMARY INSOMNIA

Moul D, Black B, Bankson L, Miewald J, Buysse D
University of Pittsburgh, Pittsburgh, PA, USA

Introduction: For insomnia patients, getting and returning to sleep are key problems, but no polysomnography exists to assess sleep onset across the night. The NLSP is designed for this assessment, but needs validation.
Methods: Primary Insomnia subjects without psychiatric, general medical, or other sleep disorders underwent a screening night of polysomnography and then two nights of NSLP procedures. In the NSLP, subjects had 1-minute wake-ups at the start of their second and third sleep cycles. For 3 weeks they received combined behavioral therapy and eszopiclone 3 mg qHS, followed by one final NSLP study while still using medication. The Pittsburgh Sleep Quality Index (PSQI) measured outcomes. Sleep onset latency was defined three ways: the start of 10-minutes´ stable sleep, first Stage 1 epoch, and first Stage 2 epoch. Log-transformed sleep latencies were regressed against night-in-study and sleep trial using mixed effects models to assess patterns of effects.
Results: Six subjects (age 46±14; 5 women) with complete data showed treatment benefit on the PSQI (t=15, df=5, p< 0.0001). In the mixed models, sleep latencies decreased across sleep trials using all sleep onset definitions (p<0.04). Sleep latencies decreased from pre- to post-treatment (maximum p<0.021). F-tests (df=2,43) for the three sleep onset definitions showed differences for sleep latency trial (p=0.06, 0.011, 0.015) and study night (p=0.07, 0.06, 0.04) effects. In exploratory post-hoc comparisons, only the second sleep latency trial of the nights showed significant decrease from baseline to follow-up (p=0.025, 0.02, 0.02).
Conclusion: These preliminary data suggest that the NSLP may provide a method to demonstrate therapeutic changes not only in initial, but subsequent sleep onsets during the night. Having a standard method to measure sleep onset across the night will enable tests of whether getting to sleep is the main problem in insomnia patients.
Support (optional): Supported by a Faculty Career Advancement Award from the American Sleep Medicine Foundation, M01 RR000056, 1 UL1 RR024153, and MH 24652-29. Medications provided by Sepracor, Inc.

0705

EFFECTS OF NG2-73 ON SLEEP ONSET, QUALITY AND NEXT DAY FUNCTION IN A TRANSIENT INSOMNIA STUDY

Zammit G,[1] Rice K,[1] Accomando W,[2] Sprenger K,[3] Aneiro L[3]
(1) Clinilabs, Inc., New York, NY, USA, (2) Accomando Consulting Enterprises, Mystic, CT, USA, (3) Neurogen Corporation, Branford, CT, USA

Introduction: NG2-73 is a partial agonist with preference for GABA(A) receptors containing the α3 subunit. This mechanism of

action may provide an important alternative to existing therapeutics for insomnia.
Methods: This double-blind, placebo-controlled, multi-center randomized trial evaluated the efficacy of 4 dose groups of NG2-73 versus placebo in reducing Latency to Persistent Sleep (LPS) in healthy adults in a sleep laboratory, single-night, polysomnographic model of transient insomnia using both first night adaptation and "phase-advance." Subjects completed questionnaires assessing sleep effects, sleep quality, and next day functioning. Safety was monitored as per usual practice. Three hundred and sixty nine adults, aged 24 – 63, with no self-reported sleep disorders were enrolled.
Results: LPS was significantly reduced, compared to placebo, at all doses of NG2-73, in a dose-dependent manner with mean LPS of 30.8 minutes for the placebo group, and 17.8, 10.6, 7.8, and 6.6 minutes for the 1, 3, 10, and 20 mg NG2-73 groups, respectively. Subjective sleep latency (sSL) was significantly reduced compared to placebo at all doses. All four NG2-73 treatment groups reported that their sleep had been significantly more refreshing than did the placebo group. At 1, 3, and 10mg, subjects felt alert and more than 87% of subjects considered their ability to concentrate as "very good" or "excellent" the morning following dosing, which was similar to the placebo group. NG2-73 was generally well tolerated with adverse events attributable to the pharmacological action of the drug. There were no deaths, or drug-related serious AEs or discontinuations, and no clinically important changes in safety labs, vital signs or ECGs.
Conclusion: NG2-73 is a potent sedative hypnotic which significantly reduced LPS at all doses tested, which was supported by subjective responses indicating rapid sSL. Most subjects expressed good concentration, alertness, and feeling refreshed the next morning. NG2-73 was generally well-tolerated.
Support (optional): Neurogen Corp.

0706

A RANDOMIZED PLACEBO-CONTROLLED TRIAL OF ACUPUNCTURE FOR PRIMARY INSOMNIA – PRELIMINARY DATA

Yeung W,[1] Chung K,[2] Zhang S,[3] Yap T[4]
(1) University of Hong Kong, Hong Kong, China, (2) the University of Hong Kong, Hong Kong, China, (3) Hong Kong Baptist University, Hong Kong, China, (4) Hong Kong Professional Teachers' Union, Hong Kong, China

Introduction: Acupuncture is a commonly used complementary therapy for insomnia. Previous studies were limited by the lack of placebo acupuncture group, proper diagnostic and blinding procedure and objective sleep assessment. The purpose of this study is to evaluate the efficacy and safety of electro-acupuncture in primary insomnia using placebo acupuncture as control.
Methods: Chinese adults aged 18-65 yr with DSM-IV primary insomnia for at least 3 months were randomized to receive electro-acupuncture or placebo acupuncture for 9 sessions in 3 weeks. The acupoints used were bilateral Ear Shenmen, Sishencong EX-HN1, Anmian, and unilateral Yingtong EX-HN3 and Baihui DU20. Streitberger placebo needles were used in the placebo group. The number, duration and frequency of treatment session were the same for the two groups. Structured Clinical Interview for DSM-IV and overnight polysomnography were used for screening. Insomnia Severity Index (ISI) (primary outcome measure), sleep diary and adverse event reporting were done at baseline, after the 5th treatment, after the 9th treatment and 1-week post-treatment. Actigraphy, PSQI, Hospital Anxiety and Depression Scale, Sheehan Disability Index were done at baseline and 1-week post-treatment. Significant treatment effect is defined as a difference of ≥ 5 ISI points between the two groups. A sample size of 20 in each group has a power of 85-100% to detect the significant treatment effect using ANCOVA.
Results: This preliminary analysis was based on the first 10 subjects in each group. Subjects receiving electro-acupuncture had significantly higher sleep efficiency by sleep diaries than those with placebo acupuncture at 1-week post-treatment (ANCOVA: $F = 5.4$, $p = 0.03$) with difference between means of 12.8% (95% CI: 2.2%-23.3%). No significant difference in other outcome measures between the two groups. No adverse event was reported in either group.
Conclusion: Electro-acupuncture seems to be effective and well tolerated in the short-term treatment of primary insomnia.

0707

DOSE-RESPONSE EFFECTS OF SUBLINGUAL TRANSMUCOSAL ZOLPIDEM 3.5MG AND 1.75MG IN MIDDLE-OF-THE-NIGHT (MOTN) INSOMNIA

Hull S,[1] Roth T,[2] Scharf M,[3] Lankford A,[4] Rosenberg R,[5] Rosenthal M,[6] Singh N,[7] Maguire Y[7]
(1) Vince and Associates Clinical Research, Overland Park, KS, USA, (2) Henry Ford Sleep Disorders Center, Detroit, MI, USA, (3) Tri-State Sleep Disorders Center, Cincinnati, OH, USA, (4) Sleep Disorders Center of Georgia, Atlanta, GA, USA, (5) NeuroTrials Research Inc, Atlanta, GA, USA, (6) California Clinical Trials, CA, USA, (7) TransOral Pharmaceuticals Inc, San Francisco, CA, USA

Introduction: Individuals with insomnia characterized by prolonged middle-of-the-night (MOTN) awakenings have no treatment option approved for dosing on a prn basis during the night following an awakening. This study assessed the efficacy of a new low-dose formulation of sublingual transmucosal (ST) zolpidem following a planned nighttime awakening.
Methods: This was a randomized, double-blind, placebo-controlled, three-way crossover study of two nights of dosing with placebo, 1.75 or 3.5 mg ST zolpidem. Eligible subjects (N=83) had a diagnosis of DSM-IV-TM primary insomnia and a history of prolonged MOTN awakenings. Subjects were awakened 4 hours after initial lights out, received study medication and kept awake for 30 minutes before returning to bed. Sleep parameters were measured by polysomnography (PSG) and by subject report.
Results: Significant, dose-related improvements in sleep initiation and maintenance parameters were seen with ST zolpidem. Latency to Persistent Sleep after the MOTN awakening (LPSmotn) had LS mean values of 9.6, 16.8 and 28.1 minutes for ST zolpidem 3.5 mg ($p \leq 0.001$), 1.75 mg ($p \leq 0.001$) and placebo, respectively. Subjective Latency to Sleep Onset (LSOmotn), Total Sleep Time (TSTmotn) and Sleep Efficiency after the experimental awakening showed significant dose-dependent improvements relative to placebo (all $p \leq 0.001$). Furthermore, subjects with severe MOTN insomnia (baseline MOTN awake time ≥60 minutes) showed proportionally greater improvements in LPSmotn with active treatment than the population as a whole (LS means 12.6, 23.2 and 37.8 minutes with ST zolpidem 3.5 mg ($p \leq 0.001$), 1.75 mg ($p=0.003$) and placebo, respectively). This subgroup also showed significant improvements in TSTmotn relative to placebo.
Conclusion: The new, low-dose formulation of ST zolpidem (Intermezzo™) produced significant dose-dependent improvements in sleep onset and duration without any next-day residual effects: with the 3.5mg adult dose such improvements were retained in patients with more severe MOTN insomnia.
Support (optional): This study was fully funded and supported by TransOral Pharmaceuticals Inc., San Francisco, CA, USA

0708

LONG-TERM EFFICACY OF ZOLPIDEM EXTENDED-RELEASE IN THE TREATMENT OF SLEEP MAINTENANCE AND SLEEP ONSET INSOMNIA WITH IMPROVEMENTS IN NEXT-DAY FUNCTIONING

Erman M,[1] Krystal A,[2] Zammit G,[3] Soubrane C,[4] Roth T[5]
(1) University of California, San Diego, San Diego, CA, USA, (2) Duke University, Durham, NC, USA, (3) Clinilabs, Inc., New York, NY, USA, (4) Sanofi-Aventis, Chilly-Mazarin, France, (5) Detroit, MI, USA

Introduction: Zolpidem extended-release 12.5 mg has been shown to improve measures of sleep maintenance and sleep onset in two 3-week studies. We present results from a 6-month study in patients with chronic insomnia taking zolpidem extended-release or placebo "as needed" 3–7 nights/week.
Methods: Multicenter, double-blind, placebo-controlled, randomized study in adult chronic insomnia patients (18–64 years; n=1025). Zolpidem extended-release 12.5 mg or placebo was taken "as needed" 3–7 nights/week for 6 months. Patient-ratings of sleep improvements and next-day function were assessed every 4th week by Patient Global Impression (PGI) and by daily morning questionnaires.
Results: 436/674 (64.7%) zolpidem extended-release and 184/351 (52.4%) placebo patients completed the 6-month treatment period. PGI—sleep duration showed a significantly greater percentage of patients treated with zolpidem-extended release, compared to placebo, rated lengthened total sleep time (e.g. Week 4: 79.6% vs 36.1%; Week 24: 86.8% vs 54.8% [$P<0.0001$ throughout]). Reported wake time after sleep onset (WASO) derived from morning questionnaires was reduced on a sustained, significant basis ($P<0.0001$ Months 1–6; range of decrease in mean WASO from baseline with zolpidem extended-release: 50.86–68.27 minutes). A significantly decreased number of awakenings was reported by zolpidem extended-release patients (mean change from baseline, Month 1: –1.34 vs –0.81; Month 6: –1.80 vs –1.31 [$P<0.0001$ vs placebo, Months 2–6]). Questionnaires also showed sustained improvements in sleep quality ($P<0.0001$ vs placebo), sleep onset latency ($P<0.0014$ vs placebo), patient-reported sleepiness in the morning ($P<0.0001$ vs placebo) and improved ability to concentrate ($P\leq 0.0014$ vs placebo) at all timepoints. Most frequent AEs were: headache, anxiety and somnolence.
Conclusion: Zolpidem extended-release (Ambien CR™) 12.5 mg, taken "as needed" 3–7 nights/week had sustained efficacy over 6 months in self-reported sleep onset and maintenance, as well as next-day function. These findings suggest the utility of long-term "as needed" insomnia pharmacotherapy.
Support (optional): Research was supported by sanofi-aventis, Inc.

0709

EFFICACY AND SAFETY OF SUBLINGUAL TRANSMUCOSAL ZOLPIDEM 3.5MG AND 1.75MG IN MIDDLE-OF-THE-NIGHT (MOTN) INSOMNIA

Roth T,[1] Scharf M,[2] Hull S,[3] Lankford A,[4] Rosenberg R,[5] Rosenthal M,[6] Maguire Y,[7] Singh N[8]
(1) Detroit, MI, USA, (2) Tri-State Sleep Disorders Center, Cincinnati, OH, USA, (3) somniTech, Inc., Overland Park, KS, USA, (4) Sleep Disorders Center of Georgia, Atlanta, GA, USA, (5) NeuroTrials Research, Atlanta, GA, USA, (6) California Clinical Trials, San Diego, CA, USA, (7) TransOral Pharmaceuticals, San Francisco, CA, USA, (8) TransOral Pharmaceuticals Inc., San Francisco, CA, USA

Introduction: There are no hypnotics currently approved that can be used on a prn basis when insomnia patients who awaken in the Middle-Of-The-Night (MOTN) and have difficulty returning to sleep. Instead, patients with MOTN awakenings dose themselves with hypnotics prophylactically on a nightly basis in anticipation of nighttime awakenings. This polysomnography (PSG) study evaluated the efficacy and safety of sublingual transmucosal (ST) zolpidem 1.75 and 3.5 mg in adults with MOTN insomnia utilizing a planned MOTN awakening.
Methods: Adults (N=83) meeting DSM-IV-TM criteria for primary insomnia and a history of prolonged nighttime awakenings were evaluated in a randomized, double-blind, placebo-controlled, three-way crossover study with 2 consecutive nights of dosing with placebo, 1.75 and 3.5 mg ST zolpidem. Four hours after initial lights-out patients were awakened for 30 minutes, and after receiving study medication they were allowed an additional 4 hours in bed. Sleep parameters were measured by PSG and by subject report.
Results: Significant reductions in Latency to Persistent Sleep post-MOTN awakening were seen with both 3.5 and 1.75 mg ST zolpidem ($p\leq 0.001$: LS means 9.6, and 16.8 minutes, respectively vs. 28.1 minutes with placebo) subject reported Latency to Sleep Onset , PSG Total Sleep Time and Sleep Efficiency were significantly improved in both active treatment groups relative to placebo (all $p\leq 0.001$). Furthermore, a significantly higher portion of subjects rated their "level of refreshed sleep" and "ability to function" as "good" or "excellent" with ST zolpidem compared to placebo (all $p<0.025$). Incidence of adverse events with ST zolpidem at both doses was not different from to placebo.
Conclusion: Low-dose ST zolpidem (IntermezzoTM) was well tolerated and produced significant, dose-related improvements in objective and subject reported sleep endpoints with no residual next day sedation. ST zolpidem´s profile is appropriate for the prn management of insomnia following nighttime awakenings.

0710

NO EVIDENCE OF REBOUND INSOMNIA IN PATIENTS WITH CHRONIC INSOMNIA TREATED WITH ZOLPIDEM EXTENDED-RELEASE 12.5 MG ADMINISTERED "AS NEEDED" 3–7 NIGHTS/WEEK FOR 6 MONTHS

Erman M,[1] Krystal A,[2] Zammit G,[3] Soubrane C,[4] Roth T[5]
(1) University of California, San Diego, San Diego, CA, USA, (2) Duke University, Durham, NC, USA, (3) Clinilabs, Inc., New York, NY, USA, (4) Sanofi-Aventis, Chilly-Mazarin, France, (5) Detroit, MI, USA

Introduction: Rebound insomnia (worsened sleep versus baseline) is often observed following abrupt discontinuation of hypnotics. We present results from a 6-month study in chronic insomnia patients taking zolpidem extended-release 12.5 mg "as needed" 3–7 nights/week to determine if rebound occurs on nights when subjects did not take medication.
Methods: Multicenter, randomized, double-blind study in adult chronic insomnia patients (18–64 years; n=1025), receiving either zolpidem extended-release 12.5 mg or placebo taken "as needed" 3–7 nights/week for 6 months. Patients completed daily morning questionnaires reporting perceived total sleep time (TST) and wake time after sleep onset (WASO). As predetermined, rebound insomnia was assessed using baseline-adjusted mean change in TST and WASO calculated within each month for each non-treatment night, which followed 4 consecutive treatment nights, and during the first 3 nights of permanent treatment discontinuation at study end.
Results: During the 6-month treatment phase, morning questionnaires from single nights without zolpidem extended-release treatment (following 4 consecutive treatment nights) demonstrated no decrease (worsening) below baseline in WASO during Months 1–6 (least-square mean WASO change [<0=improvement] above baseline each month:

-0.27, -16.64, -13.43, -18.75, -16.12, 23.99 minutes) and for TST during Months 2–6 (least-square mean TST change from baseline each month: -8.42, +13.94, +18.50, +14.15, +16.92, +13.25 minutes). For the 3 nights following permanent treatment discontinuation, no decrease (worsening) from baseline was observed in TST (change above baseline—Night 1: 17.68; Night 2: 44.53; Night 3: 42.94 minutes) or WASO (change above baseline—Night 1: –21.06; Night 2: –31.39; Night 3: –35.92 minutes).
Conclusion: Zolpidem extended-release (Ambien CR™) 12.5 mg taken "as needed" 3–7 nights/week for 6 months shows no evidence of rebound insomnia during Months 2–6 of the treatment phase and following treatment discontinuation, further supporting the potential utility of long-term "as needed" insomnia pharmacotherapy.
Support (optional): Research was supported by sanofi-aventis, Inc.

0711

NEXT-DAY DRIVING ABILITY, COGNITION AND PSYCHOMOTOR FUNCTION FOLLOWING NIGHTTIME ADMINISTRATION OF ESZOPICLONE IN PRIMARY INSOMNIACS

Boyle J,[1] Rubens R,[2] Roach J,[2] Johnsen S,[1] Trick L[1]
(1) University of Surrey, Guildford, Surrey, United Kingdom, (2) Sepracor Inc., Marlborough, MA, USA

Introduction: This study evaluated next-day on-the-road driving ability and cognitive function following nighttime administration of eszopiclone 3mg in primary insomniacs.
Methods: This randomized, double blind, placebo controlled, crossover study was performed in patients with primary insomnia (n=31). Eszopiclone 3mg was administered 30 minutes prior to lights out. On the road driving ability was assessed 9.5 to 10.25 hours after ingestion and additional objective cognitive and psychomotor testing was performed 9.75 to 10.5 hours after ingestion. Sleep and residual effects were also assessed subjectively in the morning.
Results: There were no significant differences in brake-reaction time (BRT) following nighttime administration of eszopiclone compared with placebo (p=0.39), and no significant differences between treatments on objective cognitive tests of information processing, divided attention, psychomotor tasks and working memory as assessed by Critical Flicker Fusion, Choice Reaction Time, Continuous Tracking Task, Sternberg Short Term Memory Scanning Task, Rapid Visual Information Processing and Digit Symbol Substitution Test . Neither was there any significant effect on subjective next day ratings of morning sedation, co-ordination or mood as assessed by the Leeds Analog Rating Scale (LARS). There was significant improvement compared with placebo (p<0.0001) in subjectively rated ease of getting to sleep and quality of sleep the morning following dosing, and no perceived impairment of behavior following awakening or early morning awakenings as assessed by the Leeds Sleep Evaluation Questionnaire (LSEQ). PSG demonstrated significant increases in total sleep time and sleep efficiency, and significant reductions in time awake, wake after sleep onset, sleep onset latency (latency to sleep Stage 1) and latency to persistent sleep (p-values <0.005).
Conclusion: In this study, nighttime administration of eszopiclone 3mg improved objective and subjective sleep measures in primary insomniacs and did not impair next-day driving ability or other measures of cognition and psychomotor function.
Support (optional): Support for this study provided by Sepracor Inc.

0712

INSOMNIA RELATED COMORBIDITIES AND ECONOMIC CONSEQUENCES AMONG AN INSURED POPULATION

Pollack M,[1] Joish V[2]
(1) HealthCore, Inc., Wilmington, DE, USA, (2) Sanofi-Aventis, Bridgewater, NJ, USA

Introduction: Insomnia is a prevalent condition affecting overall healthcare expenditures and has been linked to significant comorbidities as well. The aim of this study is to document the economic impact of insomnia and the prevalence of comorbid conditions.
Methods: Insomnia cohort subjects had a prescription claim for an insomnia medication or an ICD-9 insomnia-related medical claim within Medstat's MarketScan Health and Productivity Databases. The index date for this cohort was the first claim between 1/1/2001 – 12/30/2003. A control group was identified as patients having no prescription or medical claim for insomnia treatments or diagnoses during the entire study period. All subjects were continuously enrolled in the health plan with productivity data for 12-months before and after index date. Among both study cohorts, comorbidities and resource utilization were evaluated 12-months pre and post index date. Total direct healthcare and productivity costs were compared across the cohorts using t-tests for bivariate comparisons and generalized linear models with gamma functions for multivariate comparisons.
Results: : The insomnia cohort (n=2,985) had a statistically higher (p<.05) mean age (41.6 vs 42.9 years), proportion of males (52 vs. 68 %), depression (23.7 vs. 9.4%), anxiety/phobia (11.7 vs. 6.6%), stress (6.3 vs 3.1%), and muscle pain (41.6 vs. 32.4%) compared to the controls (n=14,318). Mean unadjusted total costs in the post index period were $3,708 vs. $6,989 (P <0.001) for the control and insomnia cohorts, respectively. Lost productivity costs were found to be significantly higher (P <0.001) for the insomnia group ($1,026 vs. $540). After controlling for demographic and co-morbid characteristics, insomnia patients continued to demonstrate statistically greater (p<.05) direct and indirect economic costs.
Conclusion: These results suggest a significant link between insomnia and higher rates of comorbid conditions, healthcare expenditures and productivity losses. Payers and employers should consider insomnia for disease-related case management initiatives.

0713

BEHAVIORAL MANAGEMENT OF HYPNOTIC DEPENDENT INSOMNIA: 1-YEAR FOLLOW-UP

Lichstein K,[1] Nau S,[2] Wilson N,[3] McCrae C,[4] Aguillard R,[5] Lester K,[5] Bush A[6]
(1) University of Alabama, Tuscaloosa, AL, USA, (2) University of Alabama, AL, USA, (3) University of Memphis, TN, USA, (4) Gainesville, FL, USA, (5) Methodist Hospital, TN, USA, (6) University of Tennessee, Memphis, TN, USA

Introduction: Chronic prescription hypnotic use can lead to hypnotic dependent insomnia (HDI): drug dependence, insomnia return, and daytime health risks. Adverse effects of hypnotic dependence in older adults may be more severe than in other age groups due to sluggish drug elimination, heightened site sensitivity, and polypharmacy effects. This paper presents long-term follow-up self-report data from a randomized, placebo-controlled clinical trial on the management of HDI.
Methods: Volunteers were recruited with media announcements. Qualifying participants were over age 50, free of medical/psychiatric contributors to insomnia, chronic users of prescription hypnotics, insomnia symptomatic, and free of clinically significant apnea/PLMD as per PSG screening. Participants were randomized to 8 sessions of

behavioral treatment (BT, comprising stimulus control, relaxation, sleep hygiene) followed by hypnotic weaning, placebo biofeedback followed by hypnotic weaning, or weaning only.
Results: We have complete data on 61 participants. Groups x Time ANOVA on medication consumption found a main effect for time. Combining groups, there was an 86% medication reduction at posttreatment and 69% reduction at 1-year follow-up. We tested sleep change with a covariance model equating for baseline levels across groups. Within the context of significant medication reduction, there were three primary outcomes. Not one of the six sleep variables in any group was worse at follow-up than at baseline (total of 18 pairs of means). SOL (24 min) was significantly lower in the BT group than the others at follow-up. WASO (30 min) was significantly lower in the BT group than the others at posttreatment, maintained its gains to follow-up, but the other groups reduced WASO to catch up to BT by follow-up.
Conclusion: People with HDI who wish to discontinue their medication achieve substantial success with gradual weaning without sleep deterioration to 1-year follow-up. If this is supplemented by behavioral treatment, sleep improvement may occur.
Support (optional): Research supported by National Institute on Aging grant AG14738.

0714

EVENT-RELATED POTENTIALS MEASURES IN PSYCHOPHYSIOLOGICAL AND PARADOXICAL INSOMNIA SUFFERERS

Bastien C,[1] St-Jean G,[2] Turcotte I,[3] Morin C,[3] Lamy M[3]
(1) Laval University, Ste-Foy, Quebec, Canada, (2) Laval University, Quebec, Canada, (3) Quebec, Canada

Introduction: Some preliminary QEEG studies suggest that individuals suffering from paradoxical insomnia (Para-I) display higher cortical arousal than those suffering from psychophysiological insomnia (Psy-I). Recently, our ERPs data suggested inhibition deficits in addition to cortical arousal in Psy-I relative to GS. The objective of the present study is to further circumscribe the neurophysiological basis of chronic insomnia in Para-I using ERPs.
Methods: Participants were 15 Psy-I, 10 Para-I and 15 GS. Participants underwent four consecutive nights of PSG recordings (N1 to N4). ERPs (N1, P2 and N350) in the evening and upon awakening were recorded on N3 and N4, with the addition of sleep-onset recordings on N4. Auditory stimuli consisted of `standard´ (70 dB, 2000 Hz, .85 probability) and `deviant´ (90 dB, 1500 Hz, .15 probability). Participants received the explicit instruction to ignore all stimuli at all times.
Results: Mixed model ANOVAs were used to test dependant variables (amplitudes and latencies) at each assessment phase (evening, sleep onset, morning) for each stimulus. As expected, the amplitude of all components was greater for the deviant than for the standard stimulus in all groups. The amplitude of N350 significantly differ between both insomnia groups (INS) and GS at sleep-onset, N350 being larger in GS than in INS. N350 amplitude was similar in Psy-I and Para-I. However, the amplitude of P2 was significantly greater in Para-I than in Psy-I and GS and the latency of all ERPs components was significantly shorter in Para-I compared to both Psy-I and GS.
Conclusion: These results suggest that both an inability to initiate normal sleep processes and a higher cortical activation might interfere with sleep in insomnia sufferers compared to good sleepers. Furthermore, paradoxical insomnia sufferers display greater arousal levels than psychological insomnia sufferers and are more much disturbed by the stimulation than psychological insomnia sufferers.
Support (optional): Research supported by the Canadian Institutes of Health Research (# 49500) to C. Bastien.

0715

EFFECTS OF RAMELTEON 8 MG ON LATENCY TO PERSISTENT SLEEP IN ADULTS WITH SEVERE SLEEP-INITIATION DIFFICULTY; POST-HOC ANALYSIS OF A 5-WEEK TRIAL

Mini L,[1] Wang-Weigand S,[2] Zhang J[2]
(1) Takeda Pharmaceuticals North America, Deerfield, IL, USA, (2) Takeda Global Research and Development Center, Deerfield, IL, USA

Introduction: The chronohypnotic RozeremTM (ramelteon) is a novel, highly selective MT1/MT2-receptor agonist indicated for treatment of insomnia. This study evaluated the efficacy of ramelteon in a subset of adults with chronic insomnia who had severe sleep-initiation difficulty.
Methods: A total of 405 adults with chronic insomnia (DSM-IV-TR™) lasting at least 3 months were administered ramelteon nightly for 5 weeks in a phase III, randomized, double-blind, placebo-controlled trial. From this larger trial, a subset of 127 subjects with baseline latency to persistent sleep (LPS) 60 minutes who received ramelteon 8 mg (n=65) or placebo (n=62) were selected for this post-hoc analysis. LPS was evaluated using polysomnography (PSG) at Week 1 (Nights 1-2), Week 3 (Nights 15-16), and Week 5 (Nights 29-30). Possible rebound insomnia was evaluated with a 2-day placebo run-out period. Visual Analog Scales (VAS) of mood and feelings, Digit Symbol Substitution Test (DSST), immediate and delayed recall tests, and measures of subjective levels of alertness and ability to concentrate evaluated next-morning residual effects.
Results: Compared to placebo, administration of ramelteon showed statistically significant reductions in LPS at Week 1 (change from baseline: 35.2 vs 53.0min, P=0.01), Week 3 (32.3 vs 55.8 min, P=0.002), and Week 5 (40.0 vs 58.7 min, P=0.01). During the run-out period, no rebound insomnia was observed. Assessment of DSST, memory tests, or level of alertness and ability to concentrate revealed no statistically significant differences between ramelteon and placebo groups. Both treatment groups had similar incidences of adverse events, and only 4 adverse events (headache, somnolence, fatigue, and nasopharyngitis) were reported by 5% of subjects in either group.
Conclusion: Compared to placebo, ramelteon 8 mg produced statistically significant reductions in LPS over 5 weeks in adults with severe baseline sleep-initiation difficulties without producing next-morning residual effects or rebound insomnia.
Support (optional): This research was supported by Takeda Pharmaceutical Company.

0716

RELATIVE EFFECT SIZES OF ESZOPICLONE TREATMENT FOR INSOMNIA IN PATIENTS WITH PRIMARY INSOMNIA AND INSOMNIA CO-MORBID WITH MAJOR DEPRESSIVE DISORDER, GENERALIZED ANXIETY DISORDER, PERIMENOPAUSAL TRANSITION OR RHEUMATOID ARTHRITIS

Schaefer K,[1] McCall W,[2] Krystal A,[3] Rubens R,[1] Wilson P,[4] Pfleeger K,[1] Roth T[5]
(1) Sepracor Inc., Marlborough, MA, USA, (2) Wake Forest University, Winston-Salem, NC, USA, (3) Duke University, Durham, NC, USA, (4) Sepracor Inc., MA, USA, (5) Sepracor Inc., Detroit, MI, USA

Introduction: Insomnia may be a primary medical condition or it may be comorbid with a psychiatric or medical condition. This report evaluates the relative effect sizes of eszopiclone 3mg treatment

compared with placebo in patients with primary insomnia (PI), and insomnia comorbid with Major Depressive Disorder (MDD), Generalized Anxiety Disorder (GAD), peri-menopausal transition (PMT), or rheumatoid arthritis (RA).
Methods: Sleep-wake symptoms were assessed in primary insomniacs (n=830), and in patients with insomnia comorbid with MDD (n=545), GAD (n=595), PMT (n=410), or RA (n=153) via patient-reported sleep latency (SL), wake time after sleep onset (WASO), total sleep time (TST), sleep quality and daytime functioning symptoms. In all studies, patients met DSM-IV criteria for insomnia at screening. Relative effect sizes were computed using the absolute value of the difference between the two treatment means (eszopiclone – placebo) divided by the pooled standard deviation. All patients in the psychiatric studies were treated with an open label SSRI.
Results: There were moderate (0.3) to strong (0.5) treatment effects on sleep outcomes with eszopiclone treatment across the studies as early as Week 1 (SL 0.47 - 0.63; WASO 0.40 - 0.69; TST 0.44 - 0.65; sleep quality 0.50 - 0.77) and after 4 weeks (SL 0.33 - 0.63; WASO 0.28 - 0.43; TST 0.27 - 0.61; sleep quality 0.29 - 0.61). The largest effect sizes were observed in the primary insomnia population, particularly on measures of next-day functioning. The variance observed in the primary insomnia population was similar to that observed in the comorbid populations. In the two psychiatric studies, the concomitant use of an SSRI did not diminish the insomnia-related effect sizes.
Conclusion: Eszopiclone treatment was associated with moderate to strong effects on all sleep outcomes analyzed in each insomnia population. The largest effects were generally observed in primary insomniacs.
Support (optional): Support for this study provided by Sepracor Inc.

0717

PHARMACOKINETIC EFFECT OF MULTIPLE ORAL DOSES OF DONEPEZIL ON RAMELTEON, AND VICE VERSA, IN HEALTHY ADULTS

Karim A, Bradford D, Siebert F, Zhao Z
Takeda Global Research and Development Center, Deerfield, IL, USA

Introduction: This study evaluated the pharmacokinetic effects of RozeremTM (ramelteon, a selective MT1/MT2-receptor agonist indicated for treatment of insomnia) coadministered with donepezil (a medication indicated for treatment of mild to moderate Alzheimer's type dementia) in healthy adults.
Methods: A total of 48 healthy adults (mean, 43.0 years) were enrolled in this single-center, open-label study and assigned to 1 of 2 treatment sequences. In Sequence 1, subjects received ramelteon 8mg (Day 1). A 3-day washout period followed (Days 2-4). Subjects then received donepezil 5mg once daily (QD) (Days 5-11), which increased to donepezil 10mg QD on Days 12-26. On the final day (Day 27), donepezil 10mg and ramelteon 8mg were coadministered. In Sequence 2, subjects received donepezil 5mg (Day 1). An 18-day washout period followed (Days 2-19). Subjects then received ramelteon 8mg QD on Days 20-26. On the final day (Day 27), ramelteon 8mg and donepezil 5mg were coadministered. All study medications were administered under fasting conditions. On Days 1 and 27, serial blood samples were collected post dose up to 24 hours for ramelteon and 120 hours for donepezil.
Results: Coadministration of ramelteon and donepezil 10mg, relative to ramelteon alone, increased AUC0-inf of ramelteon by 100% (7.46 vs 3.74 ng•hr/mL; 90% CI: 144.94%, 274.80%) and Cmax of ramelteon by 87% (5.43 vs 2.91 ng/mL; 90% CI: 136.47%, 255.15%). The systemic exposure of ramelteon´s major metabolite, M-II, was not affected by donepezil. Coadministration of ramelteon and donepezil, compared to donepezil alone, produced 2-3% increases in donepezil AUC0 tlqc (207.14 vs 202.49 ng•hr/mL; 90% CI: 98.84%, 105.88%) and Cmax (7.56 vs 7.38 ng/mL; 90% CI: 97.6%, 107.63%).
Conclusion: Coadministration of donepezil 10mg increased ramelteon exposure; however, given ramelteon´s highly variable inter-subject pharmacokinetic profile and wide safety margin, the increase was not considered clinically relevant. Coadministration of ramelteon did not affect exposure to donepezil.
Support (optional): This study was supported by Takeda Pharmaceutical Company.

0718

EFFECT OF RAMELTEON ON MIDDLE-OF-THE-NIGHT BALANCE, MOBILITY, AND MEMORY PERFORMANCE IN OLDER ADULTS

Wang-Weigand S,[1] Zammit G,[2] Peng X[1]
(1) Takeda Global Research and Development Center, Deerfield, IL, USA, (2) Clinilabs, Inc., New York, NY, USA

Introduction: Commonly prescribed insomnia treatments may increase the risk of falls, especially in older adults. The nonsedative, chronohypnotic RozeremTM (ramelteon) is a selective MT1/MT2-receptor agonist approved for the treatment of insomnia. This study evaluated the effects of ramelteon vs placebo on middle-of-the-night balance, mobility, and memory performance in older adults, using zolpidem as a positive control.
Methods: In a double-blind, placebo-controlled, single-dose, 3-period crossover study, 33 older adults (>65 years) with chronic insomnia received ramelteon 8 mg, zolpidem 10 mg, or placebo 5 minutes before bedtime for 1 night, followed by a 5- to10-day washout period. Subjects were awakened 2 hours after treatment administration to evaluate standing balance (NeuroCom EquiTest Sensory Organization Test [SOT]), turning speed and stability (NeuroCom EquiTest Step Quick Turn Test [SQTT]), memory (immediate and delayed word recall tests), and adverse events. Balance, as assessed by SOT composite score 2 hours post dose, was the primary evaluation variable.
Results: Mean SOT composite scores did not significantly differ between ramelteon and placebo (P=0.837). In contrast, a significant decrease in mean SOT composite scores was observed between zolpidem and placebo (P<0.001). No significant differences between ramelteon and placebo were observed on SQTT measures of turn time (P=0.776) and turn sway (P=0.982), while significant increases in turn time and turn sway were observed between zolpidem and placebo (P<0.001, both). Significantly lower immediate memory recall scores were reported with zolpidem (P=0.002), but not ramelteon (P=0.683). Delayed recall was not significantly affected by either study drug. Thirteen subjects reported adverse events during zolpidem treatment and 7 subjects each during placebo and ramelteon treatment. No serious adverse events were reported.
Conclusion: Compared to placebo, ramelteon did not impair middle-of-the-night balance, mobility, or memory performance in older adults with insomnia; in contrast, treatment with zolpidem impaired performance on these measures.
Support (optional): This study was supported by Takeda Pharmaceutical Company.

0719

RAMELTEON, UNLIKE ZOPICLONE, HAS NO EFFECT ON BODY SWAY AT PEAK PLASMA LEVELS IN INSOMNIA PATIENTS

Hajak G,[1] Ebrahim I,[2] Hibberd M,[3] Vincent S[3]
(1) University of Regensburg, Department of Psychiatry, Regensburg, Germany, (2) The London Sleep Center, London, United Kingdom, (3) Takeda Global Research and Development, London, London, United Kingdom

Introduction: Studies have found that use of hypnotic agents may be associated with an increased risk of hip fracture due to nocturnal falls. Postural sway is an indicator of instability and thought to predict risk of falls. This study examined the effect of RozeremTM (ramelteon) compared to placebo on balance platform stability at peak plasma levels on night 14 of treatment. Zopiclone was used as a reference treatment. The primary endpoint was calculated area of centre of pressure (COP), in cm2, recorded on the balance platform with eyes open.
Methods: Following a 14-night single-blind placebo run-in, 275 adults with chronic insomnia were randomised to receive placebo, ramelteon 8mg, or zopiclone 7.5mg in a 28-night double-blind treatment period. On night 14, subjects were admitted to the sleep lab 2 hrs prior to their bedtime; the balance platform task was performed at 1.5 hours before dosing. Subjects were administered their double-blinded treatment and went to sleep. At 1.5 to 2 hours post dose, subjects were awakened from sleep and the balance platform task repeated.
Results: A total of 260 adults completed the night 14 balance platform tests; placebo = 91, ramelteon = 85, zopiclone = 84. One subject on zopiclone was unable to stand on the platform for the post dose measurement. The mean log of COP post dose for placebo was 1.617 cm2 and for ramelteon 1.497 cm2, p = 0.532. For zopiclone the mean log of COP post dose was 3.539 cm2, p = <0.001 compared to placebo.
Conclusion: At peak plasma levels and following awakening from sleep, the effect of ramelteon on body sway is no different from placebo; the effect of zopiclone is significantly worse than placebo. Ramelteon offers a potentially safer alternative to traditional hypnotic agents in terms of reduction in risk of falling.
Support (optional): This research was supported by Takeda Pharmaceutical Company.

0720

SLEEP OUTCOMES FOLLOWING ESZOPICLONE DISCONTINUATION IN PATIENTS WITH PRIMARY INSOMNIA AND INSOMNIA CO-EXISTING WITH MAJOR DEPRESSIVE DISORDER OR GENERALIZED ANXIETY DISORDER

Krystal A,[1] Fava M,[2] Pollack M,[2] Rubens R,[3] Schaefer K,[3] Amato D,[4] Roth T[5]
(1) Duke University, Durham, NC, USA, (2) Massachusetts General Hospital, Boston, MA, USA, (3) Sepracor Inc., Marlborough, MA, USA, (4) Sepracor Inc, Marlborough, MA, USA, (5) Detroit, MI, USA

Introduction: Eszopiclone has been shown to improve sleep in patients with primary insomnia (PI) and patients with insomnia comorbid with Major Depressive Disorder (MDD) or Generalized Anxiety Disorder (GAD). Here we examine the effects of eszopiclone discontinuation on sleep outcomes in these patient populations.
Methods: In three double-blind, multicenter, randomized studies, patients received either eszopiclone or placebo treatment. Patients with PI (n=830) were randomized to receive either eszopiclone 3mg or placebo for 6 months. Patients with MDD (n=545) receiving fluoxetine were randomized to receive eszopiclone 3mg or placebo for 8 weeks, and patients with GAD (n=595) receiving escitalopram oxalate were randomized to receive eszopiclone 3mg or placebo for 8 weeks. A 14-day single-blind placebo run-out period (plus continued fluoxetine or escitalopram for the MDD and GAD studies, respectively) followed all double-blind periods. During the run-out, patient-reported total sleep time (TST), sleep latency (SL), and wake time after sleep onset (WASO) were collected.
Results: In all studies, following eszopiclone discontinuation, TST, SL, and WASO values remained improved from baseline at 14 days post treatment ($\leq$0.0001) and when averaged over all 14 days of the run-out period (p<0.0001). Additionally, based on a comparison of treatment group median values, rebound insomnia was not observed for any sleep parameter on any night of the run-out period. In the MDD patients, significant sleep improvements observed with eszopiclone-fluoxetine vs fluoxetine-placebo during the double-blind period were maintained following eszopiclone discontinuation, while in PI and GAD patients, significant treatment differences were not consistently observed during the run-out period.
Conclusion: Relative to baseline measures, there was no evidence of rebound insomnia after eszopiclone cessation during the 14-day discontinuation period in patients with PI, GAD, and MDD. In contrast to the PI and GAD studies, improvements in sleep were maintained in the MDD study.
Support (optional): Support for this study provided by Sepracor Inc.

0721

BASELINE SLEEP IMPAIRMENT AS ASSESSED BY THE INSOMNIA SEVERITY INDEX IN PATIENTS WITH PRIMARY INSOMNIA AND INSOMNIA CO-MORBID WITH PSYCHIATRIC OR OTHER PHYSICAL DISORDERS

Morin C,[1] Schaefer K,[2] Roach J,[2] Pfleeger K,[2] McCall W,[3] Roth T[4]
(1) Laval University, Ste-Foy, Quebec, Canada, (2) Sepracor Inc., Marlborough, MA, USA, (3) Wake Forest University, Winston-Salem, NC, USA, (4) Detroit, MI, USA

Introduction: The Insomnia Severity Index (ISI) was developed to measure patient´s perception of insomnia symptoms, and the impact of insomnia on daily living. The content of the questions corresponds with diagnostic criteria for insomnia, and it has been validated and shown to be sensitive to change. However, normative values have not been reported. We used the ISI in five studies of eszopiclone efficacy in the treatment of primary insomnia (PI), and insomnia comorbid with Major Depressive Disorder (MDD), Generalized Anxiety Disorder (GAD), peri-menopause (PM), or rheumatoid arthritis (RA). Here we present baseline values for the ISI total score for each of these populations.
Methods: All patients were required to meet DSM-IV criteria for either primary insomnia or secondary insomnia. In addition, patients were required to meet self-reported minimum criteria for insomnia, which, in all studies, included sleep latency$\geq$30 minutes and TST$\leq$6.5 hours. There were no entry criteria for ISI scores in any study. ISI total scores were categorized as 0-7: not clinically significant (NCS); 8-14: sub-threshold insomnia; 15-21: moderate insomnia; 22-28: severe insomnia.
Results: Across all studies, a small percentage of patients had insomnia NCS at baseline (0.7-9%), and ~52% and 18% of patients had moderate and severe insomnia at baseline, respectively. Mean (±SD) ISI scores were 19.7±4.3 for MDD patients, 17.9±4.1 for PI, 17.3±4.9 for GAD, 15.6±5.1 for RA and 14.7±5.1 for PM populations. Across studies, patients with PI and insomnia comorbid with MDD and GAD had the highest ISI scores, indicating more severe patient-reported baseline insomnia. In contrast, scores were generally similar and lower for the RA and PM patients.
Conclusion: These findings indicate that the ISI is a useful screening

instrument to identify and establish baseline insomnia severity in primary and comorbid insomnia. These normative values may provide guidance for future research in these populations.
Support (optional): Support for this study provided by Sepracor Inc.

0722

COST OF ILLNESS FOR INSOMNIA: MEDICAL, PHARMACY, AND WORK ABSENCE COSTS IN EMPLOYEES WITH OR WITHOUT INSOMNIA

Brook R,[1] Kleinman N,[2] Melkonian A,[2] Doan J,[3] Baran R[3]
(1) The JeSTARx Group, Newfoundland, NJ, USA, (2) HCMS Group, Cheyenne, WY, USA, (3) Takeda Pharmaceuticals North America, Deerfield, IL, USA

Introduction: The purpose of this study was to assess the annual cost of illness for insomnia among US-based employees.
Methods: A retrospective analysis was conducted using the Human Capital Management Services Research Reference Database, which contains employee data from 2001-2006 from multiple US-based employers. Data from medical and payroll records was collected as well as incidences of work absence (where available) and employee demographics. Employees were identified with insomnia based on history of hypnotic drug use or diagnosis of a sleep disorder (International Classification of Diseases [ICD-9]). Diagnostic codes for insomnia included: 307.41 (transient disorder of initiating or maintaining sleep), 307.42 (persistent disorder of initiating or maintaining sleep), 307.49 (subjective insomnia), and 780.52 (insomnia). Employees with no history of hypnotic drug use or insomnia diagnosis were designated as controls. Annual cost differences between employees in the insomnia or control group was determined using a two-part regression model, controlling for age, gender, comorbid mental disorders, job tenure, salary, geographic region, and the Charlson Comorbidity Index score.
Results: Data was collected for 294,042 employees. Employees with insomnia were on average 42.7 years of age, 63% female, and 19.8% black. Annual mean incremental costs were significantly greater (P<0.0001) for employees in the insomnia group compared to those in the control group (direct medical, $3,306 vs $1,749; prescription drugs, $1,220 vs $422; sick leave, $720 vs $325; short-term disability, $465 vs $229; long-term disability, $46 vs $10; worker´s compensation, $483 vs $280) totaling an additional $3,225 per year. Direct medical (48.3%) and prescription drugs (24.7%) represented the majority of the cost increase.
Conclusion: Insomnia is associated with substantial medical, prescription drugs, sick leave, short- and long-term disability, and workers' compensation costs in the United States. In this study, direct medical costs contributed nearly half (48.3%) of total incremental costs.
Support (optional): This research was supported by Takeda Pharmaceutical Company.

0723

DO PATIENT CHARACTERISTICS AFFECT TYPE OF MEDICATION PRESCRIBED FOR INSOMNIA? EVIDENCE FROM US NATIONAL OUTPATIENT DATA 1995-2004.

Balkrishnan R,[1] Joish V,[2] Pawaskar M[3]
(1) Ohio State University, Columbus, OH, USA, (2) Sanofi-Aventis, Bridgewater, NJ, USA, (3) The Ohio State University College of Pharmacy, Columbus, OH, USA

Introduction: Patient demographics and clinical disposition have shown to be correlated with receipt of pharmacological treatment in insomnia. The objective of this study was to evaluate whether patient characteristics affected the type of insomnia medication (benzodiazepine versus non benzodiazepines) prescribed at the time of visit in physician outpatient settings in the United States.
Methods: A cross sectional study of the National Ambulatory Medical Care Survey data was conducted from 1995-2004 in patients with an ICD-9 diagnosis of insomnia. Data were categorized according to patient demographics, clinical characteristics (including comorbidities), physician specialty and type of pharmacotherapy. Unit of analysis was individual patient visit. Multivariate logistic regression models were used to determine predictors of specific type of pharmacotherapy for insomnia.
Results: Approximately 54 million outpatient visits were made by patients who received some type of pharmacotherapy for sleep difficulties in the 10 year period. Mental comorbidities such as anxiety (15.6%) episodic mood disorders (14.9%) and depression (7%) were most prevalent in these patients. Patients with comorbid anxiety were 42% less likely to receive pharmacological treatment for insomnia than those without anxiety (OR: 0.58, 95% CI: 0.45-0.73). Among specific comorbidities examined, patients with comorbid episodic mood disorders were the only ones associated with a nearly twofold increase in odds of getting a nonbenzodiazepine prescription (OR: 1.92; 95% CI: 1.25-2.96). The likelihood of non-benzodiazepine therapy prescription decreased by 44% in Hispanic patients compared to Whites (OR: 0.56, 95% CI: 0.32-0.98). Patient visits with public insurance (as compared to private insurance), as a primary payer source were associated with decreased non-benzodiazepine prescription (OR: 0.58; 95% CI: 0.39-0.86).
Conclusion: The results revealed that certain demographic, socioeconomic and clinical characteristics of patients seem to influence both prescribing of any pharmacotherapy and specific pharmacological treatments for sleep difficulties, known to have better safety and tolerability profiles.
Support (optional): This study was funded by sanofi aventis inc.

0724

COMORBIDITIES ARE COMMON IN PATIENTS WITH INSOMNIA: EVIDENCE FROM US NATIONAL OUTPATIENT DATA 1995-2004 ON PHARMACOLOGICAL TREATMENT EFFECTS.

Balkrishnan R,[1] Seal B,[2] Pawaskar M[3]
(1) Ohio State University, Columbus, OH, USA, (2) sanofi aventis, NJ, USA, (3) The Ohio State University, Columbus, OH, USA

Introduction: Patients with insomnia are likely to have other medical conditions as well which could affect treatment choices. This study examined the prevalence of comorbidities in patients with insomnia and associated pharmacological treatment of insomnia in US primary care settings.
Methods: A retrospective data analysis of the National Ambulatory Medical Care Survey from 1995 to 2004 was performed. Patients aged 18 years and greater, who had a physician visit with an ICD-9 diagnosis of insomnia in US outpatient settings were included in this study. A descriptive trend analysis was performed to determine the prevalence of commonly occurring comorbid conditions and their correlation with prescribing pharmacotherapy for insomnia. Multivariate logistic regression models were used to examine the relationship between patient comorbidities and insomnia-specific pharmacological treatment receipt at the time of visit.
Results: Among the weighted 107.4 million visits over the 10 year period for insomnia, approximately 41% of the patients with insomnia also had a concomitant diagnosis of a mental comorbidity. Subgroup analysis revealed that anxiety (15.6%) was the most commonly

prevalent comorbidity followed by episodic mood disorders (14.9%). There was a stable prevalence of hypertension (10%), depression (7%) and diabetes (3.5%) in patients with insomnia over the decade. The mean Charlson comorbidity index in patients with sleep difficulties was 0.22 (0.68 SD). Increased number of comorbidities was associated with 19% higher likelihood of receiving pharmacological treatment for insomnia (OR: 1.19, 95% CI: 1.08-1.31). Patients with mental comorbidities were 35% less likely to receive pharmacological treatment for insomnia than those without mental comorbidities (OR: 0.65, 95% CI: 0.51-0.84).
Conclusion: Comorbidities such as episodic mood disorder, hypertension, depression and diabetes are prevalent in patients with insomnia and affect receipt of pharmacological therapy for insomnia. Healthcare professionals need to consider the impact of these comorbidities while prescribing medication therapy in patients with insomnia.
Support (optional): This study was funded by sanofi aventis inc.

0725

BASELINE INSOMNIA SEVERITY IN PATIENTS WITH PRIMARY INSOMNIA AND INSOMNIA CO-MORBID WITH MAJOR DEPRESSIVE DISORDER, GENERALIZED ANXIETY DISORDER, PERIMENOPAUSAL TRANSITION OR RHEUMATOID ARTHRITIS

Roth T,[1] Wilson P,[2] Schaefer K,[2] Rubens R,[2] Walsh J,[3] Krystal A[4]
(1) Henry Ford Hospital System, Detroit, MI, USA, (2) Sepracor Inc., Marlborough, MA, USA, (3) St. John's and St. Luke´s Hospitals, Chesterfield, MS, USA, (4) Duke University, Durham, NC, USA

Introduction: Insomnia may be a primary medical condition or it may be comorbid with a psychiatric or medical condition. In many types of comorbid insomnia, detailed sleep data are limited. This report evaluates baseline insomnia severity in patients with primary insomnia (PI), insomnia comorbid with Major Depressive Disorder (MDD), Generalized Anxiety Disorder (GAD), peri-menopausal transition (PMT), or rheumatoid arthritis (RA).
Methods: Baseline insomnia severity was assessed in primary insomniacs (n=830), and patients with insomnia comorbid with MDD (n=545), GAD (n=595), PMT (n=410), or RA (n=153) via patient-reported sleep onset (sleep latency), maintenance (wake time after sleep onset, WASO, total sleep time, (TST), sleep quality and daytime functioning (daytime alertness, ability to concentrate, physical well-being and ability to function) symptoms. All patients met DSM-IV criteria for insomnia at screening in all studies.
Results: Patients with insomnia comorbid with MDD had the most severe baseline sleep symptoms (median sleep latency 126 min, WASO 75min, TST 246min and mean sleep quality 4.1) compared with the primary insomnia and other comorbid insomnia populations (median sleep latency 59-67min, WASO 39-57min, TST 310-341min, and mean sleep quality 4.6-5.7). Baseline daytime functioning (measured on scales of 0-10 with higher scores reflecting less impairment) was also the most impaired in patients with MDD (mean daytime alertness 4.5, ability to concentrate 4.7, physical well-being 4.7 and ability to function 4.9) relative to primary insomnia and the other comorbid populations (mean daytime function ratings of 5.0-6.9).
Conclusion: Patients with insomnia comorbid with MDD had the most severe baseline nighttime and daytime symptoms relative to the other insomnia patient populations studied.
Support (optional): Support for this study provided by Sepracor Inc.

0726

CHANGES IN SLEEP OUTCOMES WITH PLACEBO TREATMENT IN PATIENTS WITH PRIMARY INSOMNIA AND INSOMNIA CO-MORBID WITH PERI-MENOPAUSAL TRANSITION OR RHEUMATOID ARTHRITIS

Rubens R,[1] Wilson P,[2] Schaefer K,[1] McCall W,[3] Roth T[4]
(1) Sepracor Inc., Marlborough, MA, USA, (2) Sepracor Inc., MA, USA, (3) Wake Forest University, Winston-Salem, NC, USA, (4) Detroit, MI, USA

Introduction: This report evaluates changes in sleep with placebo treatment in patients with primary chronic insomnia (PI) and in patients with chronic insomnia co-morbid with peri-menopausal transition (PMT) or rheumatoid arthritis (RA).
Methods: Changes in sleep after 4 weeks of placebo treatment were assessed in PI (n=830), insomnia co-morbid with PMT (n=410), or insomnia comorbid with RA (n=153) via patient-reported sleep onset (sleep latency), maintenance [wake time after sleep onset (WASO) total sleep time (TST)], sleep quality and daytime functioning (daytime alertness, ability to concentrate, physical well-being and ability to function) symptoms. All patients met DSM-IV criteria for insomnia at screening.
Results: Percent changes from baseline WASO with placebo treatment were largest in the comorbid insomnia populations compared with the PI population (-50% in PMT and -47% in RA vs -24% in PI), whereas improvements in sleep latency and TST were similar in all populations (sleep latency: -33% in PMT and -38% in RA vs -31% in PI and TST: 10% in PMT and 8% in RA vs 10% in PI). Additionally, improvements in sleep quality with placebo were similar across populations (18% for PI, 20% for PMT and 23% for RA) as were measures of daytime functioning (daytime alertness: PI 12%, PMT 13%, RA 6%; ability to concentrate: PI 8%, PMT 7%, RA 5%; physical well-being: PI 8%, PMT 7%, RA 12%; ability to function: PI 7%, PMT 5%, RA 1%).
Conclusion: Improvements from baseline in WASO with placebo treatment were greater in the co-morbid chronic insomnia populations than in primary chronic insomniacs. Improvements in daytime functioning and sleep quality were generally similar across populations with placebo treatment.
Support (optional): Support for this study provided by Sepracor Inc.

0727

CANCER-SPECIFIC FACTORS DO NOT PREDICT CHRONIC INSOMNIA IN BREAST CANCER SURVIVORS (BCS)

Bardwell W,[1] Natarajan L,[1] Dimsdale J,[2] Rock C,[1] Pierce J[1]
(1) University of California, San Diego, La Jolla, CA, USA, (2) University of California, San Diego, San Diego, CA, USA

Introduction: Chronic insomnia is common in BCS. The Women's Healthy Eating & Living (WHEL) Study is a randomized controlled trial of the impact of a dietary intervention (including 18hrs telephone counseling) on breast cancer recurrence/death. We previously reported that depression and vasomotor symptoms--not cancer-specific variables or other patient characteristics--predicted insomnia in these women at baseline (prior to randomization to WHEL intervention or comparison groups). We now examine risk for chronic insomnia.
Methods: 2101 survivors of early-stage breast cancer completed a 147-item psychosocial questionnaire at 4 timepoints: baseline, Yr1, either Yr2 or 3, and Yr4. Participants were divided into 3 groups using the Women´s Health Initiative-Insomnia Rating Scale (WHI-IRS; scores >=9 indicate significant insomnia): (1) WHI-IRS scores >=9 at all timepoints (`persistent insomnia´; 14.1%); (2) scores <9 at all timepoints (`normal sleepers´; 40.4%); and, (3) a mixed pattern

(`relapsing-remitting insomnia´; 45.5%). Data were analyzed with multinomial logistic regression (MLR; using these 3 groups as the outcome variable) and with mixed model analyses (MMA; using continuous WHI-IRS data over time).
Results: MMA of time and treatment group on WHI-IRS over time showed that mean WHI-IRS scores were stable over time and revealed no effect for the WHEL intervention on insomnia. Therefore, data from both the intervention and comparison groups were included in the following analyses. MLR, using 27 predictors on the outcome variable (the 3 WHI-IRS groups), identified enduring vasomotor symptoms, depression, and pain as the only risk factors for persistent insomnia. Consistently normal sleepers reported fewer vasomotor symptoms (OR=.166, Wald=36.259), less depression (OR=.125, Wald=29.012), and less pain (OR=.144, Wald=10.137) than women with persistent insomnia (all p<=.001). A similar but less-pronounced pattern was observed for the relapsing-remitting group vs. consistently normal sleepers. Results from MMA using longitudinal predictor variables will also be reported.
Conclusion: Cancer-specific variables are unimportant in determining which BCS will experience persistent or relapsing-remitting insomnia. Rather, enduring vasomotor symptoms, pain, and depression predict chronic insomnia in this group.
Support (optional): Susan G. Komen Foundation; Lance Armstrong Foundation; Walton Family Foundation; NCI CA69375; NIH M01-RR00070, M01-RR00079, M01-RR00827

0728

COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA IN SURVIVORS OF BREAST CANCER

Fiorentino L,[1] McQuaid J,[1] Liu L,[2] Parker B,[3] Cornejo M,[1] Lawton S,[2] Ancoli-Israel S[4]
(1) Department of Psychiatry, University of California, San Diego, San Diego, CA, USA, (2) Department of Psychiatry University of California, San Diego, San Diego, CA, USA, (3) Department of Medicine, University of California, San Diego, San Diego, CA, USA, (4) Dept. of Psychiatry, University of California, San Diego, San Diego, CA, USA

Introduction: Survivors of breast cancer often suffer from insomnia. Sleep problems and correlated symptoms can last for years after the end of treatment. The present data are from an ongoing study testing the effects of a cognitive behavioral treatment for insomnia (CBT-I) on sleep, depression, anxiety, and quality of life in breast cancer survivors.
Methods: The study is a 12-week randomized controlled crossover design, with participants being randomized to either 6 weeks of CBT-I followed by 6 weeks of follow up (i.e., group 1), or six weeks of treatment as usual (TAU) followed by six weeks of CBT-I (i.e., group 2). Self-reports of insomnia (Insomnia Severity Index: ISI) and quality of sleep (Pittsburgh Sleep Quality Index: PSQI) are assessed at baseline, 6 weeks, and 12 weeks. The CBT-I treatment is administered in 6 individual one-hour weekly sessions. The following data describe the results of the first four participants who have completed all assessments of the study protocol. Of these, 1 participant was randomized initially to CBT-I, and 3 were randomized to TAU followed by CBT-I.
Results: All 4 participants (mean age=57 years, SD=9, range=46-67) had reduced levels of insomnia and sleep disruption comparing baseline (ISI: mean=18.2, SD=3.9, range=13-22; PSQI: mean=13.5, SD=2.4, range=11-16) to after the CBT-I (ISI: mean=5.7, SD=3.9, range=2-11; PSQI: mean=5.2, SD=2.9, range=3-9). In addition, the 3 participants in group 2 did not improve during the 6 weeks of TAU (ISI: mean=18.3, SD=1.5, range=17-20; PSQI: mean=13.3, SD=2.5, range=11-16). The participant randomized to initial CBT-I continued improving during the follow up (ISI: score=0, PSQI=1).
Conclusion: Although these data are very preliminary, breast cancer survivors appear to benefit from CBT-I. After 6 sessions of CBT-I all 4 participants reported having no insomnia and better sleep quality. A larger sample size, currently being recruited, will permit statistical analysis of these differences.
Support (optional): Supported by CBCRP 11GB0049, CBCRP 11IB-0034, NCI CA112035 and the research service of the VASDHS.

0729

SLEEP MISPERCEPTION AMONG INSOMNIA SUFFERERS

Moreau V, Guay C, Ivers H, Morin C
Laval University, Quebec, Canada

Introduction: It is well recognized that individuals with insomnia, as a group, consistently overestimate the severity of their sleep disturbances relative to polysomnographic recordings. However, some individuals with insomnia are indeed good estimators and may even underestimate sleep difficulties. There is little information about the extent of sleep misperception and about its clinical correlates among individuals diagnosed with insomnia. The objective of this study was to characterize sleep misperception and to examine its relationships with various sleep, health and psychological correlates.
Methods: A total of 120 individuals (mean age = 49.2 years, 62.5% women) completed clinical and PSG (three nights) baseline assessments before a treatment trial for insomnia. Evaluation comprised the Insomnia Interview Schedule, sleep diaries, and other questionnaires (Insomnia Severity Index, Dysfunctional Beliefs and Attitudes about Sleep, Beck Depression Inventory, Beck Anxiety Inventory, Multidimensional Fatigue Inventory, SF-36). Percentage of accurate estimation of total wake time (TWT) and total sleep time (TST) were computed from PSG data of the third recording night as : [(estimated parameter – objective parameter)/objective parameter] X 100 (i.e., a positive score means an overestimation of sleep). In order to investigate subgroups of patients similar on their level of misperception, these two variables were standardized (using z scores) and submitted to a hierarchical cluster analysis (Ward method, radius = 2). Clusters were compared on various sleep, health and psychological variables.
Results: Overall, TWT was overestimated by 109.5% (SD = 177.5, median = 55.2%) but TST was underestimated by a modest 13.2% (SD = 22.8, median = 8.4%). A four-group solution was selected (R2 = 83.6%) from cluster analysis: (a) Cluster I (n = 34), underestimating TWT by 23% and overestimating TST by 9%, (b) Cluster II (n = 55), estimating both parameters accurately, (c) Cluster III (n = 20), overestimating TWT by 298% and underestimating TST by 33%, and (d) Cluster IV (n = 11), overestimating TWT by 394% and underestimating TST by 60%. Comparisons between the subgroups revealed that the two subgroups who overestimated their sleep impairments the most reported significantly more subjective sleep difficulties and more frequent sleepless nights. No significant differences were found on objective sleep continuity, sleep architecture or psychological and health variables.
Conclusion: Results are consistent with previous studies showing that individuals with insomnia as a group tend to overestimate sleep difficulties but that misperception is not ubiquitous in this population. This study did not identify reliable correlates of sleep misperception.
Support (optional): National Institute of Mental Health (MH060413)

0730

EFFICACY AND TOLERABILITY OF GABOXADOL IN ELDERLY PATIENTS WITH CHRONIC PRIMARY INSOMNIA: A 4-WEEK, DOUBLE-BLIND, PLACEBO-CONTROLLED OUTPATIENT STUDY

Hedner J,[1] Loft H,[2] Hajak G,[3] Lundahl J,[4] Hedegaard K,[4] Knoth Sorensen H,[4] Torstenson R[4]
(1) Sahlgrenska University Hospital, Göteborg, Sweden, (2) H. Lundbeck A/S, Copenhagen, Denmark, (3) University of Regensburg, Germany, (4) H. Lundbeck A/S, Denmark

Introduction: Gaboxadol, a selective extrasynaptic $GABA_A$ agonist (SEGA), has demonstrated hypnotic efficacy in short-term studies in patients with primary insomnia. This study evaluated the efficacy and safety of gaboxadol during 4-weeks of treatment in elderly insomnia patients.
Methods: Patients aged 64-91y (N=539; 62% female) met DSM-IV criteria for primary insomnia, and reported subjective Time to Sleep Onset (sTSO) ≥45min as well as subjective Total Sleep Time (sTST) <6.0h for ≥4 nights/week. Following a 1-week, single-blind, placebo run-in period, patients were randomized to 4 weeks of double-blind treatment with gaboxadol 5mg, 10mg or placebo. Daily morning and evening diary data were analysed as weekly means versus placebo using repeated-measures of observed cases (week 1 and 4 presented). Safety was assessed weekly and withdrawal symptoms were evaluated using the Tyrer scale.
Results: Both gaboxadol doses improved sTST (weeks 1 and 4, $p<0.05$), Wake After Sleep Onset (weeks 1 and 4, $p<0.05$, except week 1 for 5mg gaboxadol) and sTSO (weeks 1 and 4, $p<0.05$). Patients reported improved sleep quality (weeks 1 and 4, $p<0.01$) and felt more refreshed (weeks 1 and 4, $p<0.01$) in the morning and experienced more daytime energy (weeks 1 and 4, $p<0.05$). Gaboxadol was generally safe and well tolerated. The most frequently reported adverse events (>5%) following gaboxadol treatment were dizziness, headache and nausea with no apparent influence of dose level. The overall incidence of adverse events for both gaboxadol doses did not differ significantly from the placebo group. No withdrawal symptoms were detected after discontinuation of treatment.
Conclusion: In this 4-week study gaboxadol 5mg and 10mg improved patient reported sleep maintenance and induction. Patients felt more refreshed in the morning and reported improved energy during the day. Gaboxadol was generally safe, well tolerated and no withdrawal symptoms were detected in this elderly population of insomniacs.
Support (optional): H. Lundbeck A/S

0731

MEASURING INSOMNIA WITH THE INSOMNIA SEVERITY INDEX IN EPILEPSY PATIENTS

Talih F, Budur K, Ioachimescu O, Foldvary-Schaefer N
Cleveland Clinic Foundation, Cleveland, OH, USA

Introduction: Recent work suggests that patients with epilepsy are at increased risk for sleep complaints. Sleep deprivation has long been recognized as a seizure precipitant; epilepsy patients with insomnia may therefore be prone to poorer seizure control. No prior studies have systematically assessed insomnia in epilepsy. Our purpose was to use a validated insomnia scale (Insomnia Severity Index [ISI]) in patients with epilepsy and determine the association between insomnia and age, gender, depression status, seizure frequency (SF) and antiepileptic drug (AED) use.
Methods: This is part of a cross-sectional study of adults with epilepsy presenting to a tertiary care clinic from 2004 to 2006. Subjects completed a series of questionnaires including the ISI and the Beck Depression Inventory (BDI) and underwent a PSG and MSLT. The ISI is a 7-item measure that evaluates insomnia. A score > 7 indicates insomnia. This report includes 61 subjects who completed the ISI.
Results: The mean age was 39 years. 73% of the 61 subjects were female. Based on the ISI, 23 (37%) had sub-threshold insomnia, 15 (24%) had moderate insomnia, and 4 (6%) had severe insomnia. Based on the BDI, 20.6% of subjects had mild depression, 17.6% had moderate depression, and 10.3% had severe depression. There were no associations between ISI and SF, gender, age or number of AEDs. ISI and BDI correlated moderately (r=0.51).
Conclusion: Approximately 70% of epilepsy patients had insomnia using the ISI. A correlation between insomnia and depression was observed. Other factors, such as specific AEDs and primary sleep disorders may also be operative and deserve further analysis. These results support the need to routinely incorporate a sleep history in the evaluation of patients with epilepsy as untreated sleep complaints may adversely affect seizure control and quality of life.

0732

A MULTI-TRAIT, MULTI-METHOD APPROACH TO THE ASSESSMENT OF INSOMNIA

Gehrman P,[1] Edinger J,[2] Means M,[3] Husain A[4]
(1) University of the Sciences in Philadelphia, Philadelphia, PA, USA, (2) VA and Duke University Medical Centers, Durham, NC, USA, (3) VA Medical Center, Durham NC, NC, USA, (4) NC, USA

Introduction: Precise diagnostic categorization requires both subjective and objective measurement of sleep to determine if patients meet criteria for paradoxical insomnia vs. psychophysiological insomnia or another subtype. There is a lack of data in which multiple measures are collected on the same subjects in order to compare their psychometric properties. Therefore this study was undertaken to compare sleep logs, polysomnography, and actigraphy in patients with insomnia and healthy sleepers using a multi-trait, multi-method approach.
Methods: The sample consisted of 32 people with insomnia (mean(SD) age=28.1(5.8), 19 women) and 35 healthy sleepers (mean(SD) age=28.3(4.7), 18 women). On three consecutive nights at home subjects´ sleep was recorded with polysomnography (Medilog system) and actigraphy (Actiwatch-L) and sleep logs were completed each morning. From each assessment technique standard sleep variables were computed: total sleep time (TST), sleep efficiency (SE), sleep onset latency (SOL), and wake after sleep onset (WASO). Correlations among sleep variables were computed within and across assessment approaches to derive measures of reliability and validity.
Results: Across assessment approaches sleep variables were comparably reliable (r .75-.80) with sleep logs demonstrating the highest reliability. Reliabilities for PSG were generally higher for subjects with insomnia but the reverse was true for actigraphy, with no substantial differences in sleep logs. Agreement across measurement approaches was generally poor, particularly for actigraphy vs. sleep logs (r=.17-.38) but agreement was higher in the insomnia group. The pattern of correlations demonstrated only moderate convergent and discriminant validity.
Conclusion: These results indicate that polysomnography, actigraphy and sleep logs are all reliable measures of sleep. On the other hand they do not have strong agreement with each other, indicating that each is measuring a distinct aspect of sleep. Further research needs to determine which measure(s) has the greatest clinical relevance for patients with insomnia.

0733

PREVALENCE OF INSOMNIA AND SLEEP-RELATED SYMPTOMS AMONG PARTICIPANTS IN THE NATIONAL HEALTH AND WELLNESS SURVEY (NHWS)

Shaw J,[1] Seal B[2]
(1) University of Illinois at Chicago, Chicago, IL, USA, (2) sanofi-aventis U.S., Inc., NJ, USA

Introduction: This purpose of this study was to estimate the prevalence of insomnia and sleep-related symptoms and to describe socio-demographic differences among symptom groups.
Methods: Participants in the US arm of the 2005 National Health and Wellness Survey (NHWS) were invited to complete an online survey. 1,063 respondents were categorized based on sleep-related symptoms (A–induction, B–maintenance, C–both) and insomnia diagnosis (1–diagnosed, 2–undiagnosed but met DSM-IV criteria, 3–non-sufferer). Missing data for income, race, and Hispanic ethnicity were imputed using the weighted sequential hot deck procedure. Statistical tests of means and proportions were conducted and accounted for the sampling design of the NHWS. Estimates were weighted to the US adult civilian noninstitutionalized population in 2005. The Bonferroni procedure was applied to adjust for multiple comparisons.
Results: Population estimates are reported in brackets. The percentage of respondents classified in groups 1, 2, and 3 was 35.3% [29.3%], 53.9% [42.4%], and 28.3% [62.3%], respectively. The percentage of respondents classified in groups A, B, and C was 13.3% [15.3%], 16.6% [19.9%], and 70.2% [64.8%], respectively. The distribution of sleep symptoms varied by diagnostic group ($p<0.001$), with respondents in group B being less likely to be in groups 1 or 2 (75% [48.1%] vs. 83.0% [59.9%] for A and 93.7% [81.7%] for C) and more likely to be in group 3 (25% [51.9%] vs. 17.0% [40.1%] for A and 6.3% [18.3%] for C). Age, educational attainment, and health insurance coverage type also varied among the groups ($p<0.05$).
Conclusion: A substantial percentage of individuals with sleep-related symptoms did not report a diagnosis of insomnia. Individuals with sleep maintenance symptoms tended to be older than those with sleep induction symptoms, while persons with both induction and maintenance symptoms tended to be less educated and less likely to have health insurance than others.
Support (optional): This study was sponsored by sanofi-aventis U.S., Inc.

0734

EXAMINING POLYSOMNOGRAPHIC QUANTITATIVE CRITERIA SETS FOR DISCRIMINATING PRIMARY INSOMNIA SUFFERERS FROM NORMAL SLEEPERS

Rumble M,[1] Lineberger M,[2] Edinger J[3]
(1) Duke University, Durham, NC, USA, (2) Duke University Medical Center, Durham, NC, USA, (3) VA and Duke University Medical Centers, Durham, NC, USA

Introduction: Recent efforts have been made to develop quantitative criteria for insomnia. Furthermore, recent studies have shown some success in developing quantitative criteria for insomnia with sleep-log data. Using polysomnographic data, the current study similarly examined quantitative criteria for discriminating primary insomnia sufferers from normal sleepers.
Methods: 94 adults with primary insomnia (mean age = 49.49; 51.06% women) and 95 normal sleepers (mean age = 48.34; 49.47% women) were asked to complete 3 consecutive nights of lab-based and home-based polysomnography. Receiver-operator characteristic (ROC) curve analyses were used to compare a range of combined severity/frequency criteria cutoffs for discriminating insomnia sufferers from normal sleepers in both settings. ROC curve analyses were also used to compare a range of severity cutoffs based on 3-night mean lab- and home-based polysomnographic data. The following cutoffs were used for all analyses: SOL or WASO ≥ 20, 21, 30, 31, 40, or 60 minutes and SE ≥ 80, 85, and 90%.
Results: ROC curve analyses revealed poor sensitivity and specificity for all combined severity/frequency criteria cutoffs with the most optimal cutoff having only 72% sensitivity and 59% specificity. Similarly, analyses of mean polysomnographic data revealed poor sensitivity and specificity for all severity cutoffs with the most optimal cutoff having only 72% sensitivity and 62% specificity.
Conclusion: Thus, unlike the findings for sleep-log data, the current findings based on polysomnographic data do not suggest reliable quantitative cutoffs for defining insomnia. It may be that sleep-log data may be more useful in providing quantitative criteria for classification of primary insomnia than polysomnographic data.
Support (optional): This research was supported by Grants for the Department of Veterans Affairs Merit Review (Grant # 0009) and The National Heart, Lung, and Blood Institute (Grant # R01-HL-073259-01).

0735

DIFFERENCES IN HEALTH-RELATED QUALITY OF LIFE (HRQOL), WORKER PRODUCTIVITY, AND ACTIVITY IMPAIRMENT AMONG SUBJECTS WITH DIVERSE INSOMNIA SYMPTOMS

Shaw J,[1] Chow W[2]
(1) University of Illinois at Chicago, Chicago, IL, USA, (2) sanofi-aventis U.S., Inc., NJ, USA

Introduction: The objective of this study was to describe the relationship of insomnia symptoms with productivity and health-related quality of life (HRQoL).
Methods: 1,063 participants in the 2005 National Health and Wellness Survey (NHWS) completed an online follow-up survey that included the 12-item Short-Form Health Survey, Version-1 (SF-12v1), Work Productivity and Activity Impairment (WPAI) questionnaire, and Sleep Impact Scale (SIS). Scale scores ranged from 0 to 100, with higher numbers indicating better HRQoL or less productivity. Respondents were categorized based on sleep-related symptoms (A–induction, B–maintenance, C–both). All statistical analyses accounted for the sampling design of the NHWS.
Results: Mean±SE scale scores for groups A, B, and C were as follows: SIS: Daily Activities—58.1±2.2, 55.9±2.3, and 44.6±0.9 ($p<0.001$ vs. A, B), respectively; Emotional Well-Being—60.2±2.1, 59.0±2.2, and 47.6±0.9 ($p<0.001$ vs. A, B), respectively; Emotional Impact—60.2±2.0, 49.3±1.8 ($p<0.001$ vs. A), and 36.4±0.8 ($p<0.001$ vs. A, B), respectively; Energy/Fatigue—50.8±2.6, 45.7±2.4, and 34.3±0.8 ($p<0.001$ vs. A, B), respectively; Social Well-Being—67.9±2.4, 63.0±2.4, and 50.3±1.1 ($p<0.001$ vs. A, B), respectively; Mental Fatigue—69.4±2.3, 68.5±2.2, and 54.9±1.1 ($p<0.001$ vs. A, B), respectively; Sleep Satisfaction Sleep—47.7±1.7, 38.6±1.7 ($p<0.001$ vs. A), and 29.5±0.7 ($p<0.001$ vs. A, B), respectively; WPAI: Absenteeism—3.4±1.1, 7.9±3.0, and 5.6±0.7, respectively; Presenteeism—21.7±2.6, 26.0±3.7, and 30.1±1.4 ($p=0.01$ vs. A), respectively; Work Productivity Loss—23.9±2.8, 28.2±4.6, and 32.3±1.5 ($p=0.02$ vs. A), respectively; Activity Impairment—29.3±2.9, 34.6±3.0, and 41.0±1.3 ($p<0.001$ vs. A), respectively; SF-12v1: Physical Component Summary—47.3±1.1, 44.8±1.1, and 44.1±0.5 ($p=0.03$ vs. A), respectively; Mental Component Summary—43.7±1.0, 42.6±1.5, and 39.1±0.5 ($p<0.001$ vs. A), respectively.
Conclusion: Sleep induction and maintenance symptoms were

associated with reduced productivity and HRQoL. Maintenance symptoms were associated with increased anxiety/restlessness and reduced satisfaction with sleep than induction symptoms. In combination, induction and maintenance problems were associated with poorer outcomes than either problem alone.
Support (optional): This study was sponsored by sanofi-aventis U.S., Inc.

0736

DIFFERENCES IN SLEEP MEDICATION USE AND RATINGS OF TREATMENT SATISFACTION AMONG SUBJECTS WITH DIVERSE INSOMNIA SYMPTOMS

Shaw J,[1] Joish V[2]
(1) University of Illinois at Chicago, Chicago, IL, USA, (2) sanofi-aventis U.S., Inc., Bridgewater, NJ, USA

Introduction: Although a number of pharmaceuticals have been developed to treat problems related to sleep induction, there are fewer therapies for the treatment of sleep maintenance symptoms. The objective of this study was to describe the relationship of insomnia symptoms with sleep medication use and treatment satisfaction.
Methods: 1,063 participants in the 2005 National Health and Wellness Survey (NHWS) completed an online follow-up survey that included questions about current sleep medication use. Subjects were asked to rate their satisfaction with treatment, extent to which treatment expectations were met, and likelihood of continuing treatment on a scale ranging from 1 (worst possible response) to 10 (best possible response). They were categorized based on reported sleep symptoms (A–induction, B–maintenance, C–both). All statistical analyses accounted for the sampling design of the NHWS.
Results: Population estimates are reported in brackets. 274 respondents (25.8%) [22.0%] reported current sleep medication use. The prevalence of sleep medication use in groups A, B, and C was 22.0% [18.8%], 16.5% [11.1%], and 28.7% [26.0%], respectively ($p<0.001$). Mean±SE sleep medication ratings for groups A, B, and C were as follows: overall satisfaction with treatment—7.4±0.3, 7.1±0.4, and 6.5±0.2, respectively; treatment expectations were met—7.1±0.3, 6.8±0.3, and 6.5±0.2, respectively; likelihood of continuing treatment—7.9±0.5, 7.9±0.4, and 7.0±0.2, respectively. At the 5% level, there were no significant differences among the groups. However, there were differences among sleep medications in the percentage of users reporting an overall improvement in sleep. 95.0% [95%] of zolpidem ER users reported an improvement in sleep compared with 89.0% [89.0%] of zolpidem users, 92.7% [94.3%] of benzodiazepine users, and 74.1% [64.8%] of eszopiclone users ($p=0.001$).
Conclusion: Ratings of treatment satisfaction did not vary according to the type of sleep symptoms. However, important differences existed among sleep medications in users´ perceptions of their effect on sleep.
Support (optional): This study was sponsored by sanofi-aventis U.S., Inc.

0737

SLEEP, DAYTIME FUNCTIONING, AND INSOMNIA COMPLAINTS IN WELL-FUNCTIONING INDIVIDUALS WITH INSOMNIA

Vanderwal G,[1] Lichstein K,[2] Durrence H,[3] Taylor D,[4] Riedel B,[5] Bush A[6]
(1) University of Alabama, Northport, AL, USA, (2) University of Alabama, Tuscaloosa, AL, USA, (3) Somaxon Pharmaceuticals, CA, USA, (4) University of North Texas, Denton, TX, USA, (5) University of Memphis, TN, USA, (6) University of Tennessee, Memphis, TN, USA

Introduction: Although disturbed sleep is the paramount feature of insomnia, the majority of individuals who complain of insomnia also complain of daytime impairment. However, there are individuals who report insomnia and exhibit poor sleep by quantitative criteria, yet report no daytime impairments. The goal is to explore sleep and daytime functioning in these individuals (functioning insomniacs; FI) compared to individuals who meet criteria for insomnia (PWI), complaining good sleepers (CGS), and normal sleepers (PNI).
Methods: We recruited at least 50 men and 50 women in each decade from age 20 to 89 using random-digit dialing. Participants completed a series of daytime functioning questionnaires and 14 days of sleep diaries. Groups were identified based on diary data and the presence of sleep and daytime functioning complaints. To qualify for an FI label, participants must have identified themselves as having insomnia, shown a sleep pattern characterized by sleep latency ≥31 minutes or wake time after sleep onset ≥31 minutes, at least three times per week for six months, but reported no daytime impairment.
Results: Out of 772 participants, there were 14 FI, 137 PWI, 8 well-functioning CGS, and 125 well-functioning PNI. Groups were compared on the set of daytime functioning measures and sleep variables. A MANOVA on these dependent variables was significant, Wilks´Λ=.199, $F(84, 4380.96)=15.73$, $p<.01$. FI function significantly better than PWI, similar to CGS, and worse than PNI. All sleep variables between FI and PWI were non-significant except for subjective sleep quality, and FI sleep worse than PNI and CGS.
Conclusion: FI recognize their sleep as problematic, yet view their sleep quality as higher than PWI, who sleep similar to FI but are functioning at a poorer level. It appears that knowing their level of sleep and daytime functioning impairment may not inform whether or not an individual will make an insomnia complaint.
Support (optional): Research supported by National Institute on Aging grants AG12136 and AG14738

0738

WORK PRODUCTIVITY IN INSOMNIA

McClure T, Drake C, Roth T
Henry Ford Hospital Sleep Disorders and Research Center, Detroit, MI, USA

Introduction: Insomnia has been linked to impairment in daytime functioning; however, few studies have explored impairment within the occupational domain. While insomnia has been linked to increased rates of industrial accidents, increased rates of absenteeism, and lower overall quality of life, specific aspects of productivity have not been examined. This study presents data assessing different aspects of work productivity in a representative sample of insomniacs and age- and gender- matched controls.
Methods: Participants were drawn from the general population of the tri-county metropolitan Detroit area, and had to report working during the past week and being free of any psychiatric disease. Insomniacs had to report experiencing difficulty sleeping for at least one month sometimes or often and a severity of ≥ 6 in the past 3 months (scale 0-10). Controls were self-reported good sleepers. The final sample consisted of 77 insomniacs (42f; mean age = 44.8) and 77 controls (42f; mean age = 44.8). The Endicott Work Productivity Scale (EWPS) was used to assess the impact of illness on social and role functioning. The EWPS consists of 25 questions scored on a 5 point scale (higher score = greater impairment), and has both a high internal consistency and test-retest reliability.
Results: The total score of the EWPS was significantly higher (i.e., lower work productivity) in insomniacs when compared to controls ($p<.01$). When individual items were assessed, insomniacs scored

significantly higher on 13 of the 25 questions (p<.05). The work domains affected in insomniacs were related to memory, concentration, and interactions with co-workers and others.
Conclusion: Within the work domain, issues related to exhaustion/fatigue and interpersonal interactions appear most substantially affected by the disorder, with difficulty concentrating and forgetfulness also playing a role in decreased productivity. On the other hand, our findings suggest that counterproductive motivational work behaviors like arriving late, leaving early, taking longer breaks, working more slowly, and failing to complete tasks are unrelated to insomnia.
Support (optional): NIMH grants: 59338, 68372, and Pfizer

0739

COMPARISON OF ECOLOGICAL MOMENTARY ASSESSMENT TO ONCE A DAY METHOD IN INSOMNIACS

Diana G,[1] Gehrman P,[1] Impastato A[2]
(1) University of the Sciences in Philadelphia, Philadelphia, PA, USA, (2) University of the Sciences in Philadelphia, PA, USA

Introduction: People with insomnia complain of poor daytime functioning due to their poor sleep, but studies have failed to find evidence that they perform at a lower level than healthy sleepers. Functioning is usually measured with retrospective questionnaires that assess functioning for the entire day. An alternate approach is to use Ecological Momentary Assessment (EMA) in which participants complete measurements multiple times throughout the day. This study sought to compare daytime functioning assessed with retrospective and EMA questionnaires.
Methods: Thirty undergraduate students completed the Insomnia Severity Index (ISI) to determine the presence of any insomnia symptoms. They completed the HD-16, a quality of life instrument and the Stanford Sleepiness Scale (SSS) four times throughout the day according to how they felt at that moment. In the evening, they repeated the scales to reflect their average functioning throughout the day. Correlations between daytime and end-of-day scores were computed.
Results: The mean ISI score was 8.75 (SD= 4.15), which is in the range for subthreshold insomnia. The average SSS score from all four time periods was 2.54 and the average of the retrospective scores was 2.63 although these scores were not significantly correlated. The average EMA score for the HD-16 was 3.76 and the retrospective average was 3.86, with the scores showing significant correlation (r=.53).
Conclusion: The low ISI scores indicate that only minor symptoms of insomnia were present in this sample. Daytime functioning was consistent across the day and was similar to retrospective ratings obtained at the end of the day. Sleepiness showed greater variability across the day. Self reported averages and true averages were similar, but were not correlated, suggesting a large degree of individual variability. These results suggest that EMA may be a better way to measure sleepiness because it captures variability in functioning across the day.

0740

DETERMINANTS OF DAYTIME SLEEPINESS IN OLDER ADULTS WITH A COMPLAINT OF INSOMNIA

Benson K,[1] Friedman L,[2] Wicks D,[3] Yesavage J[4]
(1) retired, Barnstable, MA, USA, (2) Stanford University, Palo Alto, CA, USA, (3) Stanford University, CA, USA, (4) Stanford University, Stanford, CA, USA

Introduction: For primary insomniacs, daytime sleep initiation is no less difficult than it is at night. Insomniacs often attribute this difficulty to cognitive arousal rather than somatic activation. This study explores the possibility that cognitive arousal, in the form of two personality factors, contributes to daytime alertness. Neuroticism (NEO-N) and Conscientiousness (NEO-C) factors were derived from the NEO Personality Inventory. We included two additional measures that affect sleep propensity, i.e., prior sleep loss and sleep disordered breathing (SDB).
Methods: Ss were 15 older adults (ages 55+) with complaints of insomnia recruited from the community. Rigorous inclusion and exclusion criteria were imposed. Ss with AHI > 10 and/or PLM index > 10 were excluded. Ss underwent an adaptation night, two PSG nights, and the MSLT. A stepwise multiple linear regression was defined. Sleep latency (SL) derived from the MSLT was the outcome variable. Four predictors of SL were entered into the model: 1)Sleep Loss Index (SLI) represented the totality of sleep loss during the nocturnal sleep period summed over both PSG recordings; 2) SDQSA, the sleep apnea component of the SDQ served as a proxy measure of SDB; 3) NEO-N encompassed the facets of anxiety, depression, hostility, self-consciousness, impulsiveness and vulnerability;4)NEO-C encompassed the facets of competence, self-discipline, achievement-striving, dutifulness, order, and deliberation.
Results: MSLT scores ranged from 9.4 to 19.9 min. Only the SDQSA (t=-3.489, p=.004) and NEO-C (t=3.331, p=.006) met criteria for inclusion in the model. NEO-N and SLI were excluded. The multiple correlation coefficient (R) was 0.788; R square was 0.621.
Conclusion: In older adults complaining of insomnia, two variables were joint and significant predictors of daytime sleep propensity. SDB reduced SL. "Conscientiousness", a countervailing personality factor, delayed daytime sleep initiation and may be associated with cognitive arousal.

0741

EFFICACY AND TOLERABILITY OF GABOXADOL IN ELDERLY PATIENTS WITH CHRONIC PRIMARY INSOMNIA: A 6-MONTH DOUBLE-BLIND, PLACEBO-CONTROLLED OUTPATIENT STUDY

Hedner J,[1] Loft H,[2] Hajak G,[3] Lundahl J,[4] Hedegaard K,[2] Knoth Sorensen H,[2] Torstenson R[2]
(1) Sahlgrenska University Hospital, Göteborg, Sweden, (2) H. Lundbeck A/S, Denmark, (3) University of Regensburg, Germany, (4) H: Lundbeck A/S, Denmark

Introduction: Gaboxadol, a selective extrasynaptic $GABA_A$ agonist (SEGA), has shown hypnotic efficacy in short-term studies in patients with primary insomnia. This study evaluated the efficacy and safety of 10 mg fixed dose gaboxadol in elderly insomnia patients during a 6-month double-blind treatment period.
Methods: Patients aged 65-87 years (N=329; 58% female), met DSM-IV criteria for primary insomnia, and reported subjective time to sleep onset (sTSO) ≥45min as well as subjective total sleep time (sTST) <6.0h for ≥4 nights/week in a 4-week lead-in study. Following re-randomization, eligible patients received either gaboxadol 10mg or placebo in a 6-month, double-blind extension study. Assessments were based on daily morning patient diaries and monthly clinical visits. The statistical analysis compared gaboxadol and placebo by pooled weekly means of reported diary data using repeated measures of observed cases from months 1-3 and 4-6. Withdrawal symptoms were evaluated using the Tyrer scale during a placebo-controlled run-out week.
Results: Gaboxadol 10mg improved sTST during both periods versus placebo (1-3 and 4-6 months, p<0.05). Sleep quality (1-3 and 4-6 months, p<0.01) and a feeling of being refreshed (1-3 and 4-6 months, p<0.01) were improved in the morning assessments. There was no

evidence of tolerance development. sTSO was shortened (1-3 and 4-6 months) although this difference did not reach statistical significance. Gaboxadol was well tolerated. Dizziness and headache were the most commonly reported adverse events in the gaboxadol group but the overall incidence of adverse events did not differ significantly from the placebo group. No withdrawal symptoms were detected during run-out after 6 months treatment.
Conclusion: Throughout a 6-month treatment period gaboxadol improved subjective sleep maintenance and sleep quality. Patients also felt more refreshed in the morning. The safety profile was good and no withdrawal symptoms were detected in this group of elderly insomniacs.
Support (optional): H. Lundbeck A/S, Copenhagen, Denmark.

0742

GABOXADOL REDUCES THE DETRIMENTAL EFFECTS OF TRAFFIC NOISE ON SLEEP: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP STUDY IN HEALTHY SUBJECTS

Dijk D,[1] Stanley N,[2] Groeger J,[1] Legters A,[3] Deacon S[4]
(1) University of Surrey, Guildford, United Kingdom, (2) University of Surrey, United Kingdom, (3) Lundbeck B.V., Netherlands, (4) Lundbeck Ltd., Milton Keynes, United Kingdom

Introduction: To evaluate the efficacy of gaboxadol (GBX), a selective extra-synaptic GABA agonist, on sleep in a traffic noise model of transient insomnia
Methods: After a 2-night single-blind placebo run-in, 101 healthy subjects (20-78y) were randomized to receive GBX (n=50) or placebo (PBO, n=51) for 7 nights (N1-7). Treatment consisted of GBX (adults: 15mg and elderly ≥65y: 10mg) or PBO. During the treatment period both treatment groups were exposed to pre-recorded, random traffic noise throughout the night. Sleep was assessed using polysomnography and self-reported measures. Efficacy analysis used a longitudinal data analysis model of change from baseline with between-subject factor for treatment (GBX vs PBO) and covariates for baseline, age and (within-subject) night (N1-7). Overall treatment effects (N1-N7) and treatment effects for N1 are reported.
Results: The model caused the most severe disruption on N1 (PBO versus baseline). Subsequent results are versus PBO change from baseline. GBX reduced latency to persistent sleep overall (N1-7) by 4.5mins and on N1 by 11mins (both $p<0.05$). GBX increased total sleep time (TST) overall by 16mins ($p<0.001$) and on N1 by 38mins ($p<0.0001$). There was a tendency ($p<0.059$) to reduce number of awakenings overall and significantly on N1 ($p<0.05$). Wakefulness after sleep onset was reduced by 11mins overall ($p<0.01$) and by 29mins on N1 ($p<0.0001$). GBX increased slow wave sleep (SWS) consistently throughout ($p<0.05$). GBX reduced self-reported sleep onset overall by 11mins and on N1 by 28mins (both $p<0.05$). GBX increased self-reported TST overall by 18mins ($p<0.05$) and on N1 by 54mins ($p<0.01$). Subjective sleep quality improved overall ($p<0.01$) and on N1 ($p<0.0001$). All adverse events (AEs) were mild-to-moderate with no serious AEs (# subjects with AEs: GBX=78%, placebo=82%).
Conclusion: Gaboxadol significantly reduced the detrimental effects of traffic noise on sleep initiation and maintenance and also enhanced SWS. Gaboxadol was well tolerated.
Support (optional): H. Lundbeck A/S, Copenhagen, Denmark.

0743

MICROSTRUCTURE OF SLEEP IN PARADOXICAL INSOMNIA

Ozone M,[1] Yagi T,[2] Itoh H,[1] Tamura Y,[3] Inoue Y,[4] Uchimura N,[5] Nakayama K,[1] Terzano M,[6] Shimizu T[7]
(1) The Jikei University School of Medicine, Tokyo, Japan, (2) Ohta General Hospital, Tokyo, Japan, (3) Asahikawa Medical College, Tokyo, Japan, (4) Japan Somnology Center, Neuropsychiatric Research Institute, Tokyo, Japan, (5) Kurume University, Fukuoka, Japan, (6) Akita University, Parma, Italy, (7) Akita University, Akita, Japan

Introduction: Paradoxical insomnia (PI) is characterized as a complaint of severe insomnia that occurs without evidence of objective sleep disturbance, and without daytime impaired performance. There is dissociation between subjective and objective sleep assessment. However, a distinct finding in the macrostructure of sleep has not been found in PI by means of polysomnography (PSG) using conventional analysis methods.
This study aimed to clarify the microstructure of sleep in PI patients by means of the cyclic alternating pattern (CAP) method.
Methods: Step 1
1) 35 patients suffering from insomnia, meeting Criteria A, objective sleep quality was assessed using PSG. PSG recording was started from habitual bedtime for 8 hours.
Criteria (A):
a) Subjective sleep latency <30 minutes.
b) Habitual total sleep time > 6.5 hours.
2) Referring to the results of PSG (Step1), patients meeting Criteria B were defined as having PI in this study.
Criteria (B):
a) Sleep latency <15 minutes.
b) Total sleep time >6.5 hours.
c) AHI >10, or PLMI >5 were excluded.
Step 2
The PSG data from the PI patients was analyzed visually using the CAP method (Terzano, 2001).
Results: 1. 13 insomniac patients were defined as PI. (mean age: 40.7±11.9 y (M/F: 8/5))
2. Mean CAP rate (%) was 43.9±10.2.
3. CAP rate (%) in Younger PI patients (=< 40y) (YP) was significantly higher than those in elderly PI patients (>40y) (EP). (YP 49.4±11.1/, EP 37.4±3.4)
4. The mean of the difference in CAP rate (%) between the YP value and the standard value (Parma data) of each age was 17.4±11.0.
Conclusion: From the above-mentioned results, the CAP rate was higher than those of normal subjects especially in patients aged <40 years. This finding suggests that instability of sleep patterns in the younger generation may be a possible cause of PI.

0744

EFFECT OF SELECTIVE SWS/SWA DISRUPTION AND AGE ON DAYTIME SLEEP PROPENSITY AND ITS TIME COURSE IN HEALTHY SUBJECTS AGED 20-83

Dijk D,[1] Groeger J,[1] Stanley N,[2] Deacon S[3]
(1) University of Surrey, Guildford, United Kingdom, (2) University of Surrey, United Kingdom, (3) Lundbeck Ltd., Milton Keynes, United Kingdom

Introduction: To assess the contribution of SWS/SWA and age to daytime sleep propensity as quantified by the multiple sleep latency test (MSLT) at baseline and after two nights of selective SWS/SWA deprivation.
Methods: After two screening visits, including a polysomnography

(PSG) screening night and MSLT day, healthy young (20-30y, n=44), middle-aged (40-55y, n=35) and older (66-83y, n=31) subjects, without sleep complaints, received 2 nights of selective SWS/SWA disruption or no disruption, following a baseline assessment, in a parallel group design. Prior to baseline, subjects were scheduled to 8h sleep episodes for ≥5 nights at home. SWS/SWA disruption was achieved through acoustic stimulation contingent upon appearance of delta waves in the ongoing sleep EEG. PSG was performed on all laboratory nights (23:00-07:00h) and MSLT on all days (at 09:00, 11:00, 13:00, 15:00 and 17:00h).
Results: Aging was associated with a significant ($p<0.001$) reduction in SWS and SWA, and increase in number of awakenings at baseline. These age-related changes in nocturnal sleep were accompanied by an age-related reduction in sleep propensity. At baseline, older and middle-aged subjects´ daily mean MSLT were significantly longer than in young subjects ($p<0.001$, both cases) and daily mean MSLT in older subjects tended to be longer than in middle-aged subjects ($p=0.057$). These age-related increases in MSLT were observed at all 5 times of day. Experimental reduction of SWS/SWA led to an increase in sleep propensity in all three age groups. Compared with the control group, a significant reduction in daily mean MSLT was observed after one night of SWS/SWA disruption in young subjects and was significant in all three age groups after two nights of SWS/SWA disruption ($p< 0.05$ in all cases).
Conclusion: Experimental reduction of SWS/SWA leads to an increase in sleep propensity whereas healthy aging is associated with a reduction in SWS/SWA and sleep propensity.
Support (optional): H. Lundbeck A/S, Copenhagen, Denmark

0745

PROSPECTIVE COMPARISON OF SUBJECTIVE AROUSAL DURING THE PRE-SLEEP PERIOD IN PRIMARY SLEEP-ONSET INSOMNIA AND NORMAL SLEEPERS

Espie C,[1] Robertson J,[2] Broomfield N[2]
(1) University of Glasgow Sleep Research Laboratory, Glasgow, United Kingdom, (2) University of Glasgow Sleep Research Laboratory, Scotland, United Kingdom

Introduction: Psychophysiological insomnia (PI) is the most common insomnia sub-type, representing 12-15% of all sleep centre referrals. Diagnostic guidelines describe PI as an intrinsic sleep disorder involving both hyperarousal and learned sleep-preventing associations. Whilst evidence for the first component is reasonably compelling, evidence for learned (conditioned) sleep effects is markedly lacking. Indeed, to date no study has attempted to capture directly the conditioned arousal effect assumed to characterise the disorder.
Methods: The present study explored variations in subjective arousal over time in 15 PI participants (sleep onset type) and 15 Normal Sleepers (NS). Self-report measures of cognitive arousal, somatic arousal and sleepiness were taken at three time points: three hours before bedtime (early to mid-evening); one hour before bedtime (late evening); and in the bedroom at lights out (bedtime) across four, 24-hour cycles. Fluctuations in mean arousal and sleepiness values, and in day-to-day variation were examined using analyses of variance.
Results: Four out of seven analyses showed significant effects in support of less de-arousal at bedtime in the PI group. Furthermore, analyses of change scores consistently found that there were more sizeable reductions in cognitive activation, and greater increases in sleepiness, in normal sleepers in the period from 1 hour prior to bedtime and bedtime itself than there were in people with insomnia. There was also evidence from standard error data of considerably homogeneity in such de-arousal responses in normal sleepers. Participants with PI were significantly more cognitive aroused and significantly less sleepy relative to NS, within the bedroom environment. In contrast, only one analysis indicated general cognitive hyperarousal, present at all three time points.
Conclusion: As far as we are aware, this is the first study to examine systematically the process of self-reported de-arousal, during the pre-sleep period, in people with insomnia relative to normal sleepers. The results support the tenet of conditioned mental arousal to the bedroom, although competing explanations cannot be ruled out.
Support (optional): Supported in part by research funding from Chief Scientist Office (CZG/2/187) and by the Dr. Mortimer and Theresa Sackler Foundation

0746

SPECTRAL EEG PROFILE OF GABOXADOL DURING NREM SLEEP IN A MODEL OF TRANSIENT INSOMNIA: RESULTS FROM A LARGE MULTI-CENTER CLINICAL STUDY USING AUTOMATED SOFTWARE

Ma J,[1] Svetnik V,[2] Tymofyeyev Y,[2] Ray S,[2] Deacon S,[3] Walsh J[4]
(1) Merck Research Laboratories, Rahway, NJ, USA, (2) NJ, USA, (3) Lundbeck Ltd., Milton Keynes, United Kingdom, (4) Sleep Medicine and Research Center, MO, USA

Introduction: In an earlier crossover study of transient insomnia, gaboxadol, a selective extrasynaptic GABAA agonist (SEGA), has shown enhancement of low frequency EEG activity in NREM sleep. The objective of this present analysis was to evaluate the spectral profiles of differing doses of gaboxadol compared with placebo using automated software in a large multi-center parallel group study using model of transient insomnia.
Methods: Healthy subjects (18-64y) completed a randomized, double-blind, parallel-group study in which the sleep period was advanced 4h from habitual sleep time. Polysomnographic (PSG) recordings were used to compare gaboxadol 10mg (N=254) and 15mg (N=247) versus placebo (N=254). Spectral analysis was performed by custom developed high-throughput automated software which includes artifact detection and spectrum estimation algorithms. NREM specific power spectra were computed as the average of power spectra of 4 second, artifact-free EEG intervals located within NREM. In addition, average power in the slow wave activity (SWA) band and 7 other frequency bands encompassing 0.5-32 Hz was calculated. A linear mixed effect statistical model was used to compare log-transformed power spectra relative to baseline, between placebo and gaboxadol treatments with adjustment for multiplicity
Results: All results are in comparison to placebo. Gaboxadol significantly increased spectral power in the lower frequency bands (SWA [0.75-4.5Hz] and theta activity [4.5-7.75Hz]) in a dose-dependent manner (all $p<0.001$). Changes in alpha activity [7.75-12.0 Hz] were not statistically significant. Power in the spindle frequency range [11.5-15Hz] was reduced ($p<0.05$) with 15mg. There were no statistically significant effects on beta activity [13-32Hz].
Conclusion: Gaboxadol clearly and consistently increased SWA and theta activity in an apparent dose-dependent manner. These observed differences in NREM EEG power spectra are likely consequences of the mechanism of action for gaboxadol.
Support (optional): Merck Research Laboratories, West Point, PA

0747

WHO IS THE INSOMNIAC WOMEN IN MENOPAUSE LOOKING FOR SLEEP ASSISTANCE IN A SLEEP LABORATORY CENTER?

Hachul De Campos H,[1] Brandao L,[2] Bittencourt L,[3] Baracat E,[2] Tufik S[1]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, SP, (3) Univ Fed Sao Paulo, Sao Paulo, Brazil

Introduction: Questionnaire-based studies reveal that menopausal women frequently complain of sleep problems. Some studies show that women who exhibit hot flushes also experience more waking episodes, changes in sleep stages and less sleep efficiency. Sometimes they complain of insomnia and have another sleep disturbance such as apnea or periodic leg syndrome. Accounts from the literature remain unresolved in regard to sleep improvement with hormone therapy (HT). The aim of this study was to see the profile of menopausal women complaining of insomnia. Who are the women looking for help, if they have already been medicated and if they are under menopause treatment
Methods: Two hundred and six menopausal women who looked for treatment for insomnia after add were interviewed. They were questioned about frequency of insomnia, about type of insomnia, i.e., if they were having difficulty in falling asleep, experienced arousals during the night or had woken up earlier than planned. type of insomnia, (initial, middle, final insomnia). They were questioned also about age, years of menopause. If they were having hot flushes, how long do they take to sleep, how long do they sleep, if they had already done any polysomnography, if they were taking any medications, if they had any other disease, if they were under hormone therapy, or isoflavone.
Results: Age mean was 55 (min 37 and max 66 years old) Years of menopause vary form 0 to 43 years, mean 7,9. 40 women referred osteoporosis (19%), 70 were with HAS (33,9%), 12 had diabetes (5,8%), 142 complaint of hot flushes (68,9%) only 15 women had already done polysomnography (7%) only 5 women took isoflavone, and 5 were taking TH. So, 10 out of 206 (4,8%)were doing some kind of treatment to menopause. The complain of hot flushes was more frequent in young women than in old ones (p=0,0004). 8 % of them were using benzodiazepincs. The women who complaint of insomnia for more than 3 times a week referred longer sleep latency (p=0,03). Nevertheless there was no association between hot fhushes and type of insomnia (p=0,32,,0,22, 0,73).
Conclusion: We may be understimating the diagnosis of apnea in women complaining of insomnia, because in general they don´t do PSG. As well as that, most of them are not doing any sort of treatment for menopause and may be suffering from climacteric syndrome.
Support (optional): CNPq, Fapesp and AFIP.

0748

WILL MEN SEEK - AND RECEIVE - HELP FOR THEIR INSOMNIA?: AN EXPLORATORY STUDY

Brown J,[1] Archer M,[2] Idusohan H,[3] Shirley S,[3] Espie C[4]
(1) King's College London, London, London, United Kingdom, (2) Institute of Psychiatry, Kings College London, London, London, United Kingdom, (3) South London and Maudsley NHS Trust, London, London, United Kingdom, (4) University of Glasgow, Glasgow, United Kingdom

Introduction: Whilst effective psychological treatments like CBT-I have been developed for insomnia, access has been difficult given the limited awareness of them amongst referrers. In addition to the low capacity among services to provide CBT-I, there is a gender imbalance and men tend to seek help less frequently for their insomnia than women.
Methods: This paper describes the development and evaluation of a pilot study of CBT-I workshops, each for up to 25 men. These were designed specifically to be acceptable to men and were offered over a 6 month period. The CBT-I programme was based on Morin and Espie (2003), and adapted into a self-referral one-day workshop format specifically designed to improve access (Brown et al 1999).

Participants were asked to complete assessments both before and 6 weeks after each workshop. Assessment measures used included the Insomnia Severity Index (ISI) and the Beck Depression Inventory (BDI). Workshops were held on Saturdays in leisure centres. A brief satisfaction questionnaire was administered at the end of the workshop day.
Results: These workshops attracted a large number of enquiries from men (n=118), of whom 73 attended Introductory Talks preceding the workshops. Of these, 48.6% had never sought help from their GP, 65.8% suffered from clinical insomnia (ISI) and 61.6% were experiencing elevated depression symptoms (BDI over 10). At follow-up (n=53), the workshops were found to be effective in reducing insomnia ($t=7.34$, $p<0.001$) and depression ($t=2.64$, $p<0.01$). Satisfaction ratings with the workshops were very high.
Conclusion: These self-referral CBT-I workshops did successfully attract men needing help, but who may not have sought help from their GPs, and led to reductions in insomnia and depression. In view of these encouraging results, further work is proposed. This will include broadening the approach to include women, in a larger study with a longer-term follow-up.

0749

PAIN, SLEEP AND MOOD OUTCOMES IN CHRONIC PAIN PATIENTS FOLLOWING COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA

Pigeon W,[1] Jungquist C,[2] Matteson S,[2] Swan J,[2] Stoll J,[2] O'Brien C,[2] Taylor C,[2] Perlis M[2]
(1) University of Rochester, Rochester, NY, USA, (2) University of Rochester, NY, USA

Introduction: Insomnia is a highly prevalent co-morbid disorder in chronic pain patients (CPP). To date, one clinical trial has assessed cognitive behavioral therapy for insomnia (CBT-I) in this population and found that CBT-I delivered in a group format was effective in treating insomnia. We present preliminary findings from two ongoing trials assessing individual CBT-I therapy in CPP´s compared to control conditions.
Methods: Twenty-three subjects (16 females) with chronic, non-malignant pain originating in the spine with mean BMI of 26.8(4.3) and age of 47.4(8.9) were enrolled in one of two, randomized clinical trials contrasting CBT-I to a control condition. Subjects in the treatment group (n=16) received 8 sessions of CBT-I from one of two therapists. Subjects randomized to the control condition (n=7) were assigned to one of two control conditions: non-directive, supportive therapy or a wait list condition. The treatment and control groups did not differ with respect to any baseline variables.

Average weekly values of sleep latency (SL), wake after sleep onset (WASO), sleep efficiency (SE) and total sleep time (TST) were derived from daily sleep diaries for two weeks prior to the treatment phase, throughout treatment and for two weeks at a 3 month follow-up. The Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), Pain Disability Index (PDI), Multidimensional Pain Inventory (MPI), Beck Depression Inventory (BDI) were completed at baseline, post-treatment, and follow-up. Separate two-tailed, paired-sample t-tests were

performed to compare pre to post differences for each group. Pre to post change scores were calculated to assess between-group differences by independent samples t-tests.
Results: CBT-I for CPP´s had a significant positive effect on pre-post sleep diary measures of SL, WASO, and SE and scores on the ISI and PSQI (all p values<.001), whereas the control group experienced a significant reduction in SE (p=.04) only. In addition, the treatment group had significant reductions on the BDI (p=.001), PDI (p=.01), and MPI subscales for pain severity (p=.003) and pain interfering with life (p=.004). The control group had a reduction in pain interference (p=.05). The majority of gains were maintained at follow-up (total n=15).

Compared to controls at post-treatment, the tx group had greater improvements in SL, WASO, and SE (all p<.01) and on the ISI (p=.03) and PSQI (p=.05); pain and mood improvements were not significantly greater in the treatment group, though they trended in this direction.
Conclusion: These preliminary results provide additional evidence that that CBT-I for insomnia that is co-morbid with chronic pain can be effectively treated in the presence of ongoing pain. Further, these data suggest that the benefits CBT-I interventions may generalize to pain and mood outcomes, but this remains a trend at this stage in the ongoing trials.
Support (optional): NIH NS049789 (WRP); NIH NR009080 (MLP); UR School of Nursing data management team (CJ).

0750

EFFICACY AND SAFETY OF DOXEPIN 3 AND 6 MG IN ADULTS WITH PRIMARY INSOMNIA

Lankford A,[1] Hull S,[2] Scharf M,[3] Schwartz H,[4] Seiden D,[5] Jochelson P,[6] Rogowski R,[7] Roth T,[8] Group S[9]
(1) Sleep Disorders Center of Georgia, Atlanta, GA, USA, (2) Vince and Associates Clinical Research, Overland Park, KS, USA, (3) Tri-State Sleep Disorders Center, Cincinnati, OH, USA, (4) Miami Research Associates, Miami, FL, USA, (5) Broward Research Group, FL, USA, (6) Somaxon Pharmaceuticals, Inc, CA, USA, (7) Somaxon Pharmaceuticals, CA, USA, (8) Detroit, MI, USA, (9) CA, USA

Introduction: The efficacy and safety of doxepin (DXP) 3 and 6mg were evaluated in adults with primary insomnia.
Methods: This was a randomized, double-blind, placebo-controlled study of adults with insomnia. Subjects reported ≥3 months of DSM-IV-TR primary insomnia, with confirmation by polysomnography (PSG). Subjects were randomly assigned to nightly doses of placebo (PBO; N=73), DXP 3mg (N=75) or DXP 6mg (N=73) for 35 days. Efficacy was evaluated objectively (PSG) and subjectively; data from the first and last PSG assessment points, nights 1 (N1) and 29 (N29), are reported. PSG endpoints included wake-after-sleep-onset (WASO), latency-to-persistent-sleep (LPS), and sleep efficiency (SE; overall and by third-of-the-night). Primary endpoint was N1 WASO.
Results: Compared with PBO, DXP 3 and 6mg statistically significantly improved WASO at N1 (p<0.0001) and N29 (3mg p=0.0299; 6mg p=0.0012), LPS at N1 (3mg p=0.0110; 6mg p=0.0018), and overall SE at N1 (p<0.0001) and N29 (3mg p=0.0262; 6mg p=0.0003). The significant differences on N1 LPS were not observed on N29, primarily due to PBO improvement. DXP 3 and 6mg generally demonstrated statistically significant improvements in SE by third-of-the-night on N1 and N29. There were no significant group differences in next-day residual sedation, incidence of adverse events was similar between groups, and sleep architecture was generally preserved.
Conclusion: In adults with insomnia, DXP 3 and 6mg were well-tolerated and produced significant improvement on the primary endpoint WASO and on multiple secondary endpoints on N1; these improvements were maintained on N29 for sleep maintenance and duration endpoints. On sleep onset, there was significant improvement in LPS at N1 with no loss of drug effect at N29, though statistical significance was not maintained. Additionally, the incidence of adverse events was comparable to PBO; there were no reports of amnesia, no reports of anti-cholinergic effects, and no significant hangover/next-day residual effects.
Support (optional): This study was fully funded and supported by Somaxon Pharmaceuticals, Inc., San Diego, CA.

0751

THE CLOCK AS A FOCUS OF SELECTIVE ATTENTION IN THOSE WITH PRIMARY INSOMNIA

Woods H, Marchetti L, Biello S, Espie C
University of Glasgow, Glasgow, Scotland, United Kingdom

Introduction: Espie et al (2006) propose a route into primary psychophysiological insomnia (PI) along the attention-intention-effort pathway, a process hypothesized to inhibit the automaticity of normal good sleep (Espie, 2001). Within this model, selective attention to sleep cues is viewed as the start point of sleep dysregulation in PI. Likewise, Harvey's (2002) cognitive model implicates monitoring of internal and external cues in the maintenance of insomnia. Perlis et al's (1997) neurocognitive model also points to the importance of information-processing theory.
Methods: A Posner paradigm investigated clock time as a focus of selective attention in a 2x2 between participants design. Twenty-five individuals with PI and 25 normal sleepers (NS) participated. Reaction time (RT) responses to probes (: and ..) were obtained from a computerized task presenting clock times (from the normal sleep period). The RT of interest was time taken to respond to the target, when invalidly cued (that is probe appearing in the incorrect spatial location).
Results: Comparisons were made between means for selected factors. Significant differences were found between NS and PI for invalid trials ($F(1,84)=6.9$ $p<0.05$) and between invalid and valid trials for PI ($F(1,84)=19.5$ $p<0.00001$). No significant difference was found between NS and PI on the Beck Depression Inventory. PI scored significantly higher on measures of state anxiety ($p<0.05$) but no differences were found with NS on trait anxiety.
Conclusion: This study provides further evidence of attentional bias to sleep-related stimuli in PI. In this experiment we used representations of clock times. We have found similar results previously using semantic and pictorial stimuli. The Posner paradigm also enabled us to investigate component processes in attentional bias. The finding of significant effects associated with invalid cueing suggests that people with PI have particular difficulties disengaging from sleep-salient stimuli. This is consistent with the notion of sleep preoccupation.
Support (optional):

0752

SLEEP DURATION IN A SAMPLE OF BLACK AND WHITE AMERICANS: RESULTS OF THE NATIONAL HEALTH INTERVIEW SURVEY

Nunes J,[1] Jean-Louis G,[2] Zizi F,[3] Casimir G,[2] Visan A,[2] Latortue K,[2] Kasapira S[2]
(1) Sophie Davis School of Medicine, CCNY, Brooklyn, NY, USA, (2) State University of New York Health Science Center at Brooklyn, NY, USA, (3) State University of New York Health Science Center at Brooklyn, Brooklyn, NY, USA

Introduction: Inconsistent findings are reported regarding ethnic differences in sleep patterns, which have been attributed to differences in epidemiologic designs, varying cohorts, and inadequate sampling. This study compares sleep duration in a sample of Black and White Americans in the National Health Interview Survey (NHIS).
Methods: Data were obtained from 29,818 Americans (age range: 18-85 years) participating in the 2005 NHIS. The NHIS is a cross-sectional household interview survey, which uses a multistage area probability design permitting representative sampling of U.S. households. Probability samples of the civilian population of all 50 states and DC were obtained. During face-to-face interviews conducted by trained interviewers from the U.S. Census Bureau, respondents provided sociodemographic data and information about physician-diagnosed chronic conditions. They also estimated habitual sleep duration and rated their mood. The present analysis included data from Whites (85%) and Blacks (15%) of both genders: men=44% and women=56%.
Results: Black and White respondents differed regarding the prevalence of hypertension (B=36% and W=27%), heart disease (B=6% and W=8%), cancer (B=4% and W=8%), diabetes (B=12% and W=8%), and arthritis (B=22% and W=24%). Results of Fisher´s exact tests indicated Blacks were less likely to report sleeping 7hrs (population mode) than their counterparts [23% vs. 30%; $\chi^2 = 94$, $p < 0.0001$]. There was a greater likelihood for Blacks to experience both short sleep (5 hrs) [12% vs. 8%] and long sleep (9 hrs) [11% vs. 9%]; $\chi^2 = 155$, $p<0.0001$. Based on logistic regression analysis, ethnicity remained a significant predictor of sleep duration [Wald=82, $p<0.0001$] after adjustment for differences in sociodemographic factors, depression, physical activity, and medical comorbidities.
Conclusion: Regardless of geographic residence, Blacks reported both short and long sleep, suggesting greater variability in their habitual sleep time. Blacks might be at increased risks of developing diseases associated with short sleep, as may be the case in the metabolic syndrome.
Support (optional): This research was supported by funds from NIH (1R24MD001090).

0753

CARDIOVASCULAR CHANGES ASSOCIATED WITH MICRO-AROUSALS IN PRIMARY INSOMNIACS AND NORMAL SUBJECTS.

Fradette L,[1] Pennestri M,[1] Pelletier S,[2] Montplaisir J,[1] Morin C,[3] Colombo R,[4] Lanfranchi P[1]
(1) Centre d'etude du sommeil, Hopital du Sacre-Coeur, Montreal, Quebec, Canada, (2) Centre d'etude du sommeil, Hopital de Sacré-Coeur, Montreal, Quebec, Canada, (3) Laval University, Ste-Foy, Quebec, Canada, (4) (4) Department of Bioengineering, Salvatore Maugeri Foundation, Veruno, Italy

Introduction: Subjects with primary insomnia have higher sympathetic activity during steady sleep compared to controls. The aims of this study were, firstly, to compare heart rate (HR) and blood pressure (BP) changes associated with micro-arousals (MAs) in subjects with chronic primary insomnia and controls. Secondly, to measure the relationship between MA-related cardiovascular changes and demographic, clinical and sleep variables
Methods: We studied 7 subjects with chronic primary insomnia (4 women; age 44.8 ± 6.6 years; BMI=25.1 ± 5.3 Kg/m^2) and 7 age, sex and BMI matched controls. Subjects underwent a measure of brachial arterial BP in sitting position in the evening, followed by full polysomnography, which also included beat-to-beat non invasive BP (Portapres). Ten MAs occurring in stage 2 NREM sleep were selected for cardiovascular analyses in each subject. For each MA, the increase (Δ) in HR, systolic BP (SBP), diastolic BP (DBP) were calculated as the difference between the peak value and the baseline (i.e., the mean value for the beats -10 to -2, before the MA). The increments associated to MAs were compared between insomniacs and controls by unpaired t-test. Correlation analyses between cardiovascular changes (ΔHR, ΔSBP and ΔDBP) and age, BMI, clinical BP, and sleep measures (sleep latency, sleep efficiency, % sleep stages, MA index) were also assessed in all subjects pulled together.
Results: MA-related cardiovascular responses were not different between insomniacs and controls (ΔHR: 5±3 vs 6±3 bpm, p=ns; ΔSBP: 19±5 vs 16±6 mmHg, p=ns; ΔDBP: 9±3 vs 8±3 mmHg, p=ns). There was no correlation between cardiovascular changes and age and sleep variables. By contrast, ΔSBP correlated with BMI ($R=0.57$, $p<0.05$) and evening brachial SBP ($R=0.71$, $p<0.01$).
Conclusion: Cardiovascular responses associated with MAs do not differ between insomniacs and controls. BMI and clinical blood pressure appear to be important determinants of blood pressure responses to cortical arousals.

0754

INSOMNIA AND DAYTIME FUNCTIONAL IMPAIRMENT: A PILOT STUDY OF WHETHER ETHNOGRAPHIC RESEARCH HAS A ROLE IN REFINING CURRENT ASSESSMENT MEASURES

Fox S,[1] Buysse D,[2] Grubb W,[3] Ancoli-Israel S[4]
(1) Private Practice, Valatie, NY, USA, (2) University of Pittsburgh, Pittsburgh, PA, USA, (3) Neurocrine Biosciences, Inc, San Diego, CA, USA, (4) University of California, San Diego, San Diego, CA, USA

Introduction: Daytime symptom reports in insomnia are typically not matched in severity by objective neuropsychological and psychomotor performance measures. The goal of the current study was to evaluate the ecological validity of commonly used tests of functioning in insomnia to determine whether the lack of objective daytime deficits might be partly attributable to not measuring key impairment domains.
Methods: Ethnographic data were obtained on two samples of insomnia patients, in the home (N=24, ages 19-78, 75% women) and work environments (N=24, ages 18-65, 78% women). Insomnia was identified by a standard telephone screening questionnaire concerning symptoms and treatment. Complaints of daytime impairment were documented by observation, and were compared to two sets of standard daytime impairment measures: (1) common objective measures (eg, DSST, reaction time tasks); and (2) items on general functioning measures (eg, Insomnia Impact Scale). For the current pilot study, analysis was limited to descriptive statistics (eg, mean frequency counts, and percent, of specific types of impairment).
Results: Ethnographic evaluations yielded multiple domains which were not specifically assessed, or were minimally covered, on common objective measures of performance or general functional measures. Relevant domains to insomnia sufferers included interpersonal deficits (irritability, impatience), executive function deficits (problem solving, organizational abilities), reduced creativity, and delays in initiating projects (procrastination).
Conclusion: Common measures of daytime functional impairment may miss several key assessment domains identified in this ethnographic study. This may partially account for the relative lack of measurable daytime consequences found in previous studies of insomnia. Ethnographic research may provide a novel, qualitative method for improving the ecological validity of daytime impairment measures. Although qualitative research cannot directly confirm whether insomnia results in significant daytime impairment, quantitative research is more likely to identify such deficits if it uses functional and performance

measures with greater ecological and external validity.
Support (optional): Neurocrine Biosciences, Inc.

0755

PREVALENCE AND CLINICAL CHARACTERISTICS OF SPECIFIC INSOMNIA SUBTYPES: RESULTS OF A RANDOM DIGIT DIALING STUDY

Culpepper L,[1] Grubb W,[2] Ancoli-Israel S[3]
(1) Boston University Medical Center, Boston, MA, USA, (2) Neurocrine Biosciences, Inc, San Diego, CA, USA, (3) University of California, San Diego, San Diego, CA, USA

Introduction: To examine the prevalence and clinical characteristics of subtypes of insomnia in the general population.
Methods: A random digit dialing survey was performed with a sample of 14,997 community-dwelling adults in the US. Self-reported insomnia symptoms were defined using DSM-IV criteria based on a structured questionnaire. Individuals meeting DSM-IV criteria for insomnia subtypes were compared to individuals reporting insomnia who did not meet full criteria.
Results: A total of 1,270 individuals (8.5%) met DSM-IV criteria for insomnia by self-report and an additional 3,489 (23.3%) reported insomnia which did not meet DSM-IV criteria. Not included in the current analysis were individuals 1222 (8.1%) who reported non-restorative sleep without initial/middle insomnia, and 487 (3.2%) individuals whose insomnia was limited to early morning awakening. In the subgroup of individuals with DSM-IV insomnia, 9.5% were initial-only, 3.8% were middle-only, and 86.7% reported a combination of initial, middle, early awakening subtypes. Among individuals with insomnia symptoms which did not meet DSM-IV criteria, 20.1% were initial-only, 15.6% were middle-only, and 64.3% reported a combination of initial, middle, early awakening subtypes. A physician diagnosis of insomnia was low in the DSM-IV group, ranging from 12.5% for middle-only subtype up to 24.2% for combined subtypes. Pharmacologic treatment for insomnia (hypnotic and non-hypnotic) was also low in the DSM-IV group, ranging from 19% for middle-only subtype up to 31.5% for combined subtypes. Among individuals with insomnia that did not meet DSM-IV criteria, levels of insomnia chronicity were high (median duration >1 year). Furthermore, 37.8% of the non-DSM-IV insomnia subgroup reported experiencing insomnia ≥3 times per week, while 24.3% reported impaired daytime functioning. Few individuals in the early awakening only subgroup reported daytime impairment (11.8%).
Conclusion: DSM-IV insomnia appears to be under-diagnosed and under-treated. A significant number of individuals with insomnia not meeting DSM-IV criteria experience significant daytime impairment and symptom frequency.
Support (optional): Neurocrine Biosciences, Inc; and Pfizer Inc during the period of the alliance with Neurocrine Biosciences Inc.

0756

THE RELATIONSHIP BETWEEN ANXIETY AND CARDIOVASCULAR SYMPTOMS IS MEDIATED BY INSOMNIA

Zizi F,[1] Jean-Louis G,[2] Magai C,[3] Consedine N,[3] Casimir G,[2] Mckenzie D,[2] Clark L[2]
(1) State University of New York Health Science Center at Brooklyn, Brooklyn, NY, USA, (2) State University of New York Health Science Center at Brooklyn, NY, USA, (3) Long Island University, NY, USA

Introduction: Anxiety and insomnia are both associated with cardiovascular symptoms (CVS). In this study, we assessed whether the relationship between anxiety and CVS symptoms depends on the likelihood of experiencing insomnia.
Methods: Independently living women (n = 1440; mean age = 59.36 ± 6.53 yrs) in Brooklyn, NY volunteered. The sample comprises African Americans (22%), English-Speaking Caribbeans (22%), Haitians (22%), Dominicans (12%), Eastern Europeans (11%), and European Americans (11%). Recruitment was done using a stratified, cluster sampling technique. During face-to-face interviews, we obtained sociodemographic data and ratings on physical health, health beliefs, access to health care, and stress levels. We used the State-Trait Anxiety Inventory to assess anxiety level.
Results: Overall, 56% of the sample reported insomnia; 46% reported CVS, and 54% were classified as highly anxious. As expected, there was a greater likelihood for highly anxious women and those experiencing insomnia to report CVS [rs = 0.31and rs = 0.32, respectively]. Of the women reporting CVS, 63% were highly anxious [$\chi^2 = 44.86$] and 73% experienced insomnia [$\chi^2 = 139.06$]. In logistic regression analysis, the adjusted odds ratios for reporting CVS were 1.39 for insomnia and 2.79 for anxiety. With control for insomnia, we observed a three-fold reduction in the magnitude of the associations between anxiety and CVS [rp = 0.09]. Stepwise adjustments for sociodemographic factors (i.e., age, ethnicity, education, and income), risk markers (i.e., BMI, stress, smoking, and alcohol), and factors anchoring health beliefs and access to health care showed lesser impact on the relationships [rp = 0.14; rp = 0.16; rp = 0.19, respectively]. With simultaneous control for those covariates, the correlation was: [rp = 0.13]. $p<0.01$, $p<0.001$.
Conclusion: Results are consistent with previous studies finding associations of anxiety and insomnia to CVS. The relationship between anxiety levels and CVS is jointly dependent of the likelihood of experiencing insomnia.
Support (optional): This research was supported by funds from NIH (1R24MD001090 and SO6GM54650).

0757

MENOPAUSE AND HORMONE REPLACEMENT THERAPY: EFFECTS ON OBJECTIVE SLEEP PATTERNS

Bixler E,[1] Vgontzas A,[2] Lin H,[2] Vela-Bueno A[2]
(1) Pennsylvania State University, Hershey, PA, USA, (2) Pennsylvania State University, PA, USA

Introduction: Disturbed sleep is a common complaint of women entering the menopause phase of life. To date there have been limited objective sleep data supporting these complaints from population samples. The purpose of this study was to evaluate the objective sleep patterns associated with menopause and hormone replacement therapy (HRT) in a large population sample from a subset of the Penn State Cohort.
Methods: We included subjects with an AHI < 5 and without a complaint of insomnia or excessive daytime sleepiness. This resulted in a sample of 1,324 subjects (609 men and 715 women) with a mean age of 48.6±13.6 years and an average BMI of 26.9±5.1 kg/m^2. For purposes of analysis we grouped the women into those who were pre- and postmenopausal and with and without HRT.
Results: In terms of sleep latency men did not differ from premenopausal women (Diff=1.6±2.7 min, P=0.56) or post menopausal women with HRT (Diff=5.6±3.7 min, P=0.13). Postmenopausal women without HRT had significantly higher sleep latency than both men (Diff=9.5±3.3 min, P<0.01) and postmenopausal women with HRT (Diff=15.1±4.2 min, P<0.01). In terms of the presence of slow wave (SW) sleep men were equally likely to have SW sleep compared to premenopausal women (OR=1.4, P=0.06). Men were less likely to have SW sleep than either postmenopausal women without HRT (OR=2.0,

P<0.01) or with HRT (OR=4.2, P<0.01). Further, postmenopausal women without HRT were less likely to have SW sleep than those with HRT (OR=2.1, P=0.01).
Conclusion: Menopause in the absence of HRT is associated with increased sleep latency and decreased SW sleep. HRT appears to protect women from these unfavorable changes. These data provide objective support for the complaint of poor sleep in postmenopausal women as well as the symptomatic relief reported by those on HRT.
Support (optional): NIH R01 HL40916, R01 HL51931

0758

AN ANALYSIS OF THE HEALTH AND PRODUCTIVITY BURDEN OF INSOMNIA AND ITS TREATMENT

Mendelson W,[1] Hawkins K,[2] Treglia M,[3] Healey, Sr P,[4] Wang S,[5] Harnett J[4]
(1) Consultant in Psychopharmacology, Galveston, TX, USA, (2) MI, USA, (3) Pfizer Inc, Groton, CT, USA, (4) Pfizer, Inc, New York, NY, USA, (5) Thomson Medstat, Cambridge, MA, USA

Introduction: The objective of this study was to estimate the direct and indirect costs of treated and untreated insomnia in an employed population.
Methods: The Medstat MarketScan Database was used for this study. Patients were included if they had a primary diagnosis of insomnia and/or received a new prescription for a non-benzodiazepine hypnotic medication between July 1, 1999 and June 31, 2003. Total healthcare costs, plus costs due to absenteeism, were calculated for the insomnia cohort (n=5,605), and for the propensity score matched non-insomnia cohort (total n=55,580), during 6-month pre-index and post-index periods. Change in total costs were compared using an ordinary least square model for insomnia patients who were treated versus not initially treated with a prescription hypnotic within 14 days of an insomnia diagnosis.
Results: Prior to matching, the insomnia cohort was slightly younger (40 vs. 42 years), more likely to be female (44% vs 31%), and had significantly more medical and psychiatric comorbidity than the non-insomnia cohort (Charlson Comorbidity Index score 0.32 vs. 0.11; P<0.01). After using propensity score matching and second stage regressions, the difference in average total expenditures in the 6-month post-index period between the cohort of insomnia patients (n=5,584) and matched non-insomnia controls—the burden of insomnia—was $2,738 (p<0.001). Healthcare utilization contributed to 84% of total insomnia-related costs, while absenteeism contributed 16%. Six-month costs for prescription hypnotics averaged less than $100 per patient. Both the treated and initially untreated insomnia patients experienced an increase in total costs; however, the increase for treated insomnia patients was $788 less than for the initially untreated insomnia patients.
Conclusion: Insomnia has a significant impact on direct healthcare cost, and on costs related to absenteeism. Insomnia treatment appears to be cost-effective relative to non-treatment, or delayed treatment.
Support (optional): Neurocrine Biosciences, Inc, and Pfizer, Inc during the period of the alliance with Neurocrine Biosciences Inc

0759

INDIRECT COSTS OF DSM-IV INSOMNIA IN THE U.S. LABOR FORCE

O'Sullivan A,[1] Thompson D,[1] Treglia M,[2] Healey P,[3] Harnett J,[4] Weinstein M,[5] Winkelman J[6]
(1) i3 Innovus, Medford, MA, USA, (2) Pfizer Inc, New York, NY, USA, (3) Pfizer Inc, New Yok, NY, USA, (4) Pfizer, Inc, New York, NY, USA, (5) Harvard School of Public Health, Boston, MA, USA, (6) Harvard School of Public Health, Brighton, MA, USA

Introduction: The objective of this study was to estimate the annual indirect costs of chronic primary insomnia in the U.S. labor force.
Methods: Based on a review of published epidemiological data, the prevalence of DSM-IV chronic primary insomnia was estimated to be 2.3%. Population-attributable risk (PAR) attribution techniques were used to estimate the annual indirect cost of chronic primary insomnia in the U.S. labor force. The total indirect cost reflects absenteeism from work directly attributable to an insomnia diagnosis, and productivity losses attributable to the insomnia-related incidence of accidents and chronic illnesses (depression, alcohol and/or substance abuse/dependence). Productivity costs for each insomnia-attributable health consequence were calculated by multiplying estimates of annual productivity costs among U.S. workers by the corresponding PAR for DSM-IV insomnia. The literature-derived relative risks were as follows (for persons with vs. without insomnia): depression, 5.4; auto accidents, 2.5; accidental injury at home or in public, 2.5; nicotine dependence, 2.4; alcohol abuse, 2.3; drug abuse, 1.9; work accidents, 1.5.
Results: The total annual indirect cost of chronic primary insomnia in the U.S. labor force is estimated to be $13.5 billion (in 2003 dollars). Nearly three-quarters of the total is for lost productivity due to disability, while the remainder is for premature deaths. Insomnia-attributable depression comprises 42% of the total indirect costs, while alcohol abuse and nicotine dependence account for 22% and 14%, respectively.
Conclusion: A DSM-IV diagnosis of insomnia leads to considerable productivity losses in the U.S. labor force. Interventions to reduce the severity of chronic primary insomnia among U.S. workers could substantially reduce its indirect cost burden.
Support (optional): Neurocrine Biosciences, Inc; and Pfizer Inc, during the period of the alliance with Neurocrine Biosciences Inc.

0760

IMPAIRED SLEEP-RELATED MEMORY CONSOLIDATION IN PRIMARY INSOMNIA

Nissen C,[1] Kloepfer C,[1] Nofzinger E,[2] Riemann D[3]
(1) University of Freiburg, Freiburg, Baden Wuerttemberg, Germany, (2) University of Pittsburgh, Pittsburgh, PA, USA, (3) Freiburg University Medical Center, Freiburg, Baden Wuerttemberg, Germany

Introduction: Studies in animals and healthy humans suggest that sleep facilitates the consolidation of new memories. The aim of this study was to test the hypothesis that patients with primary insomnia would demonstrate deficits in sleep-related memory consolidation.
Methods: 18 drug-free patients with primary insomnia (DSM-IV criteria, 11f, 7m, 45.5±4.5ys) and 34 sex, age and IQ matched good-sleeper controls (20f, 7m, 46.2±5.0ys) spent 1 night in the sleep-laboratory with polysomnographic monitoring from 10:30 pm to 6:30 am. Performance on a declarative visual/verbal memory task and a procedural mirror-tracing task was measured at 9:00 pm before and at 7:30 am after sleep. In addition, all subjects underwent a neuropsychological test-battery in the morning and evening.
Results: Polysomnography revealed significantly disturbed sleep in patients compared to controls (decreased sleep-efficiency, stage2%, REM%, increased waking%; MANOVA, p<0.05). Performance in all memory tasks before sleep did not differ between the groups. Patients showed a significantly attenuated overnight memory consolidation compared to controls (MANOVA with factors group and test-session, multivariate F=2.6, p=0.040). Univariate testing revealed that this effect was primarily driven by impaired procedural memory consolidation (mirror-tracing draw time: F=6.5, p=0.014; partial ETA squared, PETAS=0.12 indicating a medium/large effect size). Patients also

demonstrated a trend towards decreased verbal memory consolidation (F=3.1, p=0.084; PETAS=0.06, medium effect size), but no differences for visual memory consolidation (F=1.4, p=0.241; PETAS=0.03, small effect size). Neuropsychological testing showed no significant group differences for psychomotor functioning, vigilance or attention. Overnight memory consolidation was not correlated with standard polysomnographic parameters.
Conclusion: These findings support the hypothesis that patients with primary insomnia demonstrate deficits in sleep-related memory consolidation. The results were not explained by general neuropsychological deficits. The lacking correlation between memory and polysomnographic parameters might indicate that neural processes beyond the level of visually staged sleep might underlay the observed disruption of memory consolidation in primary insomnia.

0761

IMPROVEMENT IN EXERCISE PERFORMANCE IS ASSOCIATED WITH ENHANCED SLEEP IN OLDER ADULTS WITH CHRONIC INSOMNIA

Lu B,[1] Naylor E,[1] Ortiz R,[2] Ortiz N,[2] Huber G,[2] Keng J,[2] Zee P,[1] Wolfe L[1]
(1) Northwestern University, Chicago, IL, USA, (2) Northwestern University, IL, USA

Introduction: Chronic insomnia is common in older adults. Although previous studies have shown that regular physical activity can improve sleep quality in older adults, its mechanism remains unclear. The aim of the current study is to elucidate cardiopulmonary factors that may have an intermediary role between exercise and sleep in chronic insomniacs.
Methods: Sedentary older adults (>55 yo) with chronic insomnia were randomized to 16 weeks of either aerobic exercise regimen (30-40min at 60-75% of maximal heart rate (mHR), 3-5x/wk) plus sleep hygiene education or non-physical activity program plus sleep hygiene. Patients with other sleep disorders and unstable medical or psychiatric conditions were excluded. Cardiopulmonary exercise testing (CPET), sleep questionnaires, and three nights of in-patient polysomnography were performed at baseline and post-treatment. The change in pre- and post-treatment CPET data and sleep measures were correlated with Pearson correlation coefficient.
Results: Eleven subjects have completed the study to date. mHR in the exercise group changed by 9.4 ± 12.8 bpm vs. -2.5 ± 11.9 bpm in the standard care group ($p = 0.25$). Significant correlation exists between changes in mHR and changes in latency to stage 2 sleep ($r = -0.68$, $p < 0.05$), and correlation is also seen between changes in mHR and changes in PSQI ($r = -0.54$, $p = 0.08$). No significant correlations are detected between changes in VO2max or O2 pulse and sleep measures ($p > 0.5$).
Conclusion: In older subjects with chronic insomnia, an increase in the change of mHR with exercise correlates with improvements in objective and subjective sleep measures. This provides a mechanism which links exercise regimen to improved sleep. We hypothesize that VO2max is not associated with sleep parameters because older subjects may be unable to readily augment O2 pulse in response to exercise, thus limiting the change in VO2max during exercise.
Support (optional): Research was supported by National Institutes of Health grant #: P01 AG 114 12, 5T32 HL007909-09, T32 AG020506-02 and, in part, by M01 RR-00048 from the National Center for Research Resources

0762

THE ROLE OF TRAIT VULNERABILITY TO SLEEP DISTURBANCE IN THE MODERATION OF THE RELATIONSHIPS BETWEEN STRESS AND SLEEP QUALITY

Chen J,[1] Yang C,[2] Chou C[3]
(1) National Cheng-Chi University, Taipei City, Taiwan (R.O.C.), Taiwan, (2) Taiwan (R.O.C.), (3) National Cheng-Chi University, Department of Psychology, Taipei, Taiwan, Taipei City, Taiwan (R.O.C.), Taiwan

Introduction: Individual differences in the vulnerability to sleep disturbance has been proposed to predispose the development of chronic insomnia. The vulnerability to stress-related sleep disturbance, as measured by the Ford Insomnia Response to Stress Test (FIRST), was found to predict an individual´s first night of sleep in the laboratory and daytime sleepiness. This study is to further clarify the role of the trait vulnerability in the moderation of the effect of stress on sleep.
Methods: The participants consisted of 333 college students without reported insomnia. All participants completed the FIRST, the Pittsburgh Sleep Quality Index (PSQI), and a single-item visual analog scale for the degrees of stress experienced in the previous three days.
Results: Based on the median of FIRST score, the participants were divided into a high-vulnerability (HV) group and a low-vulnerability (LV) group. While both groups showed significant correlations between stress rating and global PSQI score, the HV group demonstrated higher correlation (r=.32) than the LV group (r=.18). In addition, the profiles of correlations between stress and the subcomponents were different for the two groups. In HV group, significant correlations were obtained between stress and the components of subjective sleep quality (r=.29), sleep latency (r=.11), sleep duration (r=.17), habitual sleep efficiency (r=.11), and daytime dysfunction (r=.23). In LV group, stress correlated significantly with the components of subjective sleep quality (r=.20), sleep disturbances (r=.19), and daytime dysfunction (r=.27).
Conclusion: The results show that although participants with both levels of trait vulnerability showed associations between stress level and sleep quality, the patterns of associations were different for the two groups. Stress level predicted symptoms of insomnia in individuals with high vulnerability, and predicted other symptoms that may interfere with sleep in individuals with low vulnerability.
Support (optional): This study is partially supported by the National Science Council of Taiwan (Grant No. NSC95-2413-H-004-020-MY3).

0763

BIBLIOMETRIC ANALYSIS OF INSOMNIA-RELATED RESEARCH IN THE PERIOD OF 1991-2005

Lu S,[1] Wu C,[1] Ho Y[2]
(1) Department of Sleep, Taipei Medical University Hospital, Taipei, Taiwan, (2) Bibliometric Centre, Taipei Medical University - Wan-Fang Hospital, Taipei, Taiwan

Introduction: Our purpose was to study the insomnia research performance based on 4,692 documents published in Science Citation Index (SCI)-indexed periodicals between 1991 and 2005. These documents were analyzed and evaluated according to publication distribution and were used to determine the quantitative characteristics of the research.
Methods: Documents used in this study were based on the databases of the SCI which was accessed from the ISI Web of Science, `Insomnia´ was used as keywords to search titles, abstracts, and keywords. Parameters analyzed included type of document, page count, authorship, journal, author keywords and country of publication.
Results: Six document types were found in the total of 4,692

documents. Seventy-three percent of all documents are articles. All articles were published in the total of 781 journals. Eighty-six percent of all articles were published in journals which listed in the category of Sleep. Of the 3,376 articles in SCI, 2,116 articles had author keyword information. Among 10,484 keywords, 3,315 (32%) keywords were used only 1 time. A summary of the remaining most-frequently used author keywords is provided. The five most used author keywords were `insomnia´, `sleep´, `depression´, `sleep disorders´, and `polysomnography´. There was logarithmic relation between yearly cumulative number of publications and the year from 1991 to 2005. Yearly production has extremely increased with the United States producing 38% the articles followed by the Japan with a 7% contribution. The G7 industrial countries (U.S.A., Japan, U.K., Germany, France, Italy, and Canada) represent a share of corresponding authors of 53% of world articles.
Conclusion: Insomnia research was a constant growth rate on publications in the fifteen year. The results of the study not only offer a comprehensive picture of insomnia by bibliometric research, but also demonstrate the performance of research countries.

0764

RANDOMIZED CONTROLLED TRIAL OF AN ACCELERATED INSOMNIA THERAPY

Harris J,[1] Lack L,[1] Bootzin R[2]
(1) Flinders University of South Australia, Adelaide, South Australia, Australia, (2) University of Arizona, Tuscon, AZ, USA

Introduction: In clinical research studies Stimulus Control Therapy (SCT) has been most consistently successful for the treatment of sleep onset insomnia. However, the effort and commitment often required for SCT may reduce compliance in clinical settings. To address this potential issue we have been investigating Flinders Accelerated Sleep Therapy (FAST). The therapy involves a 40-hour period of acute sleep deprivation during which 50 sleep onset opportunities produce numerous short sleep onset latencies (most less than 6 minutes) to reduce the putative psychophysiologic conditioned response of primary insomnia. The present study evaluated FAST with a randomised controlled trial.
Methods: Sixty-eight volunteer chronic primary insomniacs with sleep latencies > 30 min (48 f, 20 m, Mean age = 41 (13) yrs) were randomly allocated to four conditions: 1. sleep hygiene control, 2. FAST, 3. Four week SCT, and 4. Combined FAST and SCT. Reported here is the short term efficacy comparing sleep diary and subjective questionnaires prior to, during, and following the four week treatment or control period.
Results: While the control group showed minimal, non-significant changes at post treatment, mean sleep latencies of the active treatment groups decreased by 25-40 minutes, wake time decreased by 20-50 min, and total sleep time increased by 32-60 min. Global assessments of sleep (PSQI, sleep self efficacy) improved more in the active groups and daytime feelings of fatigue, stress, impaired functioning, and dysfunctional sleep beliefs decreased more in the active treatment groups. A detailed week-by-week analysis during treatment consistently showed immediate improvements in the FAST group and more gradual but comparable final improvements in the SCT group. The combined group generally showed both early and further gradual improvement resulting in trends for the greatest overall improvements.
Conclusion: This preliminary analysis indicates therapeutic potential for FAST, especially in combination with follow-up SCT.
Support (optional): National Health and Medical Research Council of Australia

0765

OSTEOPATHIC TREATMENT VERSUS PLACEBO-CONTROLLED RELAXATION THERAPY IN PRIMARY INSOMNIA: EFFECTS ON PERCEIVED SLEEP QUALITY

Guetens J,[1] De Cock J,[1] De Volder I,[2] Cluydts R[3]
(1) Flanders International College of Osteopathy, Kruibeke, Belgium, (2) University Hospital Antwerp, Edegem, Belgium, (3) University of Brussels, Brussels, Belgium

Introduction: This study was designed to find out whether osteopathic treatment can improve sleep quality in primary insomnia by influencing sympathetic and parasympathetic tone.
Methods: In a study of equivalence we compared osteopathic treatment and progressive relaxation therapy, the latter proven to be superior to placebo in several studies. 24 subjects (16 women and 8 men), were randomized and received four treatments over four consecutive weeks each.
In additional to a pre versus post study Pittsburgh Sleep Quality Index (PSQI) and the Depression Anxiety Stress Scale (DASS), the Brussels Indices of Sleep Quality (BISQ) questionnaire was completed daily seven days before and after treatment, and for two days before and after the third intervention. The osteopathic treatment involved techniques that intend to decrease sympathetic tone and increase parasympathetic tone, thereby decreasing the overall level of physiological hyperarousal. The relaxation therapy consisted of a basic programme for progressive muscle relaxation.
Results: Statistical equivalence testing (critical t-value=+/-2.074; α=0.05) demonstrated that both groups were equivalent for all sleep items of the BISQ pre versus post treatment. Absolute values however showed slightly better results for the relaxation group. Equivalence was also demonstrated for the pre-post comparison on the PSQI and for the DASS Anxiety and Stress score, but not for the Depression or total DASS score. With the exception of the BISQ Sleep Efficiency score, osteopathic treatment was superior to relaxation therapy the two nights after one single intervention.
Conclusion: This study showed that during a treatment period of 4 weeks osteopathy and progressive muscle relaxation are equivalent treatment approaches for primary insomnia. These findings further investigation of this treatment modality; especially its possible long term beneficial effects have to be demonstrated.

0766

INCIDENCE AND RISK FACTORS OF INSOMNIA IN A POPULATION-BASED SAMPLE

Leblanc M, Merette C, Savard J, Morin C
Universite Laval, Quebec, Canada

Introduction: Insomnia is a prevalent condition but there is little prospective data on its incidence and risk factors. This study estimated the incidence of insomnia and examined its risk factors in a population-based sample of self-defined good sleepers followed over a one-year period.
Methods: Participants were 394 self-defined good sleepers randomly selected from the adult population. They completed three postal evaluations over a one-year period (i.e, baseline, six months and twelve months later) which included assessment of sleep and insomnia, psychological and personality variables, stressful life events and coping skills, and health-related quality of life. Participants were categorized into three subgroups: (a) good sleepers (i.e., participants who remained good sleepers at the three evaluations), (b) incident cases of insomnia symptoms (i.e., good sleepers who developed insomnia symptoms either at six month or twelve month follow-up) and (c) incident cases of

insomnia syndrome (i.e., good sleepers who developed an insomnia syndrome either at six month or twelve month follow-up).
Results: One-year incidence rates were 31.2% for insomnia symptoms and 8.6% for insomnia syndrome. When incidence rates were computed only for those individuals without any prior history of insomnia at baseline assessment, the rates decreased to 22.7% (symptoms) and 4.7% (syndrome) respectively. Incident cases of insomnia syndrome presented a pre-morbid psychological vulnerability, as evidenced by higher arousability predisposition and higher anxiety and depressive symptoms at baseline. A logistic regression indicated that five variables were significantly associated with a new onset of an insomnia syndrome (i.e., family history of insomnia, previous episode of insomnia, arousability, the NEO-FFI openness subscale and the SF-12 general health subscale). Incident cases also reported significantly more negative life events than good sleepers within the six months preceding the onset of their insomnia and an increase of bodily pain concomitant to the onset of insomnia.
Conclusion: These results provide evidence that several characteristics previously observed among individuals with insomnia in several cross-sectional studies may represent important predisposing factors to new onset of insomnia. Improved knowledge of those risk factors could guide the development of more effective public health prevention and intervention programs for insomnia.
Support (optional): Research supported by Canadian Institutes of Health Research grant (#42504).

0767

THE COMPLAINT OF INSOMNIA IS STRONGLY CORRELATED WITH THAT OF DEPRESSION AND ANXIETY

Vela-Bueno A,[1] Fernandez-Mendoza J,[2] Olavarrieta-Bernardino S,[2] Rodriguez-MuñOz A,[2] De La Cruz-Troca J,[2] Bixler E[3]
(1) Universidad Autonoma Madrid, Madrid, Spain, (2) Universidad Autonoma Madrid, Spain, (3) Pennsylvania State University, Hershey, PA, USA

Introduction: The aim was to examine the association between somatic and psychological symptoms with the insomnia complaint.
Methods: Self-reported information was obtained from questionnaires administered to first year students of the Universidad Autonoma, Madrid, Spain. The ethical committee of the University granted the fulfillment of international ethical standards. The final sample consisted of 1,276 (response rate 74.5%). Mean age was 18.74 (±24) years, range 16-23. The survey consisted in a Self-Developed Questionnaire (SDQ) with sections to asses 1) Sleep disorders (Cronbach's $\alpha = 0.67$), and 2) Health status (Cronbach's $\alpha = 0.81$). All information was referred to the last 12 months, unless otherwise stated. Multiple logistic regression analyses were applied to explore the association of psychological and somatic variables with insomnia complaint. Thus, the final multiple conditional logistic regression model with stepwise method (PIN<0.05 and POUT>0.1) included variables retaining significance (statistical significance at $p< 0.05$).
Results: The complaint of insomnia was strongly related to symptoms of depression [fatigue (OR = 2.31, CI =1.48-3.60), irritability (OR = 2.26, CI = 1.47-3.47), diminished pleasure (OR = 2.21, CI = 1.33-3.66), sadness (OR = 2.1, CI = 1.43-3.09), weight change (OR = 1.9, CI = 1.14-3.18), decreased concentration (OR = 1.82, CI = 1.16-2.85), tearfulness (OR = 1.64, CI = 1.08-2.47)], anxiety [trembling (OR = 2.66, CI = 1.51-4.69), shortness of breath (OR = 1.9, CI = 1.42-2.23), nausea (OR = 1.84, CI = 1.01-3.39) feeling dizzy (OR = 1.75, CI = 1.05-2.91)] and somatic symptoms of depression and/or anxiety [tics (OR = 2.68, CI = 2.68-5.52), diarrhea (OR = 2.05, CI = 1.22-3.43), headache (OR = 1.61, CI = 1.10-2.36)].
Conclusion: Our data show a strong association between the subjective complaint of insomnia and those of depression and anxiety.

0768

PSYCHOMETRIC PROPERTIES OF THE SLEEP HYGIENE PRACTICE SCALE

Lin S,[1] Cheng C,[2] Yang C,[3] Hsui S[4]
(1) National Chengchi University, Taipei, Taiwan, Taipei city, Taiwan, (2) Taiwan, (3) National Cheng-Chi University, The Research Center for Mind, Brain, and Learning, Taipei, Taiwan, Taipei City, Taiwan, (4) Chang Gung Memorial Hospital, Taipei, Taiwan

Introduction: Poor sleep hygiene practices can interfere with sleep and may be a contributing factor for insomnia. Only few instruments were developed to assess sleep hygiene practices. Most of them have only fair internal consistency, limited construct validity, and/or were tested only in non-clinical population. This study is aimed to evaluate the psychometric properties of the Sleep Hygiene Practice Scale (SHPS) that we developed for the measurement of poor sleep hygiene practices in both normal sleepers and insomnia patients.
Methods: The SHPS, a 30-item self-rating scale for maladaptive sleep practices was administered to 87 good sleepers and 106 insomniacs. Cronbach´s á was used as a measure of internal reliability. Exploratory and confirmatory factor analyses were used.
Results: Good sleepers and insomniacs showed similar factor structure in the SHPS, with the following four factors: sleep environment, timing and regularity of sleep, eating/drinking habits prior to sleep, and arousal related behaviors. Goodness of Fit indices of confirmatory factor analysis were within acceptable range (good sleepers: RMSEA= .063, AIC= 696.42, NNFI= .81; insomniacs: RMSEA= .10, AIC= 875.04, NNFI= .82). Cronbach´s á coefficients for the full scale were better than the other sleep hygiene scales for both subject groups (good sleepers: .88, insomniacs: .78). Internal consistency for the separate factors were fair to good (good sleepers: .65-.81; insomniacs:.58-.78).
Conclusion: The SHPS consists of four factors that categorize sleep hygiene practices into different areas in both good sleepers and insomniacs. Although Cronbach´s á coefficients were not all very good, they are within acceptable range considering the behavior practices may not be all consistent within an individual. Also, the psychometric properties of the SHPS were in general superior to the psychometric properties of previously published sleep hygiene measures. The SHPS is a reliable and valid instrument to be used for further research and clinical works.
Support (optional): Partially supported by National Science Counsel, Taiwan (Grant No. NSC93-2413-H-030-008 and NSC94-2413-H-004-004)

0769

A PLACEBO CONTROLLED, RANDOMISED, DOUBLE-BLIND, 5 WAY CROSS-OVER STUDY OF 4 DOSES OF EVT 201 ON SUBJECTIVE SLEEP QUALITY AND MORNING AFTER PERFORMANCE IN A TRAFFIC NOISE MODEL OF SLEEP DISTURBANCE

Boyle J,[1] Stanley N,[1] Hunneyball I,[2] Kemp J,[2] Tasker T,[2] Nicholson A[1]
(1) University of Surrey, Guildford, Surrey, United Kingdom, (2) Evotec Ltd, Abingdon, Oxfordshire, United Kingdom

Introduction: EVT 201 is a high affinity, partial positive allosteric modulator of the $GABA_A$ receptor. It is metabolised to a pharmacologically active metabolite with a similar affinity profile to the parent compound but with lower efficacy. The combined pharmacokinetic profile of EVT 201 (T1/2 =3h) and metabolite 1 (T1/2

=4h) would appear useful for sleep maintenance without residual effects.

A previously reported dose finding study (2.5, 5.0 and 10.0 mg doses plus placebo) using a road traffic noise model showed that the 2.5 mg dose of EVT 201 showed good hypnotic efficacy with little evidence of significant residual effects the following morning. Since it was hypothesised that 2.5 mg may represent the top end of the effective dose range, a second study of the same design investigating lower doses (1.0, 1.5, 2.0, 2.5 mg) was carried out.
Methods: Placebo controlled, 5 way cross-over, double blind polysomnography study using a validated traffic noise model of sleep disruption in healthy volunteers. Outcome variables included objective and subjective measures of sleep and psychomotor testing of residual effects.
Results: All four doses of EVT 201 (1.0 to 2.5 mg) improved the subjective assessment of quality of sleep and were free of impaired ease of awakening or behaviour after awakening the next morning and of subjectively reported residual effects. Cognitive and psychomotor tests revealed only minor and inconsistent residual effects that were neither time nor dose related.
Conclusion: EVT 201 with doses as low as 1.0 mg improves the subjective quality of sleep and with doses below 2.0 mg there is little evidence of residual cognitive and psychomotor effects the morning after dosing.
Support (optional): This study was supported Evotec AG.

0770

DEGREE AND ASSOCIATIONS OF SLEEPINESS IN INSOMNIACS AND CONTROLS

Drake C,[1] Roehrs T,[1] Schwartz J,[2] Scofield H,[1] Roth T[1]
(1) Henry Ford Hospital Sleep Center, Detroit, MI, USA, (2) Integris Sleep Disorders Center of Oklahoma, Oklahoma, OK, USA

Introduction: While the Insomnia Research Diagnostic Criteria lists sleepiness as one of the daytime consequences of insomnia, little data is available on the degree of sleepiness among insomniacs. The aims of the present study were to determine the degree of sleepiness as well as its determinants, relative to controls, in a population based sample.
Methods: Two hundred fifty eight individuals meeting DSM-IV criteria for insomnia and 258 age and sex matched controls were drawn from the general population of Southwest Michigan using random digit dialing. Sleepiness as determined by the Epworth Sleepiness Scale was compared in insomniacs versus controls. Known determinants of sleepiness (demographic and sleep characteristics) were compared to identify what characteristics differentially predict sleepiness in insomniacs using two factor ANOVAs.
Results: Insomniacs (mean and 95% confidence interval 9.9, 9.3-10.5) had significantly (P<.001) higher ESS scores relative to controls (7.6, 7.0-8.2). Fifty percent of insomniacs and 29% of controls had ESS scores greater or equal to 10. Previously reported associations with sleepiness including, age, sex, race, reported TIB, oversleeping on weekends, napping and caffeine consumption were all associated with higher ESS scores but not differentially in the two groups. However, BMI and snoring were greater predictors of sleepiness among insomniacs relative to controls.
Conclusion: Insomniacs are significantly more sleepy than matched controls. Most of the traditional predictors of sleepiness impact insomniacs similar to controls. However, factors associated with sleep apnea (elevated BMI and snoring) differentially effect insomnia. Studies are needed to determine if these results are verifiable using objective measures of sleepiness as well as determining sleepiness in different insomnia populations.

0771

A PLACEBO CONTROLLED, RANDOMISED, DOUBLE-BLIND, 5 WAY CROSS-OVER STUDY OF 4 DOSES OF EVT 201 IN A TRAFFIC NOISE MODEL OF SLEEP DISTURBANCE: PSG AND SPECTRAL ANALYSIS OF SLEEP.

Stanley N,[1] Wright N,[2] Boyle J,[1] Hunneyball I,[3] Kemp J,[3] Tasker T,[3] Nicholson A[1]
(1) University of Surrey, Guildford, Surrey, United Kingdom, (2) QinetiQ Ltd, Farnborough, Hampshire, United Kingdom, (3) Evotec Ltd, Abingdon, Oxfordshire, United Kingdom

Introduction: EVT 201 is a high affinity, partial positive allosteric modulator of the GABAA receptor with a pharmacokinetic profile of EVT 201 (T1/2 =3h) and Metabolite 1 (T1/2 =4h).

A previously reported dose finding study (2.5, 5.0 and 10.0 mg doses plus placebo) using the same road traffic noise model showed that the 2.5 mg dose of EVT 201 had displayed good hypnotic efficacy with little evidence of residual effects the following morning. Specifically, EVT 201 2.5 mg significantly improved sleep initiation and sleep continuity, enhanced Stage 4 and slow wave sleep and had no effect on the latency or duration of REM sleep.

As the 2.5 mg dose appeared to be at the top end of the effective dose range a second study investigating lower doses was carried out.
Methods: Placebo controlled, 5 way cross-over, double blind polysomnography study using a validated traffic noise model of sleep disruption in healthy volunteers. Outcome variables included objective and subjective measures of sleep and psychomotor testing of residual effects.
Results: EVT 201 produced dose-related reductions in Wake After Sleep Onset, Total Sleep Time and Sleep Efficiency Index, and an increase in duration of Stage 4 and Slow Wave Sleep; other measures of sleep architecture were not adversely affected.

Spectral analysis of the PSG data revealed that theta and alpha activity were reduced by each dose of EVT 201, demonstrating the hypnotic activity of the drug. There was also an increase in delta activity with EVT 201 that approached significance (P = 0.061).
Conclusion: EVT 201 in the dose range 1.0 to 2.5 mg posseses hypnotic efficacy in a traffic noise model of insomnia based on PSG measures including spectral analysis. The data would suggest that EVT 201 is a promising new treatment for insomnia with activity on both sleep induction and maintenance.
Support (optional): This study was supported Evotec AG.

0772

NO IMPAIRMENT OF DAYTIME BARORECEPTOR SENSITIVITY IN PATIENTS WITH PRIMARY INSOMNIA

Peter J, Glos M, Blau A, Fietze I
Charité - Universitätsmedizin Berlin, Interdisciplinary Center for Sleep Medicine, CharitéCentrum 13, Berlin, Germany

Introduction: Insomnia with varying definitions has been linked to increased cardiovascular risk and changes in autonomous function. Reduced baroreceptor sensitivity (BRS) is an adverse prognostic marker for cardiovascular disease. Previously, we showed impaired daytime BRS in 10 snoring subjects with an AHI below 5/h and even more pronounced in patients with OSA. BRS is unknown for primary insomnia and was therefore investigated.

Methods: Diagnosis of primary insomnia was made in 24 patients (20 female/ 4 male) using DSM-IV criteria plus characteristics of psychophysiological insomnia. They were assessed using history, PE, standardized interviews (MINI), questionaires (PSQI/BDI/ESS/sleep protocol), bloods, EKG and drug screening. Respiration as well as PLM were investigated using an Embletta polygraphic 6-channel device with nasal canula, abdominal and thoracic movement, body position and activity, pulsoximetry and leg movement sensors. The healthy sleepers control group had been established similarily with additional attended polysomnography (PSG).
Spontaneous BRS was cross spectrally analysed from heart rate and blood pressure variability measured by EKG and noninvasive Portapres technology using a standardized protocol which controlled for breathing frequencies (12 and 15 breaths per minute (bpm)) and for daytime (9 to 12 a.m.). BRS was calculated from 3 minute periods at the 2 given breathing frequencies. Patients and controls were matched for age, gender and BMI. The mean age was 47,8 years in both groups. BRS was compared between patients and controls at 12 and 15 bpm respectively. Statistics included Mann-Whitney-U-Test and Bonferroni-Holm-alpha-correction.
Results: Daytime BRS showed no significant differences between patients with primary insomnia and healthy controls (patients versus controls): 12 bpm: 10,0(+/4,7) versus 13,0(+/-7,6) msec/mmHg, p=0,242. 15 bpm: 10,9(+/-4,7) versus 12,0(+/-6,5) msec/mmHg, p=0,834.
Conclusion: BRS during daytime is not impaired in patients with primary insomnia. Given the known heterogeneous PSG characteristics in patients with primary insomnia further research on BRS including PSG is necessary to identify subgroups.
Support (optional): Research grant from Humboldt University, Berlin.

0773

MELATONIN AGONIST VEC-162 IMPROVES SLEEP ONSET AND MAINTENANCE IN A MODEL OF TRANSIENT INSOMNIA

Birznieks G,[1] Scott C,[1] Baroldi P,[1] Polymeropoulos M,[1] Roth T[2]
(1) Vanda Pharmaceuticals Inc., Rockville, MD, USA, (2) Henry Ford Hospital Detroit, Detroit, MI, USA

Introduction: VEC-162 is an investigational dual MT1/MT2 receptor melatonin agonist that previously demonstrated improvement in sleep onset and sleep maintenance as well as the ability to immediately phase advance the human circadian system. Confirmation of the clinical efficacy and safety of VEC-162 using a model of transient insomnia induced by both "First Night Effect" and phase advance was studied in a Phase III multi-center placebo-controlled trial.
Methods: A randomized, double-blind, placebo-controlled, multi-center study of 412 healthy adults was conducted. Transient insomnia was induced via a combination of stress inducement (by first night in a sleep laboratory) and via circadian rhythm disruption (by a 5 hour bedtime advance). Subjects received 20mg, 50mg, 100mg VEC-162 or placebo 30 minutes prior to bedtime, and sleep measures were assessed using polysomnography (PSG). The primary outcome was latency-to-persistent-sleep (LPS), and secondary outcomes included wake-after-sleep-onset (WASO), total sleep time (TST), and next-day performance assessments.
Results: LPS significantly improved for all VEC-162 doses (21.5 min., p<0.001; 26.3 min., p<0.001 and 22.8 min., p<0.001 at 20, 50, and 100mg respectively) compared with placebo. Additionally, improvements in WASO were observed (24.2 min., p<0.02; 33.7 min., p=0.001 and 17.5 min., p=0.081 at 20, 50, and 100mg respectively) compared with placebo. VEC-162 also significantly extended total sleep time (33.7 min., p<0.002; 47.9 min., p<0.001 and 29.6 min., p<0.005 at 20, 50, and 100mg respectively) compared with placebo.
Conclusion: VEC-162 demonstrated sleep onset and maintenance effects in this model of transient insomnia. Given the combined first night effect and circadian challenge in this study, efficacy may reflect the combined soporific and circadian effects of VEC-162. In this confirmatory trial, VEC-162 was safe and well tolerated.
Support (optional): Vanda Pharmaceuticals Inc.

0774

HEALTHCARE COSTS OF PATIENTS WITH INSOMNIA: HOW MUCH DOES THE HEALTH PLAN AND PATIENT PAY?

Foley K,[1] Kalsekar A,[2] Baser O,[3] Walsh J[4]
(1) Thomson Medstat, Ann Arbor, MI, USA, (2) Eli Lilly, Carmel, IN, USA, (3) Thomas Medstat, Ann Arbor, MI, USA, (4) St. John's/St. Luke´s Hospital, Sleep Medicine and Research Center, Chesterfield, MO, USA

Introduction: The objective of this study is to compare healthcare costs of patients with insomnia to those without insomnia.
Methods: This study was based on a retrospective analysis of health insurance claims data in the US. Patients were selected if they were diagnosed with insomnia (n=24,238) or received a prescription drug for insomnia (n=294,945) during 2002-3. A control group (n=1,595,915) of patients was identified during the same study period. Insomnia was defined in 5 levels of frequency of symptoms (ranging from none to > 6 days/week) determined by proxy by a medication possession ratio. Generalized linear models were used to examine the impact of insomnia on inpatient, outpatient, prescription, mental-health related and insomnia-related costs after controlling for demographic differences and comorbidities measured by Chronic Disease Score and the Psychiatric Index.
Results: Unadjusted annual health plan paid costs for insomnia patients were approximately 3 times higher ($8,978 vs $2,790) compared to controls. After controlling for demographic and comorbidities, adjusted health plan-paid inpatient costs were 48%-79% higher, outpatient costs 49%-74% higher and prescription costs 69%-100% higher for insomnia patients relative to controls. Unadjusted mental health related costs for patients with insomnia were approximately 7 times (700% higher) greater than those for controls ($461 vs $64) which reduced to 110-450% difference in multivariate models. Out-of-pocket costs for insomnia patients were roughly twice that of the control group ($1000 vs $448), which reduced to 35%-44% difference in multivariate models. Insomnia-related costs were a small proportion of total healthcare costs ($117-health plan paid and $48-patient paid). All differences between insomnia patients and controls were statistically significant. No clear trends were identifiable regarding relationship between frequency of symptoms and healthcare costs, except for models that predicted insomnia-related costs.
Conclusion: Even for controlling for associated comorbidities, health plans and patients paid significantly higher healthcare costs for patients with insomnia compared to patients without insomnia.
Support (optional): Eli Lilly

0775

EFFECTIVENESS OF NEUROFEEDBACK TRAINING IN CHRONIC INSOMNIA.

Okunola O,[1] O'Malley E,[2] O'Malley M[2]
(1) Norwalk Hospital, Norwalk, Connecticut, Norwalk, CT, USA, (2) Nowalk Hospital, Norwalk, CT, USA

Introduction: The most effective treatment for chronic insomnia is cognitive behavior therapy (CBT). Though effective over the long term, CBT requires specialized training in behavioral sleep medicine therapies. Early neurofeedback (EEG biofeedback) training protocols have been shown to be effective therapy for insomnia (Hauri et al 1982). This training involves the use of real-time, processed electroencephalographic (EEG) activity for feedback to subjects for gradually reducing hyperarousability evident in the EEG. In this pilot study we evaluated the efficacy of a simple but comprehensive neurofeedback training protocol in chronic insomniacs in our Center. Our design utilized a retrospective analysis of clinical data to assess benefit of this training in a real world clinic population.
Methods: A retrospective data analysis of consecutive patients meeting chronic insomnia diagnosis (difficulty initiating and/or maintaining sleep for at least 3 months) and given neurofeedback training NeuroCare neurofeedback system (Zengar, Inc) integrated with CBT therapy was performed. Eight patients with complete sleep logs were included in data analysis. Patients lay on a reclined chair facing displayed LCD computer generated graphics synchronized to music heard over headphones. EEG data was collected from C3 and C4 referenced unilaterally to earlobe with separate grounds. Periods with high EEG variability triggered interruptions in the audiovisual datastream (negative feedback).
Results: Analyzing pre-post sleep log data with t-tests, all patients had significant improvement in total sleep time (5.1±0.8 to 6.4±1.0 hrs, p=0.002), sleep efficiency (70±9 to 91±5 %, p = 0.00004), wake after sleep onset (1.7±0.8 to 0.5±0.4 hrs, p=0.0003), and sleep onset latency (48±40 to 12±10 min, p=0.009).
Conclusion: Neurofeedback training is an effective, integral component of CBT for insomnia. Further research is needed to determine the relative contribution of neurofeedback training to CBT for insomnia and it´s efficacy as monotherapy.
Support (optional): none

0776

QUANTITATIVE ELECTROENCEPHALOGRAPHY IN UNMEDICATED PRIMARY INSOMNIA PATIENTS

Cortoos A,[1] Verstraeten E,[2] Cluydts R[3]
(1) Vrije Universiteit Brussel, Elsene, Brussel, Belgium, (2) Swansea University, Wales, United Kingdom, (3) Vrije Universiteit Brussel, Brussel, Belgium

Introduction: Recent studies examining EEG frequencies in primary insomnia during sleep support the concept of cortical hyperarousal in this population. Higher levels of beta power were found in comparison to healthy controls and comorbid insomnia patients. The question remains, however, if this cortical hyperarousal, is also apparent in the wake EEG.
Methods: A quantitative EEG was obtained in 13 unmedicated primary insomnia patients, diagnosed according to the DSM-IV criteria. The EEG was measured during an `eyes open´ and an `eyes closed´ condition. 19 electrodes according to the International 10-20 system were used and referenced to both mastoid electrodes. EOG and EMG were measured to assure optimal artefact rejection and impedances were kept below 10 kOhm. A minimum of 90 seconds of artefact-free EEG per patient was used for further analysis using the Thatcher qEEG database. z-values were obtained for delta (1-3,5 Hz), theta (4-7,5 Hz), alpha (8-12 Hz), beta (12,5-25 Hz) and high beta (25,5-30 Hz) EEG power.
Results: The results indicate a trend of heightened high beta power (25,5-30 Hz) in the eyes open condition (Cz: z = 1.86; p.= 0.06) and a deficit in the delta range in the eyes closed condition (T3: z = 1.34; p.=0.18). Furthermore, in the eyes open condition, the excess in high beta power is significantly higher in the right hemisphere in comparison to the left, especially on Fp2 (df 12; p.= .014), F4 (df 12; p.= .011), F8 (df 12; p.= .000) and T4 (df 12; p.= .000).
Conclusion: These preliminary results suggest that the observed cortical hyperarousal reflected by heightened beta power levels in the sleep EEG, continues to be apparent in the wake EEG. Furthermore, there might be a dominance of beta power in the right hemisphere in insomniacs, which might be related to a more negative mood.

0777

MALADAPTIVE SLEEP HYGIENE PRACTICES IN GOOD SLEEPERS AND INSOMNIA PATIENTS

Yang C,[1] Lin S,[2] S.-C. H,[3] Cheng C[4]
(1) National Chengchi University, Department of Psychology, Taipei, Taiwan, Taipei, Taiwan, (2) National Cheng-Chi University, Department of Psychology, Taipei, Taiwan, (3) Chang Gung Memorial Hospital, Taoyuang, Taiwan, (4) National Cheng-Chi University, Taiwan

Introduction: Poor sleep hygiene practices are assumed to interfere with sleep. However, previous studies on the association between sleep hygiene practices and sleep quality have yielded inconsistent results. The inconsistency may result from the differences in sample populations (college students vs. clinical patients) and the various aspects of sleep hygiene practices assessed in previous studies. This study aims to examine the associations between poor sleep hygiene practices and sleep quality in both good sleepers and insomniacs.
Methods: Participants consist of 87 good sleepers and 106 insomniacs. All participants completed the Pittsburgh Sleep Quality Index (PSQI), the Insomnia Severity Index (ISI), and the Sleep Hygiene Practices Scale (SHPS). Scores for different subscales of the SHPS were compared between normal sleepers and insomniacs. Pearson correlations were also conducted between the SHPS scores and the PSQI and ISI scores.
Results: Insomnia patients scored higher than normal sleepers on two subscales of the SHPS (sleep timing and regularity: t=2.00, p<.05; arousal-related behaviors: t=11.85, p<.001), but not on the other two subscales (sleep environment, eating/drinking habits prior to sleep). In normal sleepers, all SHPS subscales correlated significantly with the ISI score (rs = .31-.54). All but the eating/drinking habits subscale correlated significantly with the PSQI score (rs = .32-.53). In insomnia patients, however, none of SHPS subscales correlated with the PSQI score. Only the arousal related behaviors correlated with the ISI score (r = .35).
Conclusion: In normal sleepers, maladaptive sleep hygiene practices did predict poor sleep quality and insomnia symptoms. Although insomnia patients engaged in more maladaptive practices than good sleepers in sleep timing and regularity and more arousal-related behaviors, poor sleep hygiene did not predict poorer sleep quality in insomniacs. In addition, only arousal-related behaviors are associated with the severity of insomnia in insomnia patients.
Support (optional): Partially supported by National Science Counsel, Taiwan (Grant No. NSC93-2413-H-030-008 and NSC94-2413-H-004-004)

0778

EFFECTS OF INSOMNIA SUBTYPES ON PERCEIVED OCCUPATIONAL FUNCTIONING: SURVEY OF NURSING PROFESSIONALS

Mallis M,[1] Gregory K,[1] Brandt S,[1] Grubb W,[2] Rosekind M[1]
(1) Alertness Solutions, Cupertino, CA, USA, (2) Neurocrine Biosciences, Inc, San Diego, CA, USA

Introduction: Sleep disturbances are considered a significant contributor to productivity loss and injuries in the workplace. However, few efforts have examined individuals´ perceptions of how sleep difficulties affect productivity and safety in work environments.
Methods: A 67-item, anonymous, online survey was made available to United States nursing professionals over a 14-day period. Responses (N=2082, 45.87±10.09 years, 93.28% female) were examined to identify the prevalence of sleep disturbances, insomnia and effects on waking function. Individuals were classified according to DSM-IV-TR primary insomnia criteria for: 1) insomnia, 2) sleep disturbances with a co-morbid condition or 3) good sleep (did not meet DSM-IV-TR primary insomnia criteria).
Results: These results focused on individuals who met the criteria for insomnia (n=567, 27.23%) and those classified as good sleepers (n=416, 19.98%). The insomnia group was subtyped further based on reports of difficulty `initiating sleep´ only (n=71, 12.52%), `staying asleep´ only (n=182, 32.10%) or a combination of both (n=314, 55.38%). Compared to good sleepers (20.19%), those with difficulty `initiating sleep' (33.80%, p<.01), 'staying asleep' (42.31%, p<.001), and a combination of both (37.26%, p<.001) more frequently reported falling asleep unintentionally or fighting to stay awake at work. Charting deviations from standard practice were more frequently reported by those with difficulty `initiating sleep' (45.07%, p<.01), `staying asleep' (41.76%, p<.001) and a combination of both (41.72%, p<.001), compared to good sleepers (23.56%). Those who reported difficulty `staying asleep´ (29.67%, p<.01) reported medication dispensing errors more frequently than good sleepers (18.75%). Negative effects of disturbed sleep on workplace productivity was reported significantly more for those with `initiating sleep' (60.56%, p<.001), `staying asleep' (59.34%, p<.001) and a combination of both (51.27%, p<.001), compared to good sleepers (30.05%).
Conclusion: Symptoms of insomnia were commonly reported among nursing professionals. All three insomnia subtypes reported significant levels of waking impairment compared to good sleepers.
Support (optional): Financial support provided by Neurocrine Biosciences and Pfizer Inc during the period of the alliance with Neurocrine Biosciences Inc. The authors thank all of the survey respondents for their participation and the many Association of Nurse Executives (AONE) personnel who supported and collaborated on the project.

0779

EFFICACY AND SAFETY OF DOXEPIN 6 MG IN A MODEL OF TRANSIENT INSOMNIA

Schwartz H,[1] Hull S,[2] Seiden D,[3] Rogowski R,[4] Jochelson P,[4] Peterson G,[4] Ludington E,[4] Durrence H,[4] Roth T[5]
(1) Miami Research Associates, Miami, CA, USA, (2) Vince and Associates Clinical Research, Overland Park, KS, USA, (3) Broward Research Group, FL, USA, (4) Somaxon Pharmaceuticals, Inc, CA, USA, (5) Detroit, MI, USA

Introduction: The efficacy and safety of doxepin (DXP) 6mg tablets was evaluated in healthy adults using a model of transient insomnia.
Methods: This was a randomized, double-blind, parallel-group, placebo-controlled study in healthy adults using a model of transient insomnia. The insomnia model incorporated a phase advance in combination with the First Night Effect. Subjects received a single nighttime dose of placebo (PBO; N=282) or DXP 6mg (N=283) in a sleep lab. Efficacy was evaluated objectively (polysomnography; PSG) and subjectively (morning questionnaire). Primary endpoint was latency to persistent sleep (LPS); secondary PSG endpoints included wake-after-sleep-onset (WASO), total sleep time (TST), wake time after sleep (WTAS) and sleep efficiency (SE; overall, by third-of-the-night and hourly); secondary subjective endpoints included latency to sleep onset (LSO), subjective WASO (sWASO), subjective TST (sTST) and sleep quality.
Results: DXP 6mg statistically significantly improved LPS (13 minute improvement versus PBO; p<0.0001), WASO (39 minute improvement versus PBO; p<0.0001), TST (51 minute improvement versus PBO; p<0.0001), WTAS (p<0.0001), overall SE (p<0.0001), SE in each third-of-the-night (p<0.0001) and SE in all eight hours (p≤0.0003), all versus PBO. Additionally, DXP 6mg statistically significantly improved subjective variables including LSO (16 minute improvement versus PBO; p<0.0001), sWASO (p=0.0063), sTST (p<0.0001), and sleep quality (p=0.0004), all versus PBO. There were no clinically meaningful effects on measures of next-day residual sedation, and sleep architecture was generally preserved. Incidence of adverse events was comparable to placebo.
Conclusion: In this model of transient insomnia, DXP 6mg demonstrated significant improvements in sleep onset, sleep maintenance, sleep duration and sleep quality. These data suggest that doxepin 6mg may improve sleep impairment in adults with transient insomnia.
Support (optional): This study was fully funded and supported by Somaxon Pharmaceuticals, Inc., San Diego, CA.

0780

COGNITIVE BEHAVIORAL TREATMENT WITH HYPNOTIC DEPENDENT OLDER ADULTS

Ustinov Y,[1] Lichstein K,[1] Nau S,[2] Wilson N,[3] McCrae C,[4] Aguillard R,[5] Lester K,[5] Bush A[6]
(1) University of Alabama, Tuscaloosa, AL, USA, (2) University of Alabama, AL, USA, (3) University of Memphis, TN, USA, (4) Gainesville, FL, USA, (5) Methodist Hospital, TN, USA, (6) University of Tennessee, Memphis, TN, USA

Introduction: Older adults who satisfied criteria for insomnia despite having taken hypnotic medications were treated using a cognitive-behavioral treatment (CBT). Treatment was composed of sleep hygiene instructions, stimulus control, and relaxation training. Participants in the CBT group were compared to a credible placebo control and a no treatment group.
Methods: Participants were screened for inclusion using two weeks of sleep diaries to validate insomnia complaints. Polysomnography was used to rule out the presence of sleep apnea or periodic limb movements. Participants were randomly assigned to one of three groups: CBT, a sham biofeedback placebo control, or no treatment. Eight one-hour sessions were conducted with participants in the treatment groups. After completion of treatment, all participants underwent supervised medication withdrawal. The Sleep Quotient (SQ) (Lichstein, 1997) was used to analyze changes in sleep. The SQ is a standardized composite measure calculated by comparing a participant´s sleep to normative data based on age, gender, and ethnicity. The SQ was contrived to have a mean of 100 and a standard deviation of 15.
Results: To control for differences in baseline SQ scores, post-treatment scores were compared with baseline SQ included as a covariate. The

analysis of covariance revealed a significant effect of treatment group on SQ scores ($F(2,59) = 5.09$, $p = .009$). Bonferroni adjusted post hoc comparisons found that participants treated with CBT had significantly greater improvement in SQ compared to those in the no treatment group. Sham biofeedback was not significantly different from CBT or no treatment.
Conclusion: CBT produced greater sleep improvements than no treatment, but did not perform better than placebo. The SQ appears to be a valid and useful composite measure of general sleep, and is an appropriate tool for assessment of sleep differences between treatments.
Support (optional): Research Supported by National Institute on Aging grant AG14738.

0781

EFFECTS OF INSOMNIA SUBTYPES ON PERCEIVED HEALTH, MOOD, AND HELP-SEEKING: SURVEY OF NURSING PROFESSIONALS

Mallis M,[1] Brandt S,[1] Gregory K,[1] Grubb W,[2] Rosekind M[1]
(1) Alertness Solutions, Cupertino, CA, USA, (2) Neurocrine Biosciences, Inc, San Diego, CA, USA

Introduction: Insomnia and sleep disruptions are often associated with increased health problems, mood decrements, and an overall reduction in quality of life. The role of insomnia subtypes in these relationships was examined in this study.
Methods: A 67-item, anonymous, online survey was made available to nursing professionals throughout the United States over a 14-day period. Responses (N=2082; 45.87±10.09 years; 93.28% female) were examined to identify the prevalence of sleep disturbances, insomnia and effects on waking function. Individuals were classified according to DSM-IV-TR primary insomnia criteria for: 1) insomnia, 2) sleep disturbances with a co-morbid condition or 3) good sleep (did not meet DSM-IV-TR primary insomnia criteria).
Results: Results focused on individuals who met the insomnia criteria (n=567, 27.23%) and those classified as good sleepers (n=416, 19.98%). The insomnia group was subtyped further based on reports of difficulty `initiating sleep´ only (n=71, 12.52%), `staying asleep´ only (n=182, 32.10%) or a combination of both (n=314, 55.38%). The proportion of individuals reporting negative effects of disturbed sleep on both health and mood respectively was significantly higher for those with difficulty `initiating sleep´ (73.24%, 80.28%), `staying asleep´ (68.13%, 82.97%) and a combination of both (70.70%, 83.76%), compared to good sleepers (33.89%, 48.56%, $p<.001$ for all comparisons). Despite significant impairment in health and mood, only a minority of nurses saw a doctor for disturbed sleep during the past 12 months in the subgroups with difficulty `initiating sleep´ (14.08%), `staying asleep´ (15.93%) and a combination of both (30.25%), compared to good sleepers (2.88%, $p<0.001$ for all comparisons). Good sleepers reported less work-related stress than all the insomnia subtypes.
Conclusion: All three insomnia subtypes reported significantly more negative effects on health and mood, and increased medical help-seeking compared to good sleepers. Nevertheless, for all three insomnia subtypes, the majority of nurses (≥70%) did not seek professional care.
Support (optional): Financial support provided by Neurocrine Biosciences and Pfizer Inc. during the period of the alliance with Neurocrine Biosciences Inc. The authors thank all of the survey respondents for their participation and the many Association of Nurse Executives (AONE) personnel who supported and collaborated on the project.

0782

GOAL SETTING'S INFLUENCE ON CBT OUTCOMES IN CANCER CAREGIVERS

Carter P,[1] Simpson C,[2] Mikan S[2]
(1) University of Texas at Austin, Austin, TX, USA, (2) The University of Texas at Austin, Austin, TX, USA

Introduction: Caregivers of cancer patients experience insomnia. CBT is effective in reducing insomnia symptoms. This study explored the effects of scaleable goal setting on insomnia CBT outcomes in family caregivers of persons with cancer.
Methods: Caregivers of cancer patients who reported symptoms of insomnia (ICSD-2 criteria), were ≥ 21 years of age, had no previous diagnosis of depression or other sleep disorders, were invited to participate and randomized to intervention or control conditions. Sixty-four individuals have completed the study protocol (32 intervention). Data presented here will be from the intervention cohort. The PSQI and Actigraph were used to assess insomnia at 6 points over 4 months. The intervention included stimulus reduction, sleep hygiene, relaxation, & cognitive behavioral education elements. Goal attainment scaling (GAS) was used to individualize the intervention. A nurse delivered content in two 2-hour sessions at study weeks 2 & 4 in participant homes.
Results: Participants were female (70%), spouses (63%) and adult children (13%) with a mean age of 50 (SD=15years). Baseline PSQI averaged 9.1. Actigraph averages were: latency 24 minutes; duration 5.9 hours; efficiency 78%. Post intervention latency improved 12 minutes, duration increased 60 minutes and efficiency increased to 85.8% on average. PSQI averaged 6.3. Caregivers´ commonly set goals to address routine, the sleeping environment, and relaxation. Reduction in stimulant use (e.g., caffeine) was among the least frequent goals set. Caregivers who exceeded their goals showed the greatest level of improvement in insomnia symptoms.
Conclusion: Family caregivers of persons with cancer exhibit moderate to severe levels of sleep disturbance and report symptoms of insomnia. One-on-one CBT for insomnia combined with GAS provided caregivers with skills and knowledge to improve their sleep quality. Scalable goal setting allows for individualization of CBT as well as providing the opportunity for greater specificity in assessing goal attainment.
Support (optional): NIMH R21MH067600

0783

COGNITIVE-BEHAVIOR THERAPY AND MEDICATION FOR PERSISTENT INSOMNIA: SHORT-TERM AND MAINTENANCE TREATMENT EFFECTS

Morin C,[1] Vallieres A,[1] Guay B,[1] Guay C,[1] Savard J,[1] Merette C,[1] Bastien C,[2] Baillargeon L,[1] Gregoire J[1]
(1) Universite Laval, Quebec, Canada, (2) Universite Laval, Ste-Foy, Quebec, Canada

Introduction: The use of cognitive-behavior therapy (CBT) in combination with medication for treating insomnia has received limited research attention. Combined approaches should theoretically optimize outcome by capitalizing on the more rapid effects of medication and the more sustained benefits of CBT. The available evidence, however, is unclear as to whether a combined intervention has an additive effect on outcome. The objectives of this study were to evaluate the short-term effects of CBT, alone and combined with medication, and to compare the efficacy of different maintenance strategies on long-term outcomes.
Methods: 160 adults (61% women; mean age of 50.3, range of 30-72 years old) with chronic insomnia (mean duration of 16.4 years) were randomized to CBT alone (n = 80) or CBT plus nightly zolpidem (n = 80) for an initial 6-week treatment trial. After completing this treatment,

they were randomized again for an extended 6-month treatment. Patients treated with CBT alone initially continued with extended individualized CBT or no additional treatment; those who received combined treatment initially continued with an extended treatment consisting of CBT plus intermittent medication (10 pills per month) or CBT without additional medication (tapering). Multiple outcome measures were used.
Results: Of the 160 patients enrolled in treatment, 148 completed acute treatment and 141 the extended treatment. CBT was equally effective when used alone or combined with medication for improving sleep continuity parameters (SOL, WASO, TWT) during the initial phase of therapy; however, there was a greater increase of total sleep time with combined therapy than with CBT alone. The addition of individualized CBT during the 6-month maintenance phase did not enhance outcome on sleep continuity variables relative to no additional treatment. However, the proportion of treatment responders was higher among those receiving additional CBT (58%) compared to those who did not receiving additional CBT (50%). Patients treated with combined therapy initially did better during maintenance therapy when medication was tapered relative to intermittent usage. The proportion of treatment responders was also higher among those who continued with CBT alone (i.e., medication discontinued) (71%) relative to those who continued using medication intermittently (59%) during the 6-month extended treatment phase.
Conclusion: These findings suggest that combined CBT and medication does not always produce an additive effect during the initial treatment trial. Although combined therapy may provide an initial advantage in increasing total sleep time, it appears best to discontinue medication after the initial short-term trial in order to enhance long-term outcome.
Support (optional): Research supported by National Institute of Mental Health (MH60413).

0784

CEREBRAL ASYMMETRY IN SLEEP: RELATION WITH BDI AND BAI SCORES IN CHRONIC PRIMARY INSOMNIA

St-Jean G,[1] Bastien C[2]
(1) Laval University, Quebec, Canada, (2) Laval University, Ste-Foy, Quebec, Canada

Introduction: While central asymmetry is a characteristic of depressive symptoms during sleep, cerebral asymmetry in relation to anxious symptoms remains unknown. The objective of the present study is to document relationships between Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) sub-clinical scores with asymmetry during sleep in chronic primary insomnia sufferers (PI) and good sleepers (GS).
Methods: Thirteen GS and 19 INS completed both inventories before undergoing four consecutive nights of PSG recordings. The first four sleep cycles of Nights 2 and 3 were retained for spectral analysis. The frequency activity (ranging from 0.00 to 35.00 Hz) was computed (C3-C4, P3-P4, F3-F4 sites). Asymmetry scores resulted from the subtraction of the log of the left EEG power from the log of the right EEG power. Mean values of both nights were averaged.
Results: Significant Pearson correlations ($p<.05$) showed that in GS, only BAI scores correlated with REM central asymmetry in the 0.00-1.00-Hz range (r=-.56). In INS, asymmetry correlated with neither questionnaire score. The INS group was further divided in psychophysiological (Psy-I, n=13) and paradoxical (Par-I, n=6). Significant correlations were observed only for Par-I. BAI scores were related to frontal asymmetries in NREM and REM [(11.00-14.00-Hz (r=-.90; r=-.96) and 20.00-35.00-Hz (r=-.97; r=-.93) bands]. Frontal asymmetries were also observed for the 7.00-11.00-Hz band (r=-.93) in NREM and the 14.00-20.00-Hz band in REM (r=-.92). Central asymmetries were observed in the 20.00-35.00-Hz band in NREM (r=-.88) and the 11.00-14.00-Hz band in REM (r=-.88).
Conclusion: Surprisingly, BDI scores were not related to asymmetry. Asymmetry was only slightly related to BAI scores in good sleepers and not at all in Psy-I. However, in Par-I, as BAI scores increased, the asymmetry in higher EEG activity in the right central and frontal regions decreased. Cerebral asymmetry can still be detected with anxiety sub-clinical scores, and especially, in paradoxical insomnia sufferers.
Support (optional): Research supported by the Canadian Institutes of Health Research (# 49500) to C.H. Bastien.

0785

CHRONIC PRIMARY INSOMNIA: RELATION BETWEEN QUALITY OF SLEEP AND COGNITIVE EVOKED POTENTIALS MEASURES

Turcotte I,[1] St-Jean G,[1] Bastien C[2]
(1) Laval University, Quebec, Canada, (2) Laval University, Ste-Foy, Quebec, Canada

Introduction: There is intra and inter-individual variations in sleep quality in psychophysiological insomnia sufferers (Psy-I). Recently, our ERPs data (N1, P2 and N350) suggested inhibition deficits in addition to cortical arousal in Psy-I relative to good sleepers (GS). The objective of the present study is to investigate the relation between sleep quality (sleep efficiency) and the amplitudes and latencies of the different ERPs in a multi-assessment protocol.
Methods: Participants, 15 Psy-I and 16 GS, underwent four consecutive nights of PSG recordings (N1 to N4). ERPs in the evening and upon awakening were recorded on N3 and N4, with the addition of sleep-onset recordings on N4. Auditory stimuli consisted of `standard´ frequent (70 dB, 2000 Hz, .85 probability) and `deviant´ rare stimuli (90 dB, 1500 Hz, .15 probability). Sleep quality/efficiency was computed on each night. The amplitude and latency of each ERP component (N1, P2 and N350) were assessed on each recording.
Results: Pearson correlations revealed that in Psy-I sufferers, the amplitude of N1 before and during sleep-onset was negatively correlated ($p < .05$) with the objective sleep efficiency of the night preceding the ERPs recordings. As such, N1 amplitude decreased as sleep efficiency increased (r = -.73; r = -.62 respectively). In the morning, P2 amplitude significantly decreased as objective sleep efficiency increased (r = -.56). There were no relationships between sleep efficiency and N350 amplitude nor with the latency of any ERP component. In GS, N1 latency was longer as sleep efficiency was higher (r = .508, p = .045). No other significant relationships were observed.
Conclusion: These results suggest that as sleep efficiency decreases, arousal increases. This is especially true for Psy-I sufferers. These results highlight once again that when information processing and/or performance are assessed, the sleep quality of the night preceding the evaluation shall be documented.
Support (optional): Research supported by the Canadian Institutes of Health Research (# 49500) to C.H. Bastien.

0786

EFFICACY OF A HAND-HELD COMPUTER FOR THE TREATMENT OF PRIMARY INSOMNIA SYMPTOMS

Applegate B,[1] Riley W,[2] Behar A[3]
(1) Personal Improvement Computer Systems, Inc., Reston, VA, USA, (2) National Institutes of Health (NIH), Bethesda, MD, USA, (3) Personal Improvement Computer Systems, Reston, VA, USA

Introduction: Although a large portion of the population experiences

chronic insomnia, few have access to effective behavioral treatments. This study evaluated the efficacy of a handheld computer (HHC) designed to treat chronic insomnia symptoms. The HHC uses the principles of sleep monitoring, sleep restriction, and behavioral prompting to modify sleep behavior. This study compared the HHC to a self-help manual (SHM) in a 7-week randomized trial.
Methods: Subject were screened for primary insomnia by a licensed clinical psychologist, and randomly assigned to either the HHC or SHM. A total of 113 subjects with DSM-IV primary insomnia diagnoses randomized. Subjects used either the HHC or SHM for a period of 7 weeks. The HHC uses an active sampling technique to detect periods of wakefulness or sleep. After 1 week of monitoring, the HHC institutes a sleep restriction program. The HHC restriction program prompts a later bed time for the user while maintaining a consistent wake up time. Outcome measures included the Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), and sleep diaries.
Results: The sample was 67% female, 83% White, and had a mean age of 53 + 13 years. Mean scores on the ISI and PSQI at baseline were 21 + 3.1 and 14.6 + 2.7, respectively, and did not differ between groups. Subjects using the HHC showed significantly less impairment on the PSQI (9.7 vs. 11.3) and greater sleep efficiency (.81 vs. .74) than SHM subjects at 7 weeks, both P´s < .05. ISI scores tended towards significance (14.9 vs. 16.7, P = .09), but self-reported hours slept showed no differences and remained static from baseline to 7 weeks. Sleep diary results are pending.
Conclusion: Data indicate that a computerized treatment is associated with improvements of insomnia symptoms and improvements in sleep efficiency compared to self-help care.
Support (optional): Research supported by the National Heart Lung and Blood Institute (HL65893).

0787

A NEW MORNING LOG FOR RECORDING THE INSOMNIA EXPERIENCE

Nau S
University of Alabama, Tuscaloosa, AL, USA

Introduction: The Insomnia Experience (IE) Log is for morning reporting of experiences that occur during unwanted wakefulness.
Methods: The IE Log is a checklist of seven IE types: excessive cognitive activity, worrying, excessive physiological arousal, negative emotions, disruptive environmental factors, sleep-disturbing visual imagery, and dream-related awakening. A daily Sleep Log is used with the IE Log, to record the amount of wakefulness.

Data was collected from a male with sleep maintenance insomnia. Based upon sleep log quality ratings, the data were divided into "good" nights with ratings of 3-5, and "bad" nights with ratings of 1-2.

IE Log data from 36 good nights and 52 bad nights were analyzed 2 ways: by the number of nights each type of insomnia experience was reported, and by the number of nights that each type of insomnia experience was rated as *the most characteristic type of experience* for the night.
Results: IE reports from good nights and bad nights included a similar mix of IE types (excessive cognitive activity, worry, excessive physiological arousal, dream-related awakening, disruptive environmental factors and negative emotions). Negative emotions were reported more from bad nights (69%) than from good nights (25%). Dream-related awakening was the most characteristic experience for good nights (50% of IE Logs rated dream-related awakening as the most characteristic experience). The experience types rated as most characteristic for bad nights were dream-related awakening (32%), excessive physiological arousal (30%), worry (18%), and excessive cognitive activity (16%).
Conclusion: The IE Log can easily be used for extended periods.

Excessive physiological arousal, worrying and excessive cognitive activity often characterized the insomnia experience during the current sample of 52 sleep maintenance insomnia nights.

The insomnia experience of dream-related awakening was the most frequently reported experience. Dream-related awakening should be asked about in future studies of the subjective insomnia experience.
Support (optional): Research supported by National Institute on Aging grant AG14738

0788

RESEARCH EVALUATING BRIEF BEHAVIORAL SLEEP TREATMENTS FOR RURAL ELDERLY (RESTORE): PRELIMINARY FINDINGS

McCrae C,[1] McGovern R,[2] Lukefahr R,[3] Stripling A[4]
(1) Gainesville, FL, USA, (2) A.T. Still University/Kirksville College of Osteopathic Medicine, MO, USA, (3) A.T. Still University, MO, USA, (4) University of Florida, FL, USA

Introduction: Chronic insomnia affects up to 35% of individuals aged 65 and older. Rural elderly are as likely to experience insomnia as urban elderly, but are even less likely to receive behavioral treatment for a variety of reasons (practitioners lack training, treatment length, travel burden, low income). We present posttreatment sleep outcome data from an on-going trial testing two brief behavioral sleep interventions with rural older adults in primary care settings.
Methods: Twenty-one older adults with insomnia (65+) were recruited from 10 rural counties in Northeast Missouri. All counties were designated mental health shortage areas (MHSAs) and geographic/low income health profession shortage areas (HPSAs). Participants were randomly assigned to either sleep hygiene education (SHE; n=11) or insomnia & stress management (ISM;n=10). Both treatments were manualized, administered by a mental health counselor, and included 2 in-person and 2 telephone sessions. ISM was a multi-component treatment consisting of stimulus control, sleep restriction, and relaxation. SHE consisted of psychoeducation and sleep hygiene. Participants completed daily sleep diaries throughout the study: 2 weeks-baseline, 2 weeks-in-person sessions, 2 weeks-telephone sessions, 2 weeks-posttreatment.
Results: At posttreatment, both ISM and SHE participants had significantly decreased waketime after sleep onset, increased total sleep time, and improved sleep efficiency. ISM participants also had significantly improved sleep onset latency (~31minutes) compared to no improvement for SHE participants. Additionally, ISM participants had significantly greater improvement than SHE participants in sleep efficiency (ISM~13.14%; SHE~5%). All ps<.05. Regarding clinical significance, 8 ISM participants no longer met diagnostic criteria for insomnia (SOL<31, WASO<31 minutes, and SE<85%) at posttreatment compared to only 2 SHE participants.
Conclusion: Brief multi-component behavioral sleep treatment substantially improved sleep in rural older adults with insomnia. Our results have implications for primary care-based behavioral treatment of late-life insomnia. Future directions include the evaluation of long-term sleep and daytime functioning outcomes.
Support (optional): HHS/SAMSHA; ORHP/MO: DO4RHOO242

0789

VALERIAN FAILS TO IMPROVE THE SLEEP OF OLDER WOMEN WITH INSOMNIA

Taibi D, Vitiello M, Anderson G, Elmer G, Barsness S, Landis C
University of Washington, Seattle, WA, USA

Introduction: Complaints of sleep disturbance are common in older adults, particularly among women, with ~10% meeting criteria for insomnia syndrome. Valerian is an herb with putative mild sedative properties commonly used as a sleep aid. We examined the efficacy of valerian to improve the sleep of older women with insomnia.
Methods: In a double-blind, randomized, crossover design, sixteen older women (mean age= 69.44 ± 8.07) meeting diagnostic criteria for chronic (> 3 months) insomnia, took either *Valeriana officinalis* extract (300 mg) or placebo thirty minutes before bedtime for 2 weeks. After a 2-week washout, participants received the other treatment for 2 weeks. Sleep latency, sleep efficiency (SE), and wake after sleep onset (WASO) were measured by diary and polysomnography, and sleep quality by diary. Participants reported mild to moderate sleep disturbance on screening Pittsburgh Sleep Quality Index 8.8 ± 2.3 (mean ± standard deviation) and Insomnia Severity Index (11.13 ± 3.91), but baseline polysomnography revealed evidence of moderate to severe insomnia (SE 68.1 ± 12.2% and WASO 121.8 ± 54.2 minutes).
Results: No significant post-treatment differences were observed between valerian and placebo on any outcome measure, polysomnographic or diary. Compared to baseline, significant improvement (p>.05) was observed diary-rated SE and WASO after 2 weeks of both valerian and placebo. Side effects did not differ significantly between conditions during treatment; however, during 2-day post-treatment washouts participants reported marginally more tiredness (p=.06) and itching (p=.07) after valerian compared to after placebo.
Conclusion: Two-weeks of a valerian extract dose commonly recommended as therapeutic (300 mg/day) failed to improve the sleep of older women with insomnia, who also reported more adverse reactions during washout from valerian. Valerian, at least at the dose studied here, cannot be recommended as a sleep aid for older women with insomnia.
Support (optional): Supported by: NCCAM R21-AT002108; NINR T32-NR07039, Center for Women´s Health and Gender Research P30-NR04001, R01-NR04011. Valerian donated by Pharmavite, LLC. (San Fernando, CA).

0790

DIFFERENT DELIVERY METHODS OF COGNITIVE-BEHAVIORAL TREATMENTS FOR INSOMNIA YIELD DIFFERENT OUTCOMES

Cousins J,[1] Bootzin R,[2] Moritz P,[3] Epstein D,[4] Miranda J,[5] Sidani S[5]
(1) University of Arizona, Tucson, AZ, USA, (2) University of Arizona, Tuscon, AZ, USA, (3) University of Colorado Health Sciences Center, CO, USA, (4) Phoenix, AZ, USA, (5) University of Toronto, Ontario, Canada

Introduction: Cognitive-behavioral treatment has been found to be an effective treatment for adults with insomnia. Less is known about the modes of treatment delivery such as group treatment and treatment booklets or about methodological variations in outcome studies. This is the first, preliminary, report of treatment outcomes from two sites of a four site study.
Methods: Baseline and post-treatment daily sleep diaries were assessed for a total of 220 participants (Tucson = 85, Denver = 135) who met criteria for insomnia (age M = 50.06, range 21-89; 153 females). There were two treatment conditions, a multicomponent group therapy and a self-guided booklet condition. In Tucson, all of the participants were randomly assigned. In Denver, the participants chose their treatment option based on preference or were randomly assigned if a preference was not expressed.
Results: 2 X 2 (Site X Group) ANOVAs revealed only one significant difference (NWAK) at baseline between the two sites. Subjects receiving multicomponent group therapy improved more than those receiving the self-guided booklet condition on all sleep variables ($p < .05$) except for TST, in which both groups improved. Effect sizes (all $p < 05$) for the group therapy were: d = .897, SOL; d = .434, NWAK; d = 1.175, WASO; d = .915, sleep quality; d = .596, better or worse than usual rating; d = .932, TIB; d = .517, TST; and d = 1.653, SE. The self-guided booklet group improved across many of the sleep variables ($p < .05$), but more modestly: d = .462, SOL; d = .529, WASO; d =.338, sleep quality; d = .482, TST; and d = .822, SE.
Conclusion: The multicomponent group therapy was substantially more effective than the booklet, although even the booklet produced some improvement. The treatments provided robust effects irrespective of site differences.
Support (optional): This research was supported by NINR/NIH grant NR05075

0791

THE RELATION BETWEEN INSOMNIA AND COGNITIVE FUNCTIONING AMONG ADULTS AGES 35-55

Wickwire E, Brian M, Schumacher J, O'Jile J, Huercamp J, Roland M
University of Mississippi Medical Center, Jackson, MS, USA

Introduction: Among older adults, complaints of insomnia have been found to be associated with general cognitive impairment. However, few studies have explicitly considered the relation between insomnia and specific neuropsychological functioning in a typical adult population. The purpose of the current study was to evaluate the relation between subjective complaints of insomnia and cognitive functioning in a sample of non-older adults.
Methods: Participants were 45 adults (including 13 insomniacs) between the ages of 35-55 referred for neuropsychological testing in a university medical center. Patients with serious neurological impairment or DSM-IV mood disorders were excluded from the study. Yes-no insomnia status was defined based on any complaint of difficulty initiating sleep, maintaining sleep, or both. Cognitive functioning was assessed using the four specific indices from the Wechsler Adult Intelligence Scale- Third Edition (WAIS-III; verbal comprehension- VCI, perceptual organization- POI, working memory- WMI, and processing speed- PSI).
Results: A series of hierarchical multiple regressions was performed to predict VCI, POI, WMI, and PSI. Gender and years of education were entered in step 1 and insomnia status in step 2 of all models. Insomnia status was a significant predictor of working memory (p=.028) and verbal comprehension (p=.055) and explained an additional 7% and 6% of variance in these dependent variables (R2 = .07 and R2 = .06, respectively).
Conclusion: These results are consistent with previous findings among older adults and extend the literature on insomnia and cognitive functioning to include men and women ages 35 to 55. Even after controlling for gender and years of education, a significant negative relation was observed between insomnia and verbal comprehension and working memory. These findings raise important questions about the largely unexplored relation between insomnia and cognitive function among adults in prime working age. Clinical implications include that insomnia symptomatology should be assessed during routine neuropsychological evaluations.
Support (optional): N/A

0792

LONG-TERM FOLLOW-UP STUDY OF INSOMNIA PATIENTS

Dolan D,[1] Rosenthal L,[2] Taylor D[1]
(1) University of North Texas, Denton, TX, USA, (2) Sleep Medicine Associates of Texas, Dallas, TX, USA

Introduction: Insomnia is believed to be a chronic condition. However, little clinical information is available on long-term outcome of patients with Insomnia. The goal of this ongoing study is to determine the clinical status of patients evaluated in 2002.
Methods: This is a prospective telephone study combined with a retrospective chart review. Consecutive patients seen in clinical consultation in 2002 are being contacted to their listed telephone numbers. Calls are attempted twice to all listed numbers and those patients agreeing to participate are asked about the status of their sleep related symptoms and treatment.
Results: To date 50 patients have been called; 26 were found to have valid telephone numbers. Of those, 16 answered the phone, and 14, or 28% of the total sample, consented to report on their current symptomology; nine answered all questions included in the survey. Those who did not answer did not differ from those who did on age, gender, Epworth score, or diagnosis at the time of consultation. Almost 64% of patients surveyed still experienced difficulty initiating and/or maintaining sleep; the majority of those (78%) endorsed both. Only five patients were actively receiving treatment; providers included two internists, a PCP, an OB-GYN, and an allergist. Prescribed medications were Ambien (60%), Lunesta (20%), and Amitriptyline (20%). No use of over the counter or alternative medicines was endorsed. Of the 38% not reporting current insomnia symptoms, three patients offered reasons for the resolution of symptoms; in two cases it "went away" and in one case treatment of ADHD reduced insomnia.
Conclusion: The results so far confirm the chronic nature of Insomnia, which requires ongoing therapy. The majority of patients with chronic symptoms reported chronic use of non-benzodiazepine hypnotic agents. The effectiveness and safety of these therapies, under such a long-term use, has not been established and require further study.

0793

FINDINGS FROM A STAGE 1A TREATMENT DEVELOPMENT CLINICAL TRIAL: THE PRE-SLEEP ROUTINE FOR TREATING INSOMNIA

Wickwire E, Schumacher J, Roland M
University of Mississippi Medical Center, Jackson, MS, USA

Introduction: Although effective, most multi-component cognitive-behavioral therapies for insomnia (CBT-I) employ similar "cover all the bases" approaches that lack thematic consistency. Clinicians and patients may benefit from an integrative approach that is easy to understand and implement. The present study is a Stage 1A clinical trial to develop a manualized intervention for chronic insomnia, the pre-sleep routine. Borrowing from the sport and performance literatures, the pre-sleep routine seeks to reduce pre-sleep arousal by standardizing and ritualizing pre-sleep behaviors. This routine then becomes associated with preparation for sleep through classical conditioning. Several established CBT-I components are included and presented in a manner thematically consistent with the routine.
Methods: Two women and one man (M age=45 years, SD = 12.8) meeting criteria for primary insomnia were recruited from a university medical center. During an initial interview, participants completed questionnaires assessing sleep and daytime functioning. Two weeks later, treatment began, consisting of four weekly 50-minute sessions and a brief booster. Participants completed sleep diaries throughout treatment. As part of the Stage 1A manual development process, participants also provided extensive feedback on the treatment, including their impressions of the utility of various aspects of the sessions and the thematic consistency of the treatment components.
Results: At post-treatment, all participants experienced significant reductions in sleep latency, number of awakenings per night, total time awake during the night, and morning awake time before arising; increases in sleep efficiency and subjective sleep quality; and significantly reduced daytime fatigue as measured by the Insomnia Severity Index. One participant increased her total sleep time from 297m to 424m. All participants reported that the pre-sleep routine treatment was easy to understand and follow.
Conclusion: These findings demonstrate the feasibility and acceptability of the four-session treatment and suggest that the intervention will influence relevant sleep behaviors during the Stage 1B phase of this trial.
Support (optional): N/A

0794

IMAGERY REHEARSAL THERAPY IMPROVES SLEEP IN INSOMNIA

Molen Y,[1] Carvalho L,[2] Carvalho J,[3] Barreto L,[4] Prado L,[5] Neves A,[2] Prado G[4]
(1) Federal University of São Paulo, Sao Paulo, Brazil, (2) Federal University of Sao Paulo, São Paulo, Brazil, (3) Federal University of Sao Paulo (UNIFESP), São Paulo, Brazil, (4) Federal University of Sao Paulo, Sao Paulo, Brazil, (5) Federal University of São Paulo, Sao Paulo, São Paulo, Brazil

Introduction: Worries seem to be a main factor in insomnia maintenance. Studies about Imagery Rehearsal Therapy (IRT) for insomnia have not been done in a systematized way. Our goal was to verify the IRT effect in insomnia severity (IS), sleep quality (SQ), dysfunctional beliefs and attitudes about sleep (DBAS), general worries (GW), and sleep disturbance (SD).
Methods: Clinical Trial single-blind, with 24 chronic insomnia patients, taking medicine or not, separated in a quasi-random way, in two groups: 12 patients (1male, 57±8 year old) in experimental group (EG), and 12 (1 male, 51±10 years old) in control group (CG), participated of a 2 hours meeting during 5 weeks for sleep education: hygiene, beliefs and attitudes, and worries. EG received instructions for practicing IRT before sleep, with an audio compact disc for relaxing and releasing worries, and CG, for reading before sleep, during 3 weeks. Measures for IS, DBAS, GW, and SD were assessed by questionnaires during treatment (T) and 4 weeks post-treatment (follow-up, FU) and for SQ during Baseline(B), T and FU.
Results: In EG, IS diminished from T (T=17.7±3.4; FU=13.3±5; $p<0.001$), DBAS improved from T (T=38.9±20; FU=62.7±17 $p<0.001$), SD diminished from T (T=40.7±8; FU=36±7; $p=0.004$) and SQ improved since B (B=14.6±4; T=10.9±5.7; $p= 0.019$); (B= 14.6±4;FU=9.1 ± 5.2; $p<0.001$); (T= 10.9± 5.7; FU= 9.1± 5.2; $p=0.02$). SQ tended to be higher at B in EG (14.58±3.2) than in CG (10.8±3.95), $p= 0.016$. In CG, IS diminished (T=14.8±4.5; FU=12.3±4.3, $p=0.002$) and GW diminished (T=56.1±15.1; FU=49.6±16; $p=0.033$). Worries about sleep, a component from IS, improved 67% in EG and 58% in CG.
Conclusion: Imagery rehearsal therapy was associated with subjective improvement in insomnia severity, sleep quality, sleep disturbance and functional beliefs and attitudes about sleep. Although GW improved only in CG, worries about sleep improved in both groups.

0795

USE OF MEDICATIONS IN PATIENTS REVEIVING CBT FOR CHRONIC INSOMNIA

Kuo T, Ong J, Manber R
Stanford University, Stanford, CA, USA

Introduction: Chronic insomnia is a highly prevalent condition. Although cognitive behavioral therapy (CBT-I) has strong empirical support, currently medication is the most common approach for treating insomnia. The aim of this study is to characterize pattern of use of medication for sleep in patients receiving CBT-I at a multi-disciplinary sleep clinic.
Methods: This study is a retrospective case review of clinical data of 362 patients (56.7% female, age M=49 ± 14 years, Insomnia Severity Index = 21.4 ±3.9, CBT-I sessions attended M=5 ± 2) who enrolled in a 7-session group CBT for chronic insomnia between 3/1999-4/2004. Patients were heterogeneous in terms co-exisitng sleep disorders, medical and psychiatric conditions. The last available sleep diary was used for outcome analyses.
Results: 88.3% of patients were on at least 1 medication (mean =1.42 ± 0.95) for sleep at the time of entry into CBT-I. In the order of frequency, the most common classes of medications used for sleep were: non-benzodiazepine GABA-receptor agonists, benzodiazepines, over-the-counter hypnotics, sedating anti-depressants, dopamine-agonists, and other sedating psychotropics (45.3, 21.7, 17.9, 14.4, 6.1, 5.4%). Use of 2 or more classes of sedating medications occurred in 52.6% of patients. At the end of the treatment, significant (33% from baseline) dose/quantity change in medication use occurred (n=239; 37.7% decreased, 14.6% increased). Medicated patients responded to CBT-I similar to patients who did not take medication during CBT-I. The 2 groups did not differ and both showed significant improvement in sleep latency, WASO, TST, sleep quality, and scores on the Insomnia Severity Index, and Beck Depression Inventory.
Conclusion: Use of medications for sleep is highly prevalent in patients with chronic insomnia. This high prevalence may reflect a more severe population that sought treatment at a tertiary setting. Poly-pharmacy is common and spans several medication classes. The findings from this study suggest that CBT-I can significantly improve sleep in patients who still have insomnia even with pharmacotherapy.
Support (optional): None.

0796

RESPIRATORY DISTURBANCE INDEX IN CHRONIC INSOMNIA PATIENTS WITHOUT SLEEP BREATHING SYMPTOMS

Krakow B,[1] Melendrez D[2]
(1) Maimonides Sleep Arts and Sciences, Albuquerque, NM, USA, (2) Quality Sleep Solutions, Albuquerque, NM, USA

Introduction: AASM practice parameters for PSG presuppose sleep-disordered breathing (SDB) is not routinely diagnosed in chronic insomnia patients.
Methods: A chart review at two sleep labs was conducted to test this paradigm´s validity. Inclusion criteria: A) Presence of Insomnia Disorder, based on AASM Workgroup guidelines; B) Absence of any sleep breathing complaints; and C) Diagnostic PSG. Insomnia Disorder required patients to: rank Insomnia or Poor Sleep Quality as the primary sleep disorder they wanted treated; report SOL or WASO > 30 min or SE% < 80%; and, link daytime impairment to insomnia. Absence of sleep breathing symptoms required that patients deny: an SDB disorder; sleep disruption due to sleep breathing difficulties; sleep-breathing-induced awakenings; and, snoring, choking, gasping, or apnea, coupled with identical bedpartner denials. PSG with pressure transducer measured full RDI (apneas + hypopneas + RERAs).
Results: Of 738 patients completing intakes, 73 met study criteria. Average age = 47 years; 73% female; 59% married; average BMI =25.6. Mean insomnia duration = 10.1 yrs; 44% hypnotic dependent; and 51% with comorbid mood or anxiety disorders. Mean Insomnia Severity Index = 18.3; mean sleep quality rating = Poor; mean SOL = 52.71 min and mean WASO = 89.42 min; mean SE% = 75%. Mean AHI = 11.64 events/hr, and mean RDI = 40.47 events/hr. Fifty-six percent met traditional SDB criteria (AHI > 5). Using full RDI defined by new AASM nosology and a conservative cut-off of 20 events/hr, 85% met SDB criteria.
Conclusion: In a series of predominantly female, non-obese, treatment-seeking, chronic insomnia patients, who along with their bedpartners denied sleep breathing symptoms, SDB was extraordinarily common, and mean RDI was severe. As SDB was not suspected in these 73 patients, no testing should have occurred, per AASM guidelines. Conversely, these findings support routine PSG testing of chronic insomnia patients.
Support (optional): No Support

0797

INSOMNIA TREATMENT WITH IMAGERY REHEARSAL THERAPY

Molen Y,[1] Carvalho L,[2] Carvalho J,[3] Barreto L,[2] Prado L,[2] Neves A,[4] Prado G[2]
(1) Federal University of São Paulo, Sao Paulo, Brazil, (2) Federal University of Sao Paulo, Sao Paulo, Brazil, (3) Federal University of Sao Paulo (UNIFESP), São Paulo, Brazil, (4) Federal University of Sao Paulo, São Paulo, Brazil

Introduction: Many insomnia treatments include sleep hygiene, therapy aiming to change dysfunctional beliefs and attitudes about sleep and imagery rehearsal therapy (IRT). Studies about IRT for insomnia have not been done in a systematized way. The goal of this study was to explore the effects of IRT in total sleep time (TST), depression and anxiety in adult insomniacs.
Methods: Clinical Trial single-blind, with 2 chronic insomnia groups (N=24), which participated, during 5 weeks, of a 2 hours meeting with education about sleep hygiene and the effect of beliefs, attitudes and worries in insomnia maintenance. Groups were separated in a quasi-random way in experimental (EG) and control group (CG). EG received instructions for practising IRT before sleep with an audio compact disc (CD), for relaxing and releasing worries and CG were instructed for reading before sleep. Participants filled sleep logs to assess TST, for 2 weeks before treatment (B), 3 weeks of treatment (EXP), and during one week after 3 weeks post-treatment (follow-up, FU). Measures for depression and anxiety were made at B, Exp and FU.
Results: Total sleep time was significantly increased at EXP (p=0,019) and FU (p=0,006) when compared to B in EG. Depression diminished in EG at FU when compared with EXP and both groups showed a tendency to significance when the comparison was between B and FU (CG: p=0,065 e EG: p= 0,058). Symptoms of anxiety state diminished significantly from B to FU (p=0,011) and from EXP to FU (p=0,022).
Conclusion: Our preliminary findings suggest that IRT produced a significant improvement in total sleep time, in depression symptoms at least in follow up and in anxiety state from baseline with maintenance till 4 weeks post-treatment.

0798

COGNITIVE BEHAVIORAL THERAPY IN PATIENTS WITH CHRONIC INSOMNIA AND OBSTRUCTIVE SLEEP APNEA

Davis K,[1] Moroz T,[2] Ong J,[1] Kuo T,[1] Manber R[1]
(1) Stanford University, Stanford, CA, USA, (2) Stanford University, Mountain View, CA, USA

Introduction: Insomnia complaints are prevalent in patients with obstructive sleep apnea (OSA). Cognitive behavioral therapy (CBT-I) is an established and effective treatment for chronic insomnia. The aim of the study was to compare treatment outcomes following CBT-I among insomnia patients with and without OSA.
Methods: A retrospective review of clinical data on patients enrolled in group CBT-I over an 18 month period was performed. Forty-nine patients met criteria for chronic insomnia and had diagnostic polysomnograms. Patients were divided into 2 groups based on RDI >10/hr (OSA group, n =26, 46% female, average age =53 years) and RDI <10/hr (insomnia only group, n =23, 48% female, average age =44 years). CBT-I consisted of seven 90-minute sessions that included standard components. Participants attended an average of 5.8 sessions. Pre-and-post measures included: Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS), Beck Depression Inventory (BDI) and weekly sleep diaries. The last available sleep diary was used for outcome analyses.
Results: At baseline, insomnia only patients reported significantly lower average ratings of sleep quality (p =.03) and experienced more nights per week with a sleep onset latency (SOL) >30 minutes (2.5 vs.1.7, p =0.02). No significant differences between the groups were found for ISI, ESS, BDI, wake time after sleep onset (WASO), total sleep time, total wake time (TWT) and sleep efficiency (SE). A main effect for pre-to-post treatment improvements was found for WASO, SOL and SE. RDI did not correlate with outcome measures such as TWT (r = -.13) or SE (r = .11).
Conclusion: Patients with chronic insomnia and co-existing OSA benefited from CBT-I. The magnitudes of improvement on measures of sleep were comparable to that of patients with very minimal OSA (RDI<10/hr). CBT-I should be considered as an important treatment component in their clinical management.

0799

COGNITIVE BEHAVIORAL THERAPY IN PATIENTS WITH CHRONIC INSOMNIA AND RESTLESS LEGS SYNDROME

Moroz T,[1] Davis K,[2] Ong J,[2] Kuo T,[2] Manber R[2]
(1) Stanford University, Mountain View, CA, USA, (2) Stanford University, Stanford, CA, USA

Introduction: RLS is associated with sleep disturbances, depression and anxiety symptoms. Cognitive behavioral therapy (CBT-I) is an effective treatment for chronic insomnia. The aim of the study was to compare the clinical presentation and response to group CBT-I in insomnia patients with (RSL group) and without RLS (NRLS group).
Methods: Clinical data on 78 insomniacs enrolled in group CBT-I over an 18 month period was retrospectively reviewed. RLS group included 19 patients (42% male, average age = 55±17 years) and NRLS group included 59 patients (47% male, average age = 44±12 years). Group CBT-I included standard components over seven 90-minute sessions. Participants attended an average of 6 sessions. Pre-and-post measures included Insomnia Severity Index (ISI), Epsworth Sleepiness Scale (ESS), Beck Depression Inventory (BDI), weekly sleep diaries and medication use. The last available sleep diary was used for outcome analyses.
Results: At baseline, no significant group differences were found for BDI, ISI, ESS, sleep onset latency (SOL), wake time after sleep onset (WASO), total sleep time (TST) and sleep efficiency (SE). Patients with RLS were more likely to be prescribed benzodiazepine (p = .001) and non-benzodiazepine (p = 0.06) sleep medications and were older (p=.01). Of those who underwent diagnostic PSG a Respiratory Disturbance Index (RDI) > 10 was present in 10/14 (71%) patients with RLS and 14/33 (42%) of NRLS patients. A main effect for pre-to-post-treatment was found with significant improvement in WASO, SOL, TST, SE and BDI.
Conclusion: Patients with RLS had similar clinical presentation on measures of sleep and depression at the time of entering into CBT-I. RLS patients, however, were older, were more likely to be on benzodiazepines, and had higher prevalence of sleep disordered breathing. Patients with RLS responded to CBT-I as well as those without RLS. Both groups achieved improvement in sleep.

0800

ACTH AND CORTISOL RESPONSES TO DEX/CRH IN PRIMARY INSOMNIA

Watson K, McClure T, Linn S, Roth T, Richardson G
Henry Ford Hospital, Detroit, MI, USA

Introduction: We have proposed that dysregulation of the hypothalamic pituitary adrenal (HPA) axis is an important pathophysiologic factor in primary insomnia (PI). The combined dexamethasone/corticotropin releasing hormone (DEX/CRH) test provides an index of functional HPA status, and has been used to characterize patients at risk for psychiatric disorders. We previously reported that ACTH responses were exaggerated in a small sample of patients with an insomnia complaint. We now report the results of a larger sample studied using both PSG and DEX/CRH.
Methods: 22 patients with PI (12f; mean age 30.0, range 19-45y) and 34 controls (17f; mean age 29.2, range 19-46 y) were evaluated with both laboratory PSG and MSLT recordings, and in a separate visit, DEX/CRH testing. Psychiatric co-morbidities were excluded using questionnaire (HAMD < 12) and interview. The DEX/CRH test consists of self-administration the previous evening of 1.5mg dexamethasone, followed the next day by IV stimulation with 100 mcg ovine CRH through an indwelling catheter. q15min plasma samples are collected for 3.75 hours beginning 1 hour before infusion. ACTH and cortisol responses are analyzed for 1) basal (pre-CRH) levels, 2) integrated response (AUC) and 3) peak response.
Results: As reported, ACTH responses (AUC and peak) were larger in patients with the insomnia complaint, but in the larger sample these differences are not significant. However, in contrast to the results from the smaller sample, both peak and integrated cortisol responses were significantly exaggerated, particularly in those insomnia patients with objective sleep disturbance (sleep efficiency <85%): Both peak (F=12.3, p<.01) and integrated (F=8.1, p<.01) cortisol responses were significantly larger in the patients with objective insomnia. Controlling for age, sex, race and non-sleep Hamilton score did not affect the relationship.
Conclusion: These data provide additional evidence for HPA abnormalities in PI. Evidence for an exaggerated cortisol response makes the findings in insomnia more consistent with previous reports of DEX/CRH testing in patients at risk for major depression.
Support (optional): Supported by MH63968 (GSR)

0801

SHORT TERM STABILITY OF SLEEP MEASURES: AN APPLICATION OF STRUCTURAL EQUATION MODELING

Wohlgemuth W,[1] Llabre M,[2] Edinger J[3]
(1) University of Miami, Miami, FL, USA, (2) University of Miami, Coral Gables, FL, USA, (3) Duke University, Durham, NC, USA

Introduction: Although understanding the measurement characteristics of sleep variables is fundamental to improving our ability to assess relationships among these variables, little attention has been focused on this area of research. We have previously reported the short-term stability of sleep measures in an elderly cohort which indicated that a single night of recording is not sufficient to provide reliable measures. The present study is a replication of that earlier study in a larger cohort of subjects with a broader age range.
Methods: Through careful screening via medical exam and structured sleep and psychiatric interviews, 100 (Age range= 21-75 yrs.) individuals meeting criteria for Primary Insomnia and 100 non-complaining normal sleepers were recruited. All subjects in each sample were randomly assigned to complete three consecutive LPSG nights and three consecutive Home PSG nights. In addition, each subject completed subjective sleep logs each morning following PSG testing. Dependent measures from both PSG and sleep logs include SOL, WASO, sleep efficiency, time in bed total sleep time. MPlus statistical sofware was used to estimate reliability coefficients for each of the variables.
Results: As we have reported previously in an elerly cohort, these sleep measures based on a single night are unreliable and multiple nights are required to improve reliability. Coefficients ranged from .30 to .60.
Conclusion: This analysis in a cohort of 100 normal sleepers and 100 primary insomnaics have replicated our previous findings demonstrating that a single night of recording is inadequate to provide sufficient reliabilty.

0802

SLEEP MISPERCEPTION IS SUPPORTED BY ALTERATIONS OF CAP AND AROUSALS

Parrino L,[1] Smerieri A,[2] Milioli G,[3] De Paolis F,[2] Terzano M[4]
(1) University of Parma , Italy, Parma, AE, Italy, (2) University of Parma, AE, Italy, (3) University of Parma, AE (Europe), (4) University of Parma, Emilia-Romagna, Italy

Introduction: Paradoxical insomnia is characterized by the disparity between subjective and objective findings. It has been hypothesized that individuals with paradoxical insomnia misperceive their sleep because they are poor estimators of time. However, the performance of patients with insomnia is not different from that of the noninsomnia group when time estimation tasks are carried out. Candidate mechanisms that underpin misperception can be searched in the investigation of sleep microstructure which is generally neglected by conventional scoring methods.
Methods: Data collected from all-night PSG recordings of 16 patients with a diagnosis of paradoxical insomnia (Polysomnographic Total Sleep Time or PTST of at least 6 ½ hours, subjective sleep latency of at least 30 minutes, and the difference between PTST and subjective total sleep time of at least 60 minutes) without coexisting neurological, medical or psychiatric disorders (misperceptors) were compared with those of 16 normal gender- and age-matched subjects (controls). Paired t-tests were used for comparisons.
Results: Patients and controls presented non significant differences in the amounts of objective sleep time (464 min vs. 447 min) and objective sleep latency (9 min vs. 8 min). However, compared to controls, misperceptors reported a significantly shorter time of perceived sleep (285 min vs. 461 min; p=0.001) and a significantly longer duration of perceived sleep latency (51 min vs. 22 min; p=0.024). At the microstructural level, arousal index (31/hour vs. 19/hour; p = 0.0001) and total CAP rate (58% vs. 35%; p = 0.0001) were significantly higher in insomniacs. In the sleep period between objective and subjective sleep onset, CAP rate was 64.4% in misperceptors and 45% in controls (p=0.05). Insomniacs showed significantly higher amounts of CAP rate in stage 1 (62.7% vs. 37.5%; p=0.001) and in stage 2 (53,3% vs. 33.1%; p=0.001).
Conclusion: These findings suggest that in misperceptors difficulty to maintain consolidated sleep is interpreted as wakefulness. In particular, if sleep between two successive awakenings is excessively fragmented, i.e, increased arousal index and CAP rate, the interval separating the two events is globally lumped together and perceived as waking time.

0803

TRICHOTILLOMANIA EXCLUSIVELY IN SLEEP; A SURVEY OF DERMATOLOGISTS

Murphy C, Redenius R, O'Neill E, Zallek S
OSF Saint Francis Sleep Disorders Center at the Illinois Neurological Institute, Peoria, IL, USA

Introduction: Trichotillomania is an impulse control disorder that creates an irresistible urge to pull out one´s own body hair. It is one cause of unexplained hair loss. It affects approximately one to two percent of Americans, many of whom go undiagnosed. It may occur in wakefulness and sleep, but until our recently published case report it had not been described to occur solely in sleep.

We reported a case of a 24-year-old woman with trichotillomania only in NREM sleep. It responded well to imiprimine as do some other NREM sleep parasomnias.

As unexplained alopecia often presents to dermatologists we sought to determine whether dermatologists have seen or suspected trichotillomania exclusively in sleep.
Methods: Eight-hundred seven practicing dermatologists in the Midwest were identified through the American Academy of Dermatologists website database. A 10-question multiple-choice survey regarding trichotillomania was mailed to each. Responses were anonymously returned by fax.
Results: Of the 107 (13%) respondents, 12 (11.2%) had seen patients with trichotillomania that occurred solely during sleep. In cases of unexplained hair loss, twenty-one (19.6%) suspected hair-pulling occurred only in sleep.

Seventy-six subjects (71%) said they had seen patients with unexplained hair loss; 67 (88%) of those respondents said they would ask those patients if they pull their hair. Only 16 (23.8%) said they would ask patients who deny hair pulling while awake if they pull their hair during sleep. Twenty (18.7%) said they ask patients diagnosed with trichotillomania if hair pulling also occurs in sleep.
Conclusion: Although trichotillomania exclusively in sleep has only recently been formally reported, some dermatologists report having recognized this entity in their own practices. When dermatologists see patients with unexplained hair loss, only a small percentage consider trichotillomania isolated to sleep. Increasing physician awareness of this disorder may allow diagnosis and treatment of many patients.
Support (optional): OSF Saint Francis Medical Center Foundation

0804

MELATONIN THERAPY FOR REM SLEEP BEHAVIOR DISORDER

Yun C,[1] Chu M,[2] Ji K,[1] Lee J,[1] Ha C,[1] Kwon O[3]
(1) Inha University Hospital, Incheon, Incheon, South Korea, (2) Hallym University College of Medicine, Anyang, Kyung-gi-do, South Korea, (3) Seoul, South Korea

Introduction: REM-sleep behavior disorder (RBD) commonly occurs in old-age group and shows a good response to clonazepam. However, clonazepam is ineffective in some patients, and can cause cognitive impairment or aggravate, even precipitate sleep-disordered breathings. Melatonin (MLT) has been reported as other treatment option and is much less likely to impair cognitions or airway patency. We performed this study to define the effectiveness and the dosage range of melatonin therapy in RBD.
Methods: We recruited consecutive patients who had RBD confirmed by standard nocturnal polysomnography. Patients with relative contraindications of MLT were excluded. MLT was started at 0.5 mg/night and increased according to clinical response. Successful response is defined when symptoms are free or reduced in frequency more than 90% compared with baseline frequency. Any physical injury or violence should not be present.
Results: Sixteen consecutive RBD patients (10 male, median age 69 years, range 54 – 89) were eligible. Eleven had significant obstructive sleep apneas (apnea-hypopnea index>15), two Parkinson´s disease, one restless legs syndrome, and two hypertension. MLT was treated (dosage range 2-8 mg/night, treatment duration range, 7 – 35 months). Twelve patients showed successful response (dosage range 2-8 mg/night) but four showed unsatisfactory response to melatonin 4-8 mg/night. Low dose clonazepam was added in these patents. Among eleven with significant obstructive sleep-disordered breathings (apnea-hypopnea index: 22.6–35.2), nine showed successful response to MLT. No significant adverse effect was observed during follow-up period.
Conclusion: MLT can be the effective treatment for controlling RBD without significant adverse effect. Effective dosage is variable. MLT could be the first-line drug in RBD, especially with co-existing significant sleep-disordered breathings.

0805

"OFFSET" HYPOTHESIS OF BEDWETTING (SLEEP ENURESIS)

Golbin A, Golbin D
Sleep and behavior Medicine Institute, vernon Hills, IL, USA

Introduction: Nocturnal Sleep Enuresis (NE) is the most common parasomnia, but its physiological mechanism is still a puzzle. The view of NE as an incomplete arousal does not fully explain its nature. Does bedwetting play any function in the sleep mechanisms?
Methods: The history and clinical course of 365 patients with NE, the age range 9-18 years old were reviewed using a factorial analysis. 33 PSG´s of 21 enuretics were compared with 20 PSG´s of non-enuretic children matched by age and sex. 12 PSG´s were repeated 6-12 months after treatment or "self-cure". PSG scorings were performed by certified polysomnographers.
Results: Five statistically significant factors were presented as NE "syndromes": 1.Bedwetting; 2. Changes in sleep architecture; 3. Alertness instability; 4. Treatment resistance; 5. Spontaneous self-cure or deterioration (appearance of other Parasomnias). Three types of sleep structure in NE were found comparing to control: 1: The first cycle was longer, increased stage 4; 2: Increased stage 2 with frequent awakenings, 3: Disorganized sleep structure.
Probability of enuresis was dependent on the length of each stage: stage 2 – 26.7%, stage 3 – 31.2%, stage 4 – 35.7%, REM – 6.4%. After enuresis sleep stages switched to another stage in 64.7% mostly to REM or awake within a few minutes. Enuresis had several "forerunning" PSG characteristics: delta wave paroxysms, spontaneous SGR, heart rate and movements variability. After Enuresis sleep structure had "normalized". Repeated PSG´s after 6 months of dry period were found to be identical to the control
Conclusion: The sleep-wake mechanisms are strongly involved in NE. Resistance to the treatment, "self-cure", "normalization" of sleep structure after an enuretic episode suggested an initially protective (compensatory) function as a physiological "switch" or "stabilizer" to "offset" immature sleep mechanisms. The "offset" hypothesis suggested the importance of the corrections of sleep problems in the treatment of NE.

0806

REM SLEEP BEHAVIOR DISORDER (RBD) AND EEG PHASIC EVENTS DURING REM SLEEP

Manni R,[1] Terzaghi M,[2] Glorioso M,[2] Zambrelli E,[3] Rustioni V,[3] Marchese D[3]
(1) Institute of Neurology, Pavia, Italy, (2) Institute of Neurology"C. Mondino Foundation", AE (Europe), (3) Institute of Neurology "C. Mondino Foundation", AE (Europe)

Introduction: Little is known about phasic EEG activities during REM sleep in RBD.
RBD clinical manifestations are thought to be strongly affected by the dream content (RBD as "enacted dream " phenomena). However the degree of brain activation during REM sleep, partially reflected by EEG phasic events , may further affect RBD triggering and motor-behavioral patterns.
This study is aimed at evaluating potential relationship between RBD episodes and sawtooth waves (STW) and alpha bursts [1].
Methods: Standard visual analysis of 128 , video polysomnographic recorded RBD episodes in 34 REM periods, was done in 17 male subjects (mean age 66.7 years, sd 7.5) affected with idiopathic RBD, each subject having at least one RBD episode .
Results: Recurrent, intra – and inter-subjects, very similar, but not stereotypical, episodes were observed:
A) Sleeptalking with minimal motor manifestations (42% of the cases)
B) Brisk, jerking movements of the entire body , torso, arms or limbs , in association with shouting or screaming (27%)
C) Semipurposeful movements (gesturing, pointing., punching) in association with utterances/talking (31%).
88.2 % of the episodes proved to be associated with at least one of the EEG phasic events, 15% with STW, 50% with alfa bursts and 23% with both.($p<0.05$) . RBD episodes type C were preceded by alfa bursts in 89.7% , RBD type B in 68% ($p < 0.05$).
Conclusion: Most RBD episodes occur in association with REM EEG phasic events , namely with the alpha burst patterns. Episodes of semipurposeful movements were preceded by alpha burst more frequently than the other types of episodes. REM alpha bursts have been hypothesized to work as "microarousal" during REM sleep [1] . It can be hypothesized that different state of brain activation may influence occurrence and clinical manifestations in RBD,analogously to what we are used to observing in arousal parasomnia during NREM sleep.

1.Cantero JL *et al.* Spectral Features of EEG Alpha Activity in Human REM Sleep: Two variants with Different Functional Role? Sleep, 23, 6, 2000:1-5.

0807

RETROSPECTIVELY REPORTED CHILDHOOD PARASOMNIAS IN PRIMARY INSOMNIA

Walsh C,[1] Buysse D,[2] Moul D,[3] Nofzinger E,[2] Miewald J,[4] Germain A[2]
(1) University of Pittsburgh School of Medicine, Department of Psychiatry, Ridley Park, PA, USA, (2) University of Pittsburgh, Pittsburgh, PA, USA, (3) Pittsburgh, PA, USA, (4) PA, USA

Introduction: Childhood parasomnias are common and often resolve with minimal intervention. However, childhood parasomnias may predispose to experiencing sleep disturbance in adulthood (Laberge et al, 2000). The goals of this study were to compare the frequency of retrospectively reported childhood parasomnias in subjects with primary insomnia (PI) and healthy subjects; and to compare the sleep quality in PI subjects who did and did not report childhood parasomnias.
Methods: Occurrence of childhood parasomnias was derived from the Survey of Sleep, a locally developed self-report measure of sleep disturbances, quality, and behaviors in 43 healthy subjects (N=14 men; Mean age = 30.6, SD =8.65) and 104 PI subjects (N=51 men; Mean age = 36.9, SD =8.51). The number of subjects who retrospectively endorsed at least one parasomnia in childhood was compared in insomnia and healthy subjects using a Chi-squared test. Group differences on the endorsed frequency of individual parasomnias (nightmares, sleep terrors, sleep walking, sleep talking, enuresis) were also explored. Sleep quality as assessed by the Pittsburgh Sleep Quality Index (PSQI) among PI subjects with and without childhood parasomnias using t-tests.
Results: Insomnia patients more frequently endorsed childhood parasomnias (72.1%) than did healthy subjects (48.8%) $Chi^2 = 7.27$, df=1, $p<.007$). A closer examination of individual parasomnias revealed only a trend for higher frequency of childhood nightmares in insomnia subjects compared to healthy subjects ($Chi^2 = 73.26$, df=1, $p = .07$). Within PI subjects, PSQI scores did not differ in those with or without childhood parasomnias.
Conclusion: Childhood parasomnias were common in both groups. A greater number of PI subjects reported childhood parasomnias than healthy subjects. The findings support the hypothesis that childhood parasomnias may be an indicator of a predisposition for sleep disturbance in adulthood.
Support (optional): This study was supported by the National Institute of Mental Health (MH24652; MH61566, MH-66227, MH01414, MH-30915, RR00056, and MH24652) and by the US Department of Defense PRMRP (PR054093).

0808

VOLTAGE-GATED POTASSIUM CHANNEL ANTIBODIES IN IDIOPATHIC REM SLEEP BEHAVIOR DISORDER

Iranzo A,[1] Graus F,[1] Vincent A,[2] Santamaria J[1]
(1) Neurology Service, Hospital Clinic de Barcelona, Barcelona, Spain, (2) John Radcliffe Hospital, Oxford, UK, Oxford, United Kingdom

Introduction: Subjects initially diagnosed with idiopathic REM sleep behavior disorder (RBD) may develop with the passage of time a neurodegenerative disease such as multiple system atrophy, Parkinson´s disease and dementia with Lewy bodies. However, some patients with idiopathic RBD have not developed a neurodegenerative disease after several years from RBD onset and clinical follow-up. It can be speculated that autoimmune-mediated mechanisms may play a role in the pathogenesis of the idiopathic RBD subgroup of individuals that do not develop a neurodegenerative disease since this parasomnia is associated with HLA class II genes and is common in subjects with the autoimmune-mediated potassium channel antibody-associated limbic encephalitis. The aim of our study was to evaluate the presence of voltage-gated potassium channel antibodies in patients with idiopathic RBD.
Methods: The diagnosis of idiopathic RBD required 1) complaint of dream-enacting behaviors, 2) polysomnographic demonstration of increased muscle activity and abnormal movements during REM sleep, and 3) no clinical evidence of a comorbid neurologic disease after extensive evaluation. Serum levels of voltage-gated potassium channel antibodies were measured by radioimmunoassays in 38 patients with idiopathic RBD diagnosed in our sleep center.
Results: High titers (>100 pM) of voltage-gated potassium channel antibodies were not found in the serum of any of the 38 patients evaluated with idiopathic RBD.
Conclusion: Voltage-gated potassium channel antibodies are not found in the serum of patients with idiopathic RBD. This finding indicates that these antibodies do not paly a role in the pathogenesis of RBD.

0809

"A DEAD BODY CLIMBED ON TOP OF ME": A STUDY OF SLEEP PARALYSIS IN MEXICAN ADOLESCENTS

Jimenez-Genchi A, Avila-Rodriguez V
Instituto Nacional de Psiquiatria Ramon de la Fuente, Mexico City, Mexico

Introduction: A previous epidemiologic study found a prevalence rate for sleep paralysis (SP) of 11.3% in Mexican population. However, those authors used a clinical description to investigate SP, while Mexicans use the expression "a dead body climbed on top of me" (se me subió el muerto) to describe an experience that seems to be equivalent to SP. Considering that the onset of SP usually ranges from 14 to 17 years, we studied adolescent subjects with the aim to elicit accurate data about frequency and features of initial SP episodes.
Methods: Adolescents were recruited from 3 high schools in Mexico City. Subjects were included if they were younger than 18 years old and chose to participate in the study. All teen-agers completed a Sleep Paralysis Questionnaire and the Epworth Sleepiness Scale.
Results: RESULTS Two hundred and thirty subjects were studied (mean age 16.2 ± .7; 71.4% female). 90% had heard about the "a dead body climbed on top of me" expression and 26.4% had experienced the phenomenon. Most of these subjects (68.3%) had presented 1-3 episodes in their lifetimes and few subjects presented such episodes several times per year (19%). The mean age of onset was 12.5 ± 3 years. In relation to the characteristics of the phenomenon, inability to move was present in 85.5% of SP episodes, inability to speak in 72.6%, chest oppression in 43.5%, sense of a presence in 46.8%, visual hallucinations in 29%, auditory hallucinations in 24.2% and, tactile hallucinations in 12.9%.
Conclusion: Our results suggest that the experience of "a dead body climbed on top of me" is identical to SP. They also show that SP is a highly frequent phenomenon among adolescents and suggest that the discrepancy between prevalence rates for SP is related to the wording of the questions used to investigate SP.

0810

IS SOMNAMBULISM ASSOCIATED WITH PERIODIC LEG MOVEMENTS IN SLEEP?

Pilon M,[1] Zadra A,[2] Montplaisir J[2]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) Universite de Montreal, Quebec, Canada

Introduction: Sleepwalking has been reported in association with other sleep disorders including periodic leg movements in sleep (PLMS). However, whether or not PLMS actually trigger somnambulism is unknown. We previously showed that sleep deprivation significantly increases sleepwalking frequency in predisposed individuals. The goal of the present study was to asses PLMS in relation to somnambulistic episodes during normal sleep and following sleep deprivation in sleepwalkers with a high PLMS index.
Methods: Seven sleepwalkers (6 males, 1 females; mean age: 30.7±9.9 years) with a PLMS index >10 were investigated during a baseline night and during recovery sleep following 25 hours of sleep deprivation. PLMS were defined as movements lasting 0.5 to 5 seconds, separated by intervals of 4 to 90 seconds and occurring in series of at least 4 consecutive movements. PLMS were analysed during sleep and in relation to each somnambulistic event.
Results: Seven somnambulistic episodes were recorded at baseline and 19 during recovery sleep. Sleep deprivation significantly increased the mean frequency of the episodes (1.0±0.8 vs 2.7±1.4, p<0.05) while significantly decreasing subjects' mean PLMS index (19.5±5.5 vs 8.3±5.5, p<0.05). The proportion of somnambulistic episodes preceded within 90 seconds by a single leg movement part of a PLMS significantly decreased from baseline (3/7 or 43%) to recovery sleep (0/19 or 0%), p< 0.03. Of the 26 episodes, only 2 (both at baseline) were preceded within 30 seconds by an individual leg movement part of a PLMS and no leg movements were observed immediately prior to any of the episodes' onset.
Conclusion: The data indicate that most sleepwalking episodes in adults with a high PLMS index are not associated to or triggered by PLMS. Moreover, significant increases in the frequency of sleepwalking episodes after sleep deprivation are accompanied by significant decreases in PLMS frequency.
Support (optional): Research supported by the Canadian Institutes of Health Research, the Natural Sciences and Engineering Research Council of Canada and the Fonds de la Recherche en Santé du Québec.

0811

NOCTURNAL SCRATCHING AS A CHRONIC, INJURIOUS PARASOMNIA IN PATIENTS WITHOUT PRIMARY DERMATOLOGIC DISORDERS

Schenck C,[1] Mahowald M[2]
(1) University of Minnesota Medical School, Minneapolis, MN, USA, (2) University of Minnesota, Minneapolis, MN, USA

Introduction: 7 publications involving polysomnographic (PSG) monitoring have reported on chronic, non-injurious, nocturnal scratching in 63 adults & 9 children with 11 pruritic dermatologic disorders, mainly atopic dermatitis, atopic eczema & lichen simplex chronicus. Nocturnal scratching was most common in stage 2 NREM sleep, but was present throughout NREM & REM sleep. Therapy was addressed in one report on 12 adults utilizing trimipramine & trimeprazine, and in one report on 9 children utilizing oral/topical corticosteroids & antibiotics, which were all ineffective. Another publication involving 34 adults with paroxysmal nocturnal arousals documented scratching & other arousal behaviors that were considered to be manifestations of nocturnal frontal lobe epilepsy (NFLE). We now report on a series of 3 cases with nocturnal scratching as a manifestation of parasomnia.
Methods: One male & 2 females presented clinically to our sleep center with a complaint of injurious, exclusively nocturnal scratching that was the sole, nightly parasomnia complaint (n=1) or was part of a frequent parasomnia symptom complex (n=2). The patients had clinical sleep/wake & psychiatric interviews, neurologic exams, psychological testing and standard overnight video-PSGs with seizure montage & fast EEG paper speeds (15 & 30 mm/sec). Treatment was then initiated.
Results: Neither clinical nor EEG seizure-like activity, sleep-disordered breathing, or PLMs were found in any patient during PSG monitoring; increased spontaneous arousal indices ranged from 25/hr to 34/hr. A 28 y.o. married man with a 1.5 year history of nightly, exclusively perianal scratching with excoriation and bleeding had perianal scratching throughout NREM sleep. Medical evaluations by multiple specialists did not detect parasites, colorectal problems, dermatologic or psychiatric disorders. Hypnotherapy, corticosteroid creams, clomipramine and antihistamines were ineffective; however, combined clonazepam (0.5 mg) & paroxetine (20 mg) therapy at hs was found to be 50% effective. A 26 y.o. African American female with longstanding nocturnal scratching & other parasomnia behaviors, including sleepwalking, developed keloids from vigorous scratching of her shoulders, back and buttocks. PSG findings were behaviorally unremarkable. Bedtime therapy with clonazepam (0.5 mg) fully controlled all parasomnia behaviors. A 50 y.o. female with a 15 yr history of injurious nocturnal scratching, bruxism & sleep terrors had 55% sleep efficiency but no

parasomnia behaviors during PSG. Treatment outcome was not available. The diagnosis of abnormal nocturnal scratching in all 3 patients was Confusional Arousals, a NREM parasomnia.
Conclusion: Injurious nocturnal scratching is a treatable variant of Confusional Arousals manifesting as a high frequency parasomnia that is either an exclusive symptom or part of a parasomnia symptom complex. Perianal scratching can be the sole nocturnal scratching behavior.

0812

PARASOMNIA BEHAVIORS AND ANXIETY IN COLLEGE STUDENTS

Impastato A, Diana G, Gehrman P
University of the Sciences in Philadelphia, Philadelphia, PA, USA

Introduction: Parasomnias are disorders with abnormal behavioral or physiological episodes that occur during sleep. Little is known about the causes of parasomnias but it has been suggested that they are related to anxiety. This study was a first look at the developmental stability of parasomnia behaviors and their relationship with anxiety.
Methods: Forty undergraduate students participated in the study for course credit. Each student completed the Pittsburgh Sleep Quality Index (PSQI) to assess general quality of sleep, the State-Trait Anxiety Inventory (STAI) – trait version to assess anxious tendencies, and a survey assessing the presence of parasomnia behaviors such as sleepwalking and teeth grinding, both current and during childhood. Descriptive statistics were computed along with correlations among the questionnaires.
Results: The mean number of parasomnia behaviors was 1.7 during childhood and 1.2 current, with 77.5% and 62.5% of the subjects reporting at least one behavior, respectively. The mean STAI score was 41.98, placing subjects at the 76th percentile of their respective age range. The mean PSQI score was 6.2, indicating mild clinical sleep disturbance. There were significant correlation between the number of childhood and current behaviors (r=.77), between the number of current behaviors and the PSQI score (r=.31), and between the PSQI and STAI scores (r=.62).
Conclusion: The results of this study suggest that the experience of abnormal sleep behaviors may be a trait that is consistent over time. In addition, individuals with a higher incidence of parasomnia behaviors were more likely to have poorer general sleep quality, and individuals with poor general sleep quality had higher levels of anxiety. Surprisingly there was no significant relationship between current anxiety and these behaviors. What was most unexpected was the high proportion of students who reported current parasomnia behaviors. Parasomnias may represent and overlooked area for college students that leads to poor sleep.

0813

EVENT-RELATED POTENTIALS IN IDIOPATHIC RAPID EYE MOVEMENTS SLEEP BEHAVIOUR DISORDER

Ferini-Strambi L,[1] Raggi A,[2] Zucconi M,[3] Consonni M,[4] Cappa S,[5] Manconi M[6]
(1) Università Vita-Salute San Raffaele, Milan, Italy, (2) Department of Neurology and Neurorehabilitation, Ospedale San Raffaele Turro Hospital, Italy, (3) San Raffaele Institute, Milan, Milan, Italy, (4) San Raffaele Institute, Milan, Italy, (5) Scientific Institute of San Raffaele, Sleep Medicine Centre, Italy, (6) Scientific Institute of San Raffaele, Sleep Medicine Centre, Milan, Italy

Introduction: REM Behaviour Disorders (RBD) has been documented to co-occur with neurodegenerative disorders with a pathological intracellular deposit of a-synucleine protein, such as Parkinson´s disease, multiple-system atrophy and dementia with Lewy bodies. Aim of the present study was to assess psychophysiological parameters in idiopathic rapid eye movements sleep behaviour disorder (RBD), in order to identify possible markers for pre or sub-clinical cognitive abnormalities.
Methods: Sixteen consecutive unmedicated patients with idiopathic RBD and 16 age- and sex-matched controls performed active and 15 passive auditory oddball paradigms and an attentional test. RBD was excluded in the control group by means of history and polysomnographic data, while in the patient group the clinical RBD onset preceded of 41.2 ± 30.94 months in mean (range 6– 120 months) our evaluation. Both patients and controls underwent a standard encephalic MRI.
Results: Except for the PLMS index, which was greater in the patient group, no other significant differences were observed in sleep parameters between controls and patients. No significant differences between controls and patients were observed in: N100 latency and amplitude; P200 latency and amplitude; N200 latency and amplitude to rare stimuli, and P300 latency and amplitude. No significant differences were found in the following inter-peaks: mean P2–N2; mean N2–P3. The two groups showed a difference in the inter-17 peak interval between N100 and P200 in the active condition. A significant correlation between attentional matrices scores and N100 amplitude at Fz and Cz to standard stimuli in the passive condition was found in controls but not in patients.
Conclusion: In RBD there are minimal event-related potentials (ERPs) abnormalities involving the early stages of information 20 processing. ERPs are not sensitive to pre or sub-clinical cognitive abnormalities in RBD. In alternative, these findings might support the existence of a truly idiopathic RBD.

0814

RELATIONSHIP BETWEEN SLEEP BRUXISM AND MENTAL HEALTH

Fitzmorris M,[1] Tatum J,[2] Bramoweth A,[2] Taylor D,[2] Gardner C,[3] Williams J,[2] Zimmerman M,[2] Roane B,[2] Grieser E[2]
(1) University of North Texas, fort worth, TX, USA, (2) University of North Texas, Denton, TX, USA, (3) TX, USA

Introduction: The current study examines the relationship between Sleep Bruxism (SB) and mental health in college students. SB is defined as "a stereotyped movement disorder characterized by grinding or clenching of the teeth during sleep" (Lavigne & Manzini, 2000). A single mechanism or theory cannot explain SB pathophysiology. Rather, this motor activity is more likely a result of biological and psychosocial influences within an individual (Lavigne & Manzini, 2000). In a current study, we examined the relationship between SB and mental health.
Methods: Participants (N=387) completed a health survey to assess psychological well- being, which included a self report of teeth grinding at night. We used the Symptom Check List (SCL-90) as our dependent varible. The SCL-90 is a 90-item questionnaire that assesses nine symptom dimensions; somatization (SOM), obsessive-compulsive (O-C), interpersonal sensitivity (I-S), depression (DEP), anxiety (ANX), hostility (HOS), phobic anxiety (PHOB), paranoid ideation (PAR) and psychoticism (PSY), as well as a global severity index.
Results: An ANOVA revealed that people with SB had significantly higher GSI ($p < .01$) scores than people without SB. Further analyses showed that people with SB also scored higher on SOM ($p < .01$), O-C ($p < .01$), I-S ($p < .01$), DEP ($p < .01$), ANX ($p < .01$), HOS ($p < .01$), PAR ($p < .01$), and PSY ($p < .01$).
Conclusion: Preliminary results indicate that a relationship exists

between SB and many mental health components, however, further research is required in order to gain a comprehensive understanding of the disorder.

0815

PREVALENCE OF RESTLESS LEGS SYNDROME (RLS) IN SUBJECTS WITH ADULT ADHD

Zak R,[1] Fisher B,[2] Moss N,[2] Couvadelli B,[3] Walters A[3]
(1) Gaylord Sleep Services, New Rochelle, NY, USA, (2) United Psychological Services, Washington Township, MI, USA, (3) New Jersey Neuroscience Institute at JFK Medical Center, Edison, NJ, USA

Introduction: There is growing evidence that Restless Legs Syndrome (RLS) and Attention Deficit Hyperactivity Disorder (ADHD) occur more frequently together than by chance alone. Members of this group have already established an increased prevalence of ADHD in adults with RLS. This study explores the relationship further by seeing if there is an increased prevalence of RLS in the adult ADHD population.
Methods: Subjects referred for an ADHD evaluation were recruited. Attempts to decrease bias include excluding subjects also referred for evaluation of RLS and informing subjects that the study would assess the prevalence of medical conditions that might be related to ADHD without mentioning RLS. Inclusionary criteria were fulfillment of criteria for ADHD based on CAARS-Self Report (LV) and the DSM-IV symptom checklist and no history to warrant a DSM-IV diagnosis for depression, anxiety, bipolar disorder, or substance abuse, determined by self-reports and screening based on the Beck Depression Inventory, Beck Anxiety Inventory and a bipolar screening questionnaire. If positive for ADD/ADHD, subjects were then administered a specific battery of diagnostic neuropsychometric tests. Qualified subjects were then contacted by a neurologist over the phone, who screened them for RLS using the John Hopkins Telephone Diagnostic Interview. If diagnostic criteria were met for RLS, the RLS Rating Scale was also administered.
Results: The clinical sample comprised 32 subjects, ranging in age from 19 to 65 years old (M = 44.4). Results indicated that 18.75% (6/32) of the subjects were positive for RLS. This percentage is higher than the general population prevalence estimates of 4.1% to 9.7%.
Conclusion: These preliminary results support the belief that RLS and adult ADHD are related disorders. Even though this study did not include a control group and may be underpowered, clinicians should be aware that the two conditions may often be co-morbid, which in turn could have therapeutic implications.

0816

THE SLEEPMED INSOMNIA INDEX, EPWORTH SLEEPINESS SCALE, AND INTERNATIONAL RESTLESS LEGS SCALE AS CLINICAL MEASURES IN TREATED SUBJECTS WITH MODERATE TO SEVERE PRIMARY RESTLESS LEGS SYNDROME

Turner J,[1] Bogan R,[1] Mahaffey D,[2] James D[3]
(1) SleepMed, Inc., Columbia, SC, USA, (2) SleepMed Inc., Columbia, SC, USA, (3) SleepMed, Columbia, SC, USA

Introduction: The most common symptom associated with restless legs syndrome (RLS) is sleep disturbance leading to reduced quality of life. The SleepMed Insomnia Index (SMI) is a simple patient administered tool that quantifies the severity of insomnia in clinical practice. The Epworth Sleepiness Scale (ESS) is a validated measure of daytime sleepiness. This analysis describes the correlation between the SMI, ESS, and International Restless Legs Scale (IRLS) scores pre and post therapy in subjects with primary moderate to severe RLS. The Clinical Global Impression (CGI) is used to assess severity and improvement.
Methods: Nineteen consecutive subjects presenting to our sleep clinic with primary RLS and with IRLS scores >15 were included. Each subject had a CGI-S(severity) in the moderate to severe category at baseline to be included. No subjects were included with other underlying sleep disorders or significant medical or psychiatric illnesses. Post therapy assessments were performed on stable doses of medication. The mean scores, standard deviations, t-tests, and Pearson correlations for the pre and post treated groups were assessed.
Results: Scores for the groups were pre SMI 26(8), post SMI 8(7), pre IRLS 30(3), post IRLS 7(6), pre ESS 10(5) and post ESS 5(4) with t-tests showing statistically significant improvement with therapy. Correlation was seen with pre IRLS and pre SMI $r=0.5$ $p<0.01$. Mean change of scores with treatment was SMI 18(9), IRLS 23(6), and ESS 5(5) with t-tests significant with IRLS and SMI $p<0.03$. Correlation was seen in change of score with post IRLS and post SMI scores $r=0.6$ $p<0.004$. All subjects showed improvement in the CGI-I(improvement) scale with treatment.
Conclusion: The SMI correlates with IRLS as to the severity of RLS and efficacy of therapy.

0817

CARDIOVASCULAR CHANGES ASSOCIATED WITH PERIODIC LEG MOVEMENTS DURING SLEEP IN NORMAL SUBJECTS

Pennestri M,[1] Lanfranchi P,[1] Fradette L,[1] Richard M,[1] Colombo R,[2] Montplaisir J[1]
(1) Centre d'étude du sommeil, Hôpital du Sacré-Coeur, Montreal, Quebec, Canada, (2) Department of Bioengineering, Salvatore Maugeri Foundation, Veruno, Italy

Introduction: Several studies have shown a high prevalence of periodic leg movements during sleep (PLMS) in healthy normal subjects, especially in older populations. The clinical significance of PLMS in normal non-complaining subjects is still controversial. Recently, we have demonstrated that PLMS in patients with restless legs syndrome (RLS) are associated with a significant increase not only in heart rate (HR), but also in blood pressure (BP). The aim of this study was to assess HR and BP changes associated with PLMS with and without micro-arousals (MA) in healthy subjects.
Methods: We studied eight normal subjects (3 women; age=44.4±10.9 yrs) with normal BP at rest (systolic BP(SBP)=108.8±11.1mmHg, diastolic BP(DBP)=68.4±9.1mmHg). Beat-to-beat non invasive BP (Portapres) was continuously recorded during one night of polysomnography. Ten PLMS with MA and 10 PLMS without MA were analysed in each subject. Only movements which were separated by at least 20 seconds were selected for analysis, to avoid the overlapping of cardiovascular responses. For each movement, the increase in HR, SBP and DBP was calculated as the difference between the peak value and the baseline (mean value for beats –10 to –4, before the movement). The within-subject comparison of increments associated with PLMS with and without MA was assessed by paired t-tests.
Results: Significant increments of HR and BP were associated with all PLMS. PLMS with MA, compared to PLMS alone, were associated with a higher rise of HR(11.0±4.3 versus 6.5±2.3bpm,$p=0.003$), SBP(21.9±6.1 versus 14.2±4.5mmHg,$p=0.0006$) and DBP(12.3±4.7 versus 6.9±1.8mmHg,$p=0.003$).
Conclusion: These results show important increases of HR and BP in association with PLMS in normal non-complaining subjects, similar to what we observed in RLS patients. Studies have shown that enhanced BP variability is associated with the development of vascular and cardiac damage. PLMS-related repetitive BP fluctuations could thus be harmful to the cardiovascular system, even in normal subjects.
Support (optional): Supported by the Canadian Institutes of Health Research, "Les Fonds de la Recherche en Santé du Québec" and the Canadian Government Senior Chair on Sleep Disorders (J.Montplaisir).

0818

ASSOCIATION OF RESTLESS LEGS SYNDROME AND CARDIOVASCULAR DISEASE IN THE SLEEP HEART HEALTH STUDY

Winkelman J,[1] Shahar E,[2] Sharief I,[3] Gottlieb D[4]
(1) Brigham and Women's Hospital, Sleep Health Centers, Brighton, MA, USA, (2) The University of Arizona, Tuscon, AZ, USA, (3) University of Arizona, Tuscon, AZ, USA, (4) Boston University, Boston, MA, USA

Introduction: Objective: This study evaluates the cross-sectional association between RLS and prevalent CVD in a large community-based sample of middle-aged and elderly subjects.

Background: Previous limited epidemiological data suggests an association of RLS, and coronary artery disease (CAD) and cardiovascular disease (CVD). The basis for this relationship may be the repetitive EEG arousals and/or autonomic hyperactivity during sleep observed in patients with RLS and associated PLMS.
Methods: This is a cross-sectional observational study of 1730 men and 2101 women (mean age of 67.7 years) who were enrolled in the Sleep Heart Health Study, a community-based study of the cardiovascular consequences of sleep-disordered breathing. RLS was defined by positive responses on a self-administered questionnaire to the four IRLSSG diagnostic criteria, with symptoms occurring at least five times per month and associated with at least moderate distress. Coronary artery disease (CAD) was determined by self-report of doctor-diagnosed angina, myocardial infarction, or coronary revascularization procedure. Total cardiovascular disease included CAD or history of physician-diagnosed stroke or heart failure. The relation of RLS to prevalent CAD and CVD was examined by multivariable logistic regression models with adjustment for age, gender, race, BMI, use of antihypertensive or antidiabetic medications, systolic blood pressure, sleep apnea, and smoking and alcohol use.
Results: RLS was present in 6.4% (N=134) of females and 3.4% (N=58) of males. The adjusted odds ratios for CAD and CVD were 1.98 (95% CI 1.36-2.88) and 2.03 (1.43-2.89), respectively, for subjects with RLS compared to those without RLS. The associations of RLS with CAD and CVD were only apparent in those with RLS symptoms at least 16 times per month and were stronger in those with severe than in those with moderately bothersome symptoms.
Conclusion: RLS is positively associated with prevalent CAD and CVD. This association appears stronger in those with greater frequency or severity of RLS symptoms.
Support (optional): National Heart, Lung, and Blood Institute

0819

DIRECT AND INDIRECT COSTS OF RESTLESS LEGS SYNDROME (RLS)

Happe S,[1] Stiasny-Kolster K,[2] Peglau I,[3] Mayer G,[4] Giani G,[5] Geraedts M,[5] Trenkwalder C,[6] Dodel R[2]
(1) Klinikum Bremen-Ost/University of Goettingen, Bremen, Germany, (2) Dept. of Neurology, University of Marburg, Marburg, Germany, (3) Private Neurological Practice, Berlin, Berlin, Germany, (4) Hephata Klinik Schwalmstadt-Treysa, Schwalmstadt-Treysa, Germany, (5) Dept. of Biometrics and Epidemiology and School of Public Health, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany, (6) Paracelsus Elena Klinik Kassel, Kassel, Germany

Introduction: Objective: To determine the direct and indirect costs of patients with RLS in Germany.

Background: About 10% of the population suffer from RLS. Sensorimotor symptoms are often associated with sleep disturbances, problems at work, and reduced quality of life. Approximately 1% to 3% of the population are assumed to need an RLS-specific treatment.
Methods: 292 patients (190 females, 65.5 +/- 10.5 years) were recruited in four specialized movement disorders clinics and one private neurological practice. Inclusion criteria were: 1) Visiting one of the centers during the last 12 months. 2) Fulfilling the diagnostic criteria according to the International RLS Study Group 3) No participation in other clinical or epidemiological trials. Patients were either asked to fill in the questionnaire during their visit in one of the participating centers or to fill in and send back a mailed questionnaire. Sociodemographic, clinical and health-related status of all RLS patients was documented. In addition, health care resource utilization depending on RLS as well as indirect costs were sampled. Costs (2005 €) were derived from various German medical economic resources and were calculated from the societal perspective.
Results: Total costs for the three months evaluation period were €1300 +/- 2850. Indirect costs amounted to €850 +/- 2510 and were calculated based on the productivity loss using the human capital approach. Direct costs were €450 +/- 990, including inpatient stay (€60), drugs (€370), out-patient consultation (€13), costs for physiotherapy (€20) and others. Approximately 80% of the drug costs are due to dopamine agonists.
Conclusion: This is the first study evaluating the costs due to RLS. Indirect costs are the main cost components along with drug costs. Further studies evaluating the cost-effectiveness of different treatment options are necessary to provide evidence for a rational therapeutic use of available drugs in RLS.
Support (optional): Unrestricted grant (01GI0201) from the German Federal Ministry of Education and Research.)

0820

CLINICAL CHARACTERISTICS OF RESTLESS LEGS SYNDROME IN PSYCHIATRIC INPATIENTS TAKING ANTIPSYCHOTICS

Kim T, Lee D
National Gongju Hospital, Gongju, Chungnam, South Korea

Introduction: Restless leg syndrome (RLS) has been suggested as a disorder of subortical dopaminergic systems. It is known that dopamine antagonists that cross the blood-brain barrier can exacerbate RLS symptoms. In this study, we investigated clinical characteristics of RLS in a subpopulation taking antipsychotics in a psychiatric ward.
Methods: We recruited 207 patients (107 males, 100 females) who had been taking antipsychotics among the psychiatric inpatients. We evaluated the patients with diagnostic criteria of RLS in the second edition of International Classification of Sleep Disorders (ICSD). Clinical variables for each patient were reviewed. In addition, International RLS Study Group Rating Scale (IRLS) (version 2.1), Barnes Akathisia Rating Scale (BARS), Positive and Negative Syndrome Scale (PANSS) were performed. Statistical analysis was done.
Results: Fifteen patients (7.5%) were categorized as RLS group, showing significantly higher IRLS score than non-RLS group (t=2.789, p=0.009). There was no significant differences (p>0.05) between RLS and non-RLS group in gender, present age, duration and kind of antipsychotic medications, scores of BARS and PANSS. There was no correlation between duration of antipsychotic medications and score of IRLS(r=-0.188, p=0.136). Thirteen patients with RLS (86.7%) didn't have symptoms of RLS until they started antipsychotic medications. In addition, 13 patients (86.7%), not the same as the foregoing 13 patients, had early-onset (< age 45) RLS and 2 patients (13.3%) had late-onset (>

age 45) RLS.
Conclusion: Although antipsychotics can precipitate patients to RLS, psychiatric inpatients taking antipsychotics showed no more RLS than general population of previous epidemiologic studies did. While duration and kind of antipsychotic medications didn't show difference between RLS and non-RLS grpup, many of patients started RLS after antipsychotic medications. In RLS group of this subpopulation, early-onset was more common than late-onset.
Support (optional): None

0821

WISH FOR TREATMENT IN INDIVIDUALS WITH DIAGNOSED AND UNDIAGNOSED

Happe S,[1] Vennemann M,[2] Evers S,[2] Berger K[2]
(1) Klinikum Bremen-Ost/University of Goettingen, Bremen, Germany, (2) University of Muenster, Muenster, Germany

Introduction: The restless legs syndrome (RLS) is a frequent sleep disorder with a prevalence of 5% to 15% in the Caucasion population. Dopaminergic treatment is effective but it is not known what proportion of all individuals affected has an active desire for treatment, especially among those with only moderate or infrequent symptoms. Aim of this study was to assess the wish for treatment due to RLS symptoms and to analyze its determinants in a population based, cross-sectional survey in Germany.
Methods: In 1312 participants of the Dortmund Health Study, randomly selected from the city registry and aged 25 to 75 years, face-to-face interviews were done and RLS assessed using a validated and published set of questions addressing the four minimal diagnostic criteria for RLS. Treatment wish was assessed with a single question asking for the desire for medication if this would improve symptoms.
Results: The prevalence of RLS was 7.3% based on the symptom questionnaire and 2.3% based on a known doctor diagnosis of RLS yielding an overall prevalence of 8.8%. Symptoms at least 1/week were reported by 53.0% of all cases. 23% of cases with a known and 14% with an unknown RLS diagnosis had a wish for medication to improve symptoms. It was more frequent in men than women, those with frequent symptoms and among cases with a known family history of RLS.
Conclusion: The prevalence of individuals with a known diagnosis of RLS starts to increase in the community. Medication wish is present in 16.5% of all RLS cases, translating into 1.45% individuals in the general population being RLS affected and wishing treatment.
Support (optional): The Dortmund Health Study is supported by equal, unrestricted grants of equal share from the German Migraine and Headache Society and the following companies: Astra Zeneca, Berlin Chemie, Boots Healthcare, GSK, McNeil Pharma, MDS Sharp & Dome, Pfizer.

0822

THE USE OF THE INTERNATIONAL RLS RATING SCALE IN OLDER ADULTS: IMPACT OF SEVERITY OF SYMPTOMS ON SLEEP QUALITY, SLEEPINESS, FATIGUE, DEPRESSION, AND QUALITY OF LIFE

Cuellar N,[1] Strumpf N,[2] Ratcliffe S,[2] Cantor C,[2] Chien D,[2] Hyslop A[2]
(1) University of Pennsylvania, Ambler, PA, USA, (2) University of Pennsylvania, Philadelphia, PA, USA

Introduction: RLS affects 10.6% of older adults with symptoms worsening with age, often occurring daily, despite medications. Most of the research in RLS focuses on primary RLS in a younger age group. The number of publications on RLS in the older adult is sparse with only 1% of RLS research published in geriatric journals. The objective of the study was to examine the impact of RLS symptom severity on sleep quality, sleepiness, fatigue, depression, and quality of life in older adults.
Methods: Using a descriptive, comparative, cross-sectional design, 39 adults with RLS over the age of 65 were recruited from Sleep Centers and RLS Support Groups. Participants were stratified by symptom severity based on scores from the RLS Symptom Severity Scale. Sleep quality (primary outcome), was measured by the Pittsburgh Sleep Quality Index. Sleepiness, fatigue, depression, and quality of life (secondary outcomes) were measured by the Epworth Sleepiness Scale, Fatigue Severity Scale, Center for Epidemiological Studies – Depression, and RLS-Quality of Life Instrument, respectively.
Results: Significant differences were found in severity of symptoms on sleep quality (p=.007), sleep duration (p=.042), and PSQI global score (p=.007). Significant differences were found in all of the components of QLI. Sleep quality (b=-0.12, 95% CI=[-0.18,-0.06], p<.001) and sleepiness (b=0.35, 95% CI=[0.09,0.61], p=.010) were significantly related to PSQI global score and QLI , respectively. Subjects with severe symptoms were 5 times more likely to use medication to treat RLS (OR=5.3, 95% CI=1.2 - 22.2).
Conclusion: The severity of RLS symptoms in older adults affects not only sleep but many aspects of quality of life. These findings are significant for older adults who may already have poor sleep and quality of life related to the aging process. RLS may impact issues of falls, reasoning, focusing, hopelessness, and ability to perform tasks, all factors affecting quality of life.
Support (optional): We gratefully acknowledge support for this study from the Hartford Center of Geriatric Nursing Excellence and the Frank Morgan Jones Fund at the University of PA School Of Nursing, Philadelphia, PA.

0823

ROPINIROLE CR – A NOVEL EXTENDED-RELEASE FORMULATION – DEMONSTRATES ONSET OF SYMPTOM IMPROVEMENT FROM THE FIRST NIGHT OF TREATMENT IN PATIENTS WITH MODERATE-TO-SEVERE PRIMARY RESTLESS LEGS SYNDROME

Becker P,[1] Bogan R,[2] Earl N[3]
(1) University of Texas Southwestern Medical Center at Dallas, Dallas, TX, USA, (2) SleepMed of South Carolina, Columbia, SC, USA, (3) GlaxoSmithKline, Research Triangle Park, NC, USA

Introduction: Restless Legs Syndrome (RLS) is characterized by an irresistible urge to move the legs. Although some patients experience nighttime-only symptoms, many patients also experience RLS symptoms in the late afternoon/early evening and throughout the night. The onset of effect of ropinirole CR extended release was assessed in patients with moderate-to-severe primary RLS.
Methods: In a 12-week, pivotal study (protocol 101468/205), patients with RLS experiencing symptoms in the evening and throughout the night were randomized to ropinirole CR (n=189), 0.5–6mg/day, or placebo (n=195), titrated as needed and tolerated, taken once daily (4pm or later), 1–2 hours before usual RLS symptom onset. Primary endpoint: mean change from baseline in IRLS total score at Week 12 LOCF. Onset of effect was assessed by proportion of responders (rated `very much´ or 'much´ improved) on the Patient Global Improvement (PGI) scale at Days 2–4, IRLS score at Week 1 OC, and the physician-rated Clinical Global Impression-Improvement (CGI-I) scale at Week 1 OC.
Results: Beginning at Week 1 OC through Week 12 LOCF, mean change from baseline in IRLS total score was significantly greater (improved) for ropinirole CR (–9.9 to –15.4) vs. placebo (–6.2 to –9.6)

(adjusted mean treatment difference: Week 1 OC, –3.8; Week 12 LOCF, –5.9, both p<0.001). Significantly greater proportions of PGI scale responders were seen for ropinirole vs. placebo treatment on Days 2 (30% vs. 12%; after first treatment night), 3 (35% vs. 18%), and 4 (42% vs. 24%) (all p<0.001). The proportion of CGI-I scale responders at Week 1 OC was also significantly greater in the ropinirole group vs. placebo (adjusted odds ratio: 2.6; p<0.001).
Conclusion: Ropinirole CR improves RLS symptoms, with onset of effect beginning with the first night of ropinirole (0.5mg) treatment in 30% of patients with moderate-to-severe primary RLS.
Support (optional): Study supported by GlaxoSmithKline R&D.

0824

STRONG ASSOCIATION BETWEEN CYCLIC ALTERNATING PATTERN A1 AND SLOW WAVE ACTIVITY IN SLEEP BRUXERS AND CONTROL SUBJECTS.

Huynh N,[1] Macaluso G,[2] Rompré P,[3] Guilleminault C,[4] Parrino L,[5] Terzano M,[5] Lavigne G[6]
(1) Stanford University, Palo Alto, CA, USA, (2) Universita degli Studi di Parma, Italy, (3) Universite de Montreal, Quebec, Canada, (4) Stanford University, Stanford, CA, USA, (5) University of Parma, Italy, (6) Universite de Montreal, Montreal, Quebec, Canada

Introduction: The cyclic alternating pattern (CAP) is a spontaneous periodic EEG activity observed during NREM sleep. It is divided into phase A (A1, A2, A3) and phase B. It was previously reported that sleep bruxism (SB) is associated to CAP A3. This study aims to examine CAP phase A of SB subjects in comparison to control subjects.
Methods: 8 SB subjects (mean age 22.8 (min-max; 21-27); 5M, 3W) were compared to 8 control sleepers (mean age 23.0 (20-26); 4M, 4W). SB subjects were selected according to tooth grinding history ≥3 nights/week and clinical exam. Polysomnographic recordings were made for all subjects over 2 consecutive nights for SB diagnosis and to rule out other sleep disorders (e.g., apnea, periodic limb movement). Sleep variables, masticatory muscle tone of masseter and suprahyoid muscles were analysed using Harmonie software (Stellate, Canada). Statistical analysis was assessed for the first four sleep cycles of each study group using ANOVA and t-tests. Correlations were done between sleep (slow wave activity (SWA) and micro-arousals) and CAP variables. Statistical analyses were done with SYSTAT (USA) and SPSS (USA).
Results: CAP A1 rate is strongly correlated to SWA in both SB (r=0.70, p<0.001) and control subjects (r=0.79, p<0.001). A similar distribution is observed between these two variables with a quadratic distribution of NREM sleep (p<0.02) and a linear decrease from the first to the fourth sleep cycle (p<0.01). Both CAP A2 and A3 rates peaked strongly and slightly during the transition phase between NREM and REM sleep within each cycle, respectively.
Conclusion: The strong association between CAP A1 rate and SWA seem to suggest neurological synchronisation during NREM sleep.

0825

AGE-RELATED CHANGES OF LEG MOVEMENT ACTIVITY DURING SLEEP IN RESTLESS LEGS SYNDROME

Ferri R,[1] Zucconi M,[2] Manconi M,[2] Lanuzza B,[1] Cosentino F,[1] Bruni O,[3] Ferini-Strambi L[4]
(1) Oasi Institute, Troina (EN), EN, Italy, (2) San Raffaele Institute, Milan, Milan, MI, Italy, (3) University of Rome "La Sapienza", Roma, Italy, (4) Università Vita-Salute San Raffaele, Milan, MI, Italy

Introduction: Recently, we have suggested a new approach for the study of the periodicity of the leg motor activity during sleep, based on a statistical measurement called "Periodicity Index" (PI). A new study has been planned for the analysis of periodic leg movements during sleep (PLMS) in patients with RLS of different age groups (7.5-85 years).
Methods: A series of parameters were extracted from the tibialis anterior EMG activity during sleep and their age-related changes were analyzed statistically, in order to derive information in this wide age-range. Particular attention was paid to the periodicity of the motor activity; it is known that, in normal controls, PLMS can be found after the age of approximately 40 years and that the amount of these movements increases with age.
Results: We found that in the interval histogram representing all activities (periodic and nonperiodic), the peak of PLMs increases gradually in amplitude, from the youngest to the oldest individuals, and shows an age-related shift from values of 22-24 s, in patients aged 7.5-45 years, to 16-18 s in patients aged >65 years. Both PLMS index and PI increase nonlinearly with age; however, their course is different because PLMS index increases soon maintaining a plateau between 25 and 65 years, after this age it shows a new very prominent increase. On the contrary, PI increases gradually up to the age of 35-45 years and remains stable afterwards. Finally, PLMS index and PI show no statistical correlation.
Conclusion: PLMS index and PI can be considered as independent measures in RLS, probably describing two independent phenomena with a different correlation with age. The application of the same scoring criteria to different age groups is able to provide us reliable information on the development of the quantitative aspects of PLMS and on their time arrangement (periodicity).

0826

ROTIGOTINE TRANSDERMAL PATCH IN PATIENTS WITH IDIOPATHIC PARKINSON´S DISEASE: CONTROL OF NOCTURNAL AND EARLY MORNING MOTOR SYMPTOMS

Trenkwalder C,[1] Leuchtenberg U,[2] Boroojerdi B,[3] Chaudhuri K[4]
(1) Paracelsus-Elena-Kliniken, Kassel, Germany, (2) SCHWARZ PHARMA AG, Monheim, Germany, (3) SCHWARZ BIOSCIENCES, Monheim, Germany, (4) National Parkinson Foundation Centre of Excellence, Kings College and Hospital, London, United Kingdom

Introduction: Neupro® (Rotigotine transdermal system) is a broad-spectrum, non-ergolinic D3/D2/D1 dopamine receptor agonist, which has been developed as a transdermal patch for the treatment of idiopathic Parkinson´s disease (PD). Given the stable 24-hour plasma levels achieved with this system, beneficial effects on PD symptoms during night and day are expected. Effects of rotigotine treatment on nocturnal and related PD symptoms (early morning motor function, number of nocturias, daytime sleepiness) are reported.
Methods: In 3 double-blind, placebo-controlled trials with advanced PD patients, status on waking was assessed with a diary (n=449 (229 Rotigotine, 120 PBO), 506 (204 Rotigotine, 201 comparator, 101 PBO) and 324 (240 Rotigotine, 84 PBO). In an open-label trial with 54 patients the Parkinson´s Disease Sleep Scale (PDSS), Epworth Sleepiness Scale (ESS) and UPDRS Part IV were used.
Results: Compared to baseline status after waking (mean change from "off" to "on" without troublesome dyskinesias) improved by 24.1 %, 15.6%, and 25.5% for Rotigotine and 8%, 4.3% and 11.5% for Placebo in the 3 trials after up to 6 months of treatment. In the open-label trial, the mean change from baseline (9.4) in PDSS was 11.6 (p< 0.001) after 3 months of treatment. ESS sum score improved from 7.3 to 6.1. A total of 58% of patients, who had sleep disturbances at baseline according to UPDRS Part IV were free of symptoms at the end of the 3 month treatment phase. The frequency of nocturia decreased from 2.12

to 1.41 after 3 months of treatment with Rotigotine transdermal patch.
Conclusion: Treatment with rotigotine transdermal system consistently improved nocturnal and early morning motor symptoms of PD without increasing daytime sleepiness in these trials.

0827

DISTRESSING DREAMS AND NIGHTMARES IN NON-DEMENTED PARKINSONIAN PATIENTS IS ASSOCIATED WITH REDUCED SLOW-WAVE SLEEP AND FRONTAL DYSFUNCTION

McNamara P,[1] Auerbach S,[2] Varghese S,[1] Harris E,[3] Durso R[3]
(1) Boston University School of Medicine and Boston VA Medical Center, Boston, MA, USA, (2) Boston University School of Medicine, MA, USA, (3) Boston University School of Medicine and Boston VA Medical Center, MA, USA

Introduction: Nightmares occur in patients with mid-stage Parkinson's disease (PD), but little is known about their clinical correlates, prevalence or cognitive features. The aim of the study was to assess selected cognitive abilities in non-demented PD patients who reported frequent distressing dreams in order to identify specific neuropsychological correlates of such phenomena.
Methods: Fifty consecutive patients with PD and Mini Mental State Examination (MMSE) > or = 23 were examined for the presence of distressing dreams and assessed on standardized mood and neuropsychological tasks for executive cognitive function (Stroop and verbal fluency). Twenty of these patients also underwent polysomnography to assess correlations between sleep architecture and distressing dreams. We used Question 6 of the Parkinson´s Disease Sleep Scale (PDSS; Chaudhuri *et al.*, 2002) to identify patients experiencing distressing dreams or nightmares in the past week.
Results: Eleven (22%) of 50 patients reported frequent distressing dreams or nightmares `in the past week´. There was no difference between those with and those without distressing dreams on age, Hoehn-Yahr stage or carbidopa dose. Patients with nightmares scored significantly lower than patients without nightmares on the Stroop interference task ($p = 0.03$), and on semantic and phonological fluency tasks ($p = 0.001$ and $p = 0.001$, respectively). Scores on Question 6 of the PDSS scale correlated moderately (Pearson r=.28; n.s.) with REM sleep duration and inversely with Stage 4 (r=-.36; p=.05).
Conclusion: Our results suggest that PD patients who report frequent distressing dreams or nightmares show reduced performance on tasks that tap executive functioning and reduced Stage 4 slow wave sleep duration.

0828

LONG-TERM PRAMIPEXOLE THERAPY FOR RESTLESS LEG SYNDROME

Vida Z, Szakacs Z
Central Hospital of the Hungarian Home Defence Force, Budapest, Hungary

Introduction: Patients started on pramipexole in 2001 and 2002 were identified among the 134 RLS patients undergoing follow-up care currently at our laboratory. 25 out of these 40 patients are still receiving uninterrupted pramipexole monotherapy (24 patients have idiopathic and 1 has secondary RLS caused by renal failure). 13 patients discontinued pramipexole owing to the lack of efficacy (n=6), the occurrence of side effects (n=5), or both (n=2). Currently, the dose range of pramipexole is between 0.125 and 1.0 mg/day; mean duration of treatment is 60 months (range: 51 to 70 months). Augmentation occurred in 2 cases and warranted switching to another treatment. Mean age of male (n=18) and of female patients (n=33) was 55.2±15.1 years and 55.9±13.3 years, respectively. Therapeutic efficacy was monitored using the International Restless Legs Scale (IRLS), actigraphy, and the Forced Immobilization Test.
Methods: Patients started on pramipexole in 2001 and 2002 were identified among the 134 RLS patients undergoing follow-up care currently at our laboratory. Twenty-five out of these 40 patients are still receiving uninterrupted pramipexole monotherapy (24 patients have idiopathic and 1 has secondary RLS caused by renal failure). Thirteen patients discontinued pramipexole owing to the lack of efficacy (n=6), the occurrence of side effects (n=5), or both (n=2). Currently, the dose range of pramipexole is between 0.125 and 1.0 mg/day; mean duration of treatment is 60 months (range: 51 to 70 months). Augmentation occurred in 2 cases and warranted switching to another treatment. Mean age of male (n=18) and of female patients (n=33) was 55.2±15.1 years and 55.9±13.3 years, respectively. Therapeutic efficacy was monitored using the International Restless Legs Scale (IRLS), actigraphy, and the Forced Immobilization Test.
Results: IRLS scores, actigraphy, and the SIT index revealed more than 85-per-cent improvement of RLS manifestations. Adverse reactions observed during the initial phase of treatment include nausea (n=5), dizziness (n=5), fatigue (n=4), and drowsiness (n=3). After the start of treatment, dosage with pramipexole was temporarily suspended (for 7 to 14 days) in 4 patients owing to the occurrence of side effects. Notwithstanding this, pramipexole could be re-introduced subsequently and these patients are still continuing on this drug. Currently, 3 per cent of patients reports mild adverse reactions. Augmentation occurred in 2 cases; switching to another drug was necessary in both.
Conclusion: Long-term pramipexole monotherapy accomplished a significant improvement of symptoms in more than 60 per cent of patients with RLS. The efficacy of the drug remained unchanged during treatment for 60 months on average. Side effects occurred in 22.5% of patients and necessitated discontinuation of dosage in 12.5% of subjects. Augmentation occurred in 2 cases (5%). As shown by these results, pramipexole monotherapy proves effective for the treatment of RLS on the long-term (i.e. over 51- to 70 months).

0829

OCCLUSAL SPLINTS FOR TREATING SLEEP BRUXISM – COCHRANE SYSTEMATIC REVIEW

Macedo C, Juliano M, Lentine-Oliveira D, Machado M, Sugaya H, Carvalho F, Prado L, Silva A, Prado G
Federal University of Sao Paulo, SP, Sao Paulo, Brazil

Introduction: Several treatments for sleep bruxism (SB) have been proposed such as pharmacological, psychological, and dental. The main goal of this study was to evaluate the effectiveness of occlusal splints for treatment of SB with alternative interventions or no treatment.
Methods: We searched the Cochrane library, MEDLINE; EMBASE, LILACS, Brazilian Odontology Bibliographic, and hand-searched abstracts of particular importance to this review. Additional reports were identified from the reference lists of retrieved reports and from article reviews about treating SB. There were no language restrictions. We selected randomised or quasi-randomised controlled trials (RCTs), in which splint therapy was compared concurrently to no treatment, other occlusal appliances, or any other intervention in participants with SB. Data extraction was carried out independently and in duplicate. Validity assessment of the included trials was carried out at the same time as data extraction. Discrepancies were discussed and a third reviewer consulted. The author of the primary study was contacted when necessary.
Results: Thirty potentially relevant RCTs were identified. Twenty-three

trials were excluded leaving six RCTs for analysis. Splint occlusal was compared to: palatal splint, double arch device, TENS, and no treatment. There was just one common outcome (arousal index) which was combined in a meta-analysis. No significant differences between occlusal splint and control group were found in the meta-analyses.
Conclusion: The evidence is insufficient for affirming that the occlusal splint is effective for treating SB. Indication of its use is questionable with regard to the sleep outcomes, but it may be that there is some benefit with regard to tooth wear. This review suggests the need for further investigation in more controlled RCTs that pay attention to method of allocation, study design, outcome assessment, large sample size, and enough duration of follow up. A standardisation of the outcomes of the treatment of SB should be established in the RCTs.

0830

PATIENT SATISFACTION WITH ROPINIROLE CR, A ONCE-DAILY EXTENDED-RELEASE TREATMENT FOR MODERATE-TO-SEVERE PRIMARY RESTLESS LEGS SYNDROME – RESULTS FROM A 12-WEEK PIVOTAL STUDY

Becker P,[1] Castiglia M[2]
(1) University of Texas Southwestern Medical Center at Dallas, Dallas, TX, USA, (2) GlaxoSmithKline, Research Triangle Park, NC, USA

Introduction: Many patients with moderate-to-severe Restless Legs Syndrome (RLS) experience symptoms in the late afternoon/early evening and throughout the night. Patient satisfaction with a new extended-release formulation – ropinirole CR – was assessed in patients with moderate-to-severe primary RLS.
Methods: In a 12-week pivotal study (protocol 101468/205), patients with RLS experiencing symptoms in the evening and throughout the night were randomized to ropinirole CR (n=189), 0.5–6 mg/day, or placebo (n=195), titrated as needed and tolerated, taken once daily (4pm or later) 1–2 hours before usual RLS symptom onset. Primary endpoint: mean change from baseline in International Restless Legs Scale (IRLS) total score at Week 12 LOCF. Patient satisfaction with treatment was assessed at Week 12 LOCF by the proportion of patients responding 1 or 2 (`satisfied´ or ´very satisfied´) on a 7-point Likert scale. Patient response to treatment was assessed by the proportion of responders (rated 1 `very much improved´ or 2 `much improved´) on the Patient Global Improvement (PGI) scale at Days 2–4.
Results: Mean change in IRLS total score at Week 12 LOCF was significantly greater for the ropinirole CR group vs. placebo (adjusted mean treatment difference: –5.9; p<0.001). At Week 12 LOCF, more patients receiving ropinirole CR vs. placebo reported being `satisfied´/'very satisfied´ with treatment (80% vs. 51%, respectively). In addition, there were significantly greater proportions of responders on the PGI scale for ropinirole CR vs. placebo treatment on Days 2 (30% vs. 12%; after first treatment night), 3 (35% vs. 18%), and 4 (42% vs. 24%) (p<0.001 for all).
Conclusion: Ropinirole CR significantly improves RLS symptoms, and is associated with patient-assessed improvement beginning the first night of treatment in patients with moderate-to-severe RLS. More patients on ropinirole CR report satisfaction with their study medication compared with placebo.
Support (optional): Study supported by GlaxoSmithKline R&D.

0831

ROPINIROLE CR EXTENDED RELEASE IMPROVES SYMPTOMS IN PATIENTS WITH MODERATE-TO-SEVERE PRIMARY RESTLESS LEGS SYNDROME: RESULTS FROM A PIVOTAL, 12-WEEK EFFICACY AND TOLERABILITY STUDY

Bogan R,[1] Castiglia M[2]
(1) SleepMed Inc. of South Carolina, Columbia, SC, USA, (2) GlaxoSmithKline, Research Triangle Park, NC, USA

Introduction: Many patients with Restless Legs Syndrome (RLS) have symptoms that present in the late afternoon/early evening and continue through the night. The efficacy, safety, and tolerability of a novel extended-release, once-daily treatment formulation – ropinirole CR – were assessed in patients with moderate-to-severe primary RLS.
Methods: Study 101468/205 was a 12-week, randomized, double-blind study. Patients with moderate-to-severe primary RLS experiencing symptoms in the evening and throughout the night were randomized to ropinirole CR (n=189), 0.5–6mg/day, or placebo (n=195), titrated as needed and tolerated, taken once daily (4pm or later), 1–2 hours before usual onset of RLS symptoms. Primary endpoint: mean change from baseline in International Restless Legs Scale (IRLS) total score at Week 12 LOCF. Secondary endpoints included the proportion of responders (rated `very much´ or `much' improved) on the Clinical Global Impression-Improvement (CGI-I) scale at Week 12 LOCF. Tolerability was assessed by adverse-event (AE) reporting and discontinuations.
Results: Baseline demographics were comparable between treatment groups. At Week 12 LOCF, mean (SD) dose was 2.5 (1.9) and 3.8 (2.1) mg/day for ropinirole CR and placebo, respectively. Mean (SD) IRLS total score at baseline was 25.2 (5.0) and 25.3 (5.1) for ropinirole CR and placebo groups, respectively. Mean (SD) change from baseline in IRLS total score at Week 12 LOCF was significantly greater (improved) for ropinirole CR vs. placebo (adjusted mean treatment difference: –5.9; p<0.001), as was the proportion of patients classified as responders on the CGI-I scale (ropinirole: 79%; placebo: 50%; adjusted odds ratio: 4.6; p<0.001). The three most common AEs were nausea (28% and 7%), headache (20% and 18%), and somnolence (9% and 6%) in the ropinirole CR and placebo groups, respectively.
Conclusion: Ropinirole CR demonstrates RLS symptom improvement and is generally well tolerated in patients when taken once-daily for late afternoon/early evening and nighttime treatment coverage.
Support (optional): Study supported by GlaxoSmithKline R&D.

0832

ROPINIROLE CR EXTENDED RELEASE REDUCES SLEEP DISTURBANCE IN PATIENTS WITH MODERATE-TO-SEVERE PRIMARY RESTLESS LEGS SYNDROME: RESULTS FROM A 12-WEEK, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

Bogan R,[1] Monaghan E[2]
(1) SleepMed Inc. of South Carolina, Columbia, SC, USA, (2) GlaxoSmithKline, Research Triangle Park, NC, USA

Introduction: Many patients experience bothersome Restless Legs Syndrome (RLS) symptoms beginning in the late afternoon/early evening that continue through the night and are often associated with disturbed sleep. The efficacy, tolerability, and effects on sleep of a novel once-daily, extended-release formulation – ropinirole CR – were assessed in patients with moderate-to-severe primary RLS.
Methods: In a 12-week pivotal study (protocol 101468/205), patients were randomized to receive ropinirole CR (n=189), 0.5–6 mg/day, or placebo (n=195), titrated as needed and tolerated, taken once daily (4pm or later), 1–2 hours before usual onset of RLS symptoms. Primary

endpoint: mean change from baseline in International Restless Legs Scale (IRLS) total score at Week 12 LOCF. Secondary endpoints included changes in each of the four domains of the Medical Outcomes Study (MOS) Sleep Scale at Week 12 LOCF. Tolerability was assessed by adverse event (AE) reporting and discontinuations.
Results: Baseline demographics were comparable between treatment groups. At Week 12 LOCF, mean (SD) doses for ropinirole CR and placebo were 2.5 (1.9) and 3.8 (2.1) mg/day, respectively. Mean change in IRLS total score at Week 12 LOCF was significantly greater (improved) for ropinirole CR vs. placebo (adjusted mean treatment difference [AMTD]: –5.9; $p<0.001$). Ropinirole CR was also associated with significantly greater improvements, compared with placebo, in each of the MOS Sleep Scale domains at Week 12 LOCF (sleep disturbance, sleep adequacy, daytime somnolence, sleep quantity: AMTD: –13.9, 12.0, –7.9, 18.6, respectively; all $p<0.05$). The three most frequent AEs were nausea (28% and 7%), headache (20% and 18%), and somnolence (9% and 6%) in the ropinirole CR and placebo groups, respectively.
Conclusion: Ropinirole CR improves RLS symptom severity and associated sleep disturbance, with improved sleep adequacy and quantity and less daytime tiredness, and is generally well tolerated in patients with moderate-to-severe primary RLS.
Support (optional): Study supported by GlaxoSmithKline R&D.

0833

THE IMPACT OF RESTLESS LEGS SYNDROME ON DIAGNOSED AND UNDIAGNOSED SUFFERERS: RESULTS OF A WEB-BASED PATIENT SURVEY

McLeod L,[1] Fehnel S,[1] Zografos L,[1] Sander S,[2] Curtice T,[2] Shah H[2]
(1) Research Triangle Institute (RTI), RTP, NC, USA, (2) Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, USA

Introduction: The purpose of this study was to evaluate the impact of RLS in sufferers with and without a confirmed diagnosis.
Methods: A Web-based survey was presented to a multimillion member panel of US adults. To be eligible, participants had to be ≥ 18 years old and currently experiencing RLS symptoms (≥ once weekly) as determined using IRLSSG diagnostic criteria. In addition to evaluating treatment and symptom frequency/intensity, validated patient-reported instruments were administered to assess overall health status (SF-12v2), sleep (MOS Sleep), work productivity (WPAI and WLQ), and psychological distress (CES-D). Where possible, scores were compared to population norms.
Results: Participants included 702 RLS sufferers (396 were diagnosed, 306 were never told by a healthcare professional they had RLS). While 15% (26% of diagnosed, 0.3% of undiagnosed) reported currently being treated with dopaminergic therapy, the vast majority in both groups reported treating their leg symptoms with medications such as prescription sleep aids (39%), antidepressants (35%), and prescription analgesics (23%). Symptoms occurred "often" or "very often" in 46% of undiagnosed and 75% of diagnosed. Symptoms were "very distressing" or "extremely distressing" in 30% of undiagnosed and 63% of diagnosed. Fifty-six percent of undiagnosed and 70% of diagnosed met the cut-off score for depression on the CES-D. In both groups, all eight subscales of the SF-12v2 were below population norms. Both groups showed impairments in sleep and work productivity.
Conclusion: A large percentage of undiagnosed RLS sufferers reported seeking treatment for and having symptoms of high frequency and intensity. Diagnosed participants also had substantial impairments in all domains and reported use of a variety of treatments, focusing more on problems that may result from RLS symptoms and less on reducing the intensity of their leg problems. A more focused treatment and management approach may relieve some of the burden of RLS.
Support (optional): Research supported by Boehringer Ingelheim Pharmaceuticals, Incorporated

0834

PSYCHOSOCIAL FEATURES OF RESTLESS LEGS SYNDROME IN BRAZILIAN PATIENTS

Varela M,[1] Varela M,[2] Potasz C,[1] Feliciano R,[1] Canepa R,[1] Carvalho J,[1] Carvalho L,[3] Prado L,[4] Prado G[4]
(1) Federal University of Sao Paulo (UNIFESP), São Paulo, Brazil, (2) University of Sao Paulo (UNIFESP), São Paulo, Brazil, (3) Federal University of Sao Paulo (UNIFESP, São Paulo, Brazil, (4) Department of Emergency and Evidence, São Paulo, Brazil

Introduction: The Restless Legs Syndrome (RLS) is a neurological condition that affects sleep and is characterized by an irresistible urge to move the legs followed by uncomfortable and unpleasant sensations, mostly at night. In Brazil, we are just starting to recognize and care RLS, what brings us a question regarding the way our patients have represented their suffering and how they are dealing with it in their social environment.
To recognize the different terms in Brazilian Portuguese that allows patients to express their suffering experience with RLS, their relationship with family and health professionals.
Methods: We identified 60 patients (42 female; 26-85 years old), with confirmed RLS diagnosis, among 2000 medical file from the outpatient Clinic Neuro-Sono, UNIFESP.
Preliminary data of 15 recorded one-hour semi-structured interviews was analyzed (ten female, 25-79 years old). We asked about their feelings, physical sensations, names they describe their condition, and about relationship with family and physicians.
Results: All patients used names that describes their physical sensations (deep itch), feelings (restless), movement (walking bugs), and depth (something is eating deep inside). Regarding suffering, they express shame, embarrassment, the feeling of "going crazy", and something annoying to others. Regarding social suffering, they referred family´s impatience and lack of knowledge when the loss of body control is not recognized as a disease. They also referred how physicians have been misreading their symptoms as vascular, orthopedics, psychological, or psychiatrics.
Conclusion: Psychosocial features of RLS patients point to a suffering caused by an uncomfortable body and the misunderstanding regarding to the family´s and physicians´ lack of knowledge about it. This social suffering that includes patients relationships is as important as individual complaints about RLS. The misunderstanding may eventually move these patients away from the neurological treatment indicated, revealing the need to make public, more information about this disease in Brazil.

0835

ATTENUATION OF ORAL DYSKINESIA DURING SLEEP: A QUANTITATIVE STUDY

Rompre P, Lavigne G, Guitard F, Montplaisir J, Blanchet P
Universite de Montreal, Montreal, Quebec, Canada

Introduction: Oral dyskinesia (OD) originating from various sources remains a significant issue particularly in the elderly. The impact of sleep on OD has been little investigated. The aim of the present study was to investigate changes and persistence in involuntary motor activity during sleep.
Methods: A group of 15 subjects at least 60 years of age (mean 67, range 61-77) with OD participated in this study. Ten were diagnosed as

having edentulous orodyskinesia (EOD) and 5 were classified as antipsychotic drug-induced tardive dyskinesia (TD). The subjects were recorded in the sleep laboratory for 2 nights. Video and polygraphic recordings were taken for 15 minutes in the sitting position, in the waking state before bedtime and upon awakening in the morning. Sleep was recorded and scored according to standard methods. Orofacial and body movements were scored overnight and during wakefulness in the sitting position, based on polygraphic and audio-video recordings. Statistics included Friedman two-way ANOVA, Wilcoxon test and Mann-Whitney U test.
Results: The frequency of orofacial movements decreased by more than 65% during sleep (median 9.3 movements/hour) compared to the waking state during daytime (evening 28.0 movements/hr and morning 52.0 movements/hr, $p<0.01$) or to the waking state during nighttime (30.5 movements/hr, $p<0.001$). The same trend was observed for body movements. The subjects displayed few episodes of rhythmic muscle activity during sleep (median 0.1 episodes/hr, range 0.0-7.1). TD cases displayed more orofacial activities when awake in the morning than those with EOD (median 82.1 and 26.3 movements/hr for TD and SOD subjects, respectively; $p=0.02$). The sleep of these subjects was within normal range.
Conclusion: This quantitative study shows that orofacial motor activities in different types of OD are remarkably reduced but persist during sleep. However, polygraphy cannot be used to discriminate EOD from TD.
Support (optional): Canadian Institutes of Health Research and Quebec Health Research Fund.

0836

IMPULSE CONTROL DISORDERS IN PATIENTS WITH RESTLESS LEGS SYNDROME TREATED WITH DOPAMINE AGONISTS

Tippmann-Peikert M, Silber M, Park J, Shepard J, Boeve B
Mayo Foundation for Medical Education and Research, Rochester, MN, USA

Introduction: Impulse control disorders, such as pathological gambling and compulsive shopping, occur in about 6% of patients with Parkinson´s disease (PD) treated with dopamine agonists. They are thought to be due to an altered function of the dopaminergic reward system. To our knowledge, impulse control disorders have not to date been reported in patients receiving dopaminergic agents for treatment of conditions other than PD.
Methods: We identified six patients with restless legs syndrome treated with pramipexole or ropinirole who developed impulse control disorders. Records were reviewed, and data collated and analyzed.
Results: Four patients were treated with pramipexole; two with ropinirole. None of the patients had a history of Parkinson´s disease or signs of Parkinsonism. Five patients developed pathological gambling. All patients had previously gambled for pleasure on occasion without any significant financial losses. The sixth patient, who had a tendency to shop excessively in the past, developed compulsive shopping. Behaviors in all patients resulted in psychological distress and serious financial loss. The mean pramipexole dose at the onset of impulse control disorders was 0.53 mg daily (range 0.125-0.75 mg) while the mean dose of ropinirole was 1.13 mg daily (range 1.0-1.25 mg). The average treatment duration prior to the onset of symptoms was 11.2 months (range 0-24 months). Discontinuation of dopaminergic therapy was associated with marked improvement of symptoms to the premorbid level in 4 patients, and complete resolution in 2 patients.
Conclusion: Impulse control disorders may occur as a side effect of dopaminergic agonist therapy in patients with restless legs syndrome in the absence of PD. The mean dose inducing the behaviors in our patients with RLS was markedly lower than the doses reported in patients with PD. Clinicians need to be aware of this potential side effect and the important social and financial implications for the patient.

0837

SODIUM OXYBATE FOR EXCESSIVE DAYTIME SLEEPINESS IN PARKINSON'S DISEASE: A POLYSOMNOGRAPHIC STUDY

Ondo W,[1] Perkins A,[2] Swick T,[3] Hull K,[4] Jimenez E,[5] Pardi D[6]
(1) Baylor College of Medicine, Houston, TX, USA, (2) Sleep Medicine Program at Raleigh Neurology, Raleigh, NC, USA, (3) The Institute of Sleep Medicine, Houston, TX, USA, (4) Raleigh Neurology Associates, PA, NC, USA, (5) Baylor College of Medicine, TX, USA, (6) Jazz Pharmaceuticals, Palo Alto, CA, USA

Introduction: Parkinson´s disease (PD) is strongly associated with sleep abnormalities. PD patients have both excessive daytime sleepiness, as assessed by subjective scales and multiple sleep latency tests, and numerous nocturnal sleep abnormalities including fragmented sleep, REM sleep behavioral disorder, periodic limb movements, and sleep apnea. Few studies have evaluated treatment of these problems. In this currently ongoing study, we are evaluating sodium oxybate, which is currently FDA approved to treat cataplexy and excessive daytime sleepiness (EDS) in patients with narcolepsy, in a multi-center, open-label, polysomnogram (PSG) study in PD patients with sleep disorders.
Methods: Inclusion requires an Epworth Sleepiness Scale (ESS) score greater than 10 and any subjective nocturnal sleep complaint. Patients are on stable PD medications but no sleep medications. We first perform an acclimation and screening PSG to exclude subjects with meaningful sleep disordered breathing. Patients then undergo another PSG, followed by an "off" medicine Unified Parkinson Disease Rating Scale (UPDRS), ESS, and fatigue severity scale (FSS) the next morning. Patients then start sodium oxybate, which is titrated from 3 g to 9 g given nightly in two equal divided doses (at bed time and 4 hours later) over 6 weeks. They then return at 12 weeks after initiating therapy for a third PSG, "off" UPDRS, ESS, and FSS.
Results: Twenty-six subjects have currently enrolled. Four failed screening secondary to sleep apnea (3) and depression (1). Twenty have completed the study; two dropped out. Mean scores for those 20 patients showed improvements in ESS [16.1(4.3) to 9.3(5.8), $p<0.001$], FSS [44.1(13.1) to 36.8(16.0), $p<0.005$], and slow-wave sleep time [44.9(30.5) minutes to 86.3(61.2) minutes ($p<0.01$)]. No other PSG features changed. "Off" UPDRS scores were stable [28.9(9.3) to 25.3(9.7), NS]. AEs included enuresis (1) and rebound morning tremor (1).
Conclusion: Overall, nocturnal sodium oxybate improved EDS and fatigue in PD, possibly due to improved in slow-wave sleep.
Support (optional): This study (JIIT-X007) was supported by Jazz Pharmaceuticals, Inc.

0838

TRACING THE DOPAMINERGIC BORDERS OF PERIODIC LEG MOVEMENTS DURING SLEEP IN RESTLESS LEGS SYNDROME

Manconi M,[1] Ferri R,[2] Zucconi M,[3] Fantini M,[3] Castronovo V,[3] Ferini-Strambi L[3]
(1) Scientific Institute of San Raffaele, Sleep Medicine Centre, Milan, Italy, (2) Oasi Institute, Troina (EN), Italy, (3) Italy

Introduction: Periodic leg movements during sleep (PLMS) are characterized by repetitive tibialis anterior jerks lasting from 0.5 to 5 (or10) seconds, separated by interval ranging from 5 to 90 seconds,

organized in series of 4 or more consecutive leg movements (LM). Aim of the study was to re-delineate the borders of PLMS by a new pharmacological approach, trying to identify a LM group with a common dopaminergic origin.
Methods: A single-blind placebo-controlled study in 43 consecutive idiopathic RLS de-novo patients with a PLMS index greater than 10 was carried out. Patients underwent: clinical and neurophysiological evaluation, hematological screening and two consecutive full-night polysomnographies. On the second night, all patients received 0.25 mg of pramipexole or. An off-line analysis was conducted on LM parameters such as duration, amplitude, interval, and periodicity.
Results: Compared to placebo, pramipexole strongly cut PLMS, with a significantly selective inhibition on LM ranging between 2 and 4 s in duration, with an inter-movement interval greater than 6 and lower than 64 s, and with an high periodicity. No effect of pramipexole was observed on isolated LM.
Conclusion: Low dose of pramipexole suppress PLMS in RLS patients since the first night of treatment, with significant implications for possible future dopamine-agonists exploitation in on-demand therapy and in a pharmacological test for RLS diagnosis. Results stand for a heterogeneous genesis of the LM in RLS patients, which may be non-dopaminergic in isolated LM and dopaminergic in part of PLMS classified with the current criteria. To include a pathogenetically uniform cluster of PLMS, more restrictive scoring criteria might be indicated.

0839

DOES RESTLESS LEGS SYNDROME INCREASE THE RISK OF CEREBRAL MICROVASCULAR ISCHEMIC DISEASE?

Silveira D,[1] Siddiqui F,[1] Strus J,[1] Karel F,[1] Moussouttas M,[1] Walters A[2]
(1) Seton Hall University, Edison, NJ, USA, (2) New Jersey Neuroscience Institute at JFK Medical Center, Edison, NJ, USA

Introduction: We evaluated whether restless legs syndrome (RLS) is an independent risk factor for cerebral microvascular ischemic disease (MVD) when other potential risk factors for stroke are controlled. RLS has been associated with stroke risk factors, including heart disease and hypertension. However, it is not known whether RLS itself increases the risk of stroke.
Methods: Eight patients with RLS and 11 age- and sex-matched control subjects with migraine headaches were evaluated. All patients had a normal neurological exam and no previous history of stroke. Both patients and controls had similar number of risk factors for stroke, including hypertension, hyperlipidemia, coronary artery disease, diabetes and tobacco use. A Neurology stroke specialist (MM) blinded to the experiment scored the volume of cerebral MVD (Digital Image Analysis, ImageJ program, version 1.37).
Results: We did not find evidence that RLS alone significantly affected the load of MVD in the brain. Although not statistically significant, patients with RLS plus stroke risk factors had a tendency ($p = 0.153$) to have a higher brain MRI volume load of MVD than controls. The increased brain load of MVD was not associated with the presence or absence of obstructive sleep apnea as determined polysomnographically.
Conclusion: Our preliminary data showed a trend towards a relationship between an increased load of MVD in patients with both RLS and stroke risk factors, which may indicate that the presence of RLS is a contributing factor for MVD. However, a larger number of patients are necessary to confirm or rule out this possibility.
Support (optional): ACKNOWLEDGEMENT: Authors thank Barry Cohen, PhD for statistical analysis.

0840

ACCURACY AND REPRODUCIBILITY OF THE JOHNS HOPKINS TELEPHONE DIAGNOSTIC INSTRUMENT FOR RESTLESS LEGS SYNDROME.

Bourguet C,[1] Ober S,[2] Steiner R,[3] Baughman K,[1] Panzner M[4]
(1) Northeastern Ohio Universities College of Medicine, Rootstown, OH, USA, (2) Cleveland Veterans Administration Medical Center, Cleveland, OH, USA, (3) University of Akron, Akron, OH, USA, (4) Cleveland Veterans Administration Medical Center, OH, USA

Introduction: A need exists for a valid and reliable instrument to identify RLS cases in epidemiologic studies. This instrument would employ the criteria of the IRLSSG and, when administered by trained non-physician interviewers, would accurately identify RLS cases who have not been previously diagnosed. We evaluated the Johns Hopkins Telephone Diagnostic Instrument (TDI) using these criteria.
Methods: Study members were veterans who were recruited at an office visit to a VA outpatient clinic. They were participants in a larger study of RLS and had previously completed the TDI by telephone with a trained non-clinician (Time 1). The TDI was re-administered face to face by a nurse (Time 2). The gold standard was a diagnostic interview conducted by a physician. We calculated the reproducibility of the TDI between two administrations, and the sensitivity and specificity of the TDI at two time points relative to the gold standard.
Results: Eighty-five (39%) of eligible patients completed both TDI´s and 74 (34%) completed the entire study. They were predominantly male (88%) and Caucasian (89%). The mean interval from Time 1 to Time 2 TDI was 13.9 months (range: 3-25 months). Reproducibility was low (kappa = 0.34, $p<.01$), but was higher for interviews repeated within one year (kappa = 0.55, $p<.01$). By gold standard, 43% were definite cases and 11% were probable cases. Including those reporting ≥ 3 symptoms as cases, sensitivity of the TDI ranged from 63% (Time 1) to 75% (Time 2). Specificity ranged from 88% (Time 1) to 71% (Time 2).
Conclusion: The sensitivity and specificity of the TDI have been reported to be over 90%. Previous studies have distinguished diagnosed cases from non-cases. The lower accuracy which we report likely results from greater symptom overlap between previously undiagnosed cases and normals. These results are applicable to epidemiologic studies in primary care or community settings.
Support (optional): Supported by DAMD17-03-1-0082 from the US Army Medical Research and Materiel Command and a grant from Pfizer Pharmaceutical Corporation.

0841

IMPROVEMENTS OF DAYTIME SYMPTOMS AND ACTIVITIES OF DAILY LIVING IN PATIENTS WITH RESTLESS LEGS SYNDROME - 24 MONTHS RESULTS FROM A MULTI-NATIONAL, MULTI-CENTRE, OPEN-LABEL, FOLLOW-UP TRIAL WITH THE ROTIGOTINE TRANSDERMAL SYSTEM.

Oertel W,[1] Trenkwalder C,[2] Poewe W,[3] Gracia-Borregoero D,[3] Schollmayer E,[3] Keffel J[4]
(1) University of Marburg, Marburg, Hessen, Germany, (2) Paracelsus Elena Klinik Kassel, Kassel, Niedersachsen, Germany, (3) Austria, (4) Schwarz Biosciences, Monheim, Germany

Introduction: Rotigotine, a non-ergolinic D3/D2/D1 dopamine agonist formulated as a once-daily transdermal delivery system, is licensed in Europe for the treatment of Parkinson´s disease and in development for RLS. The patch technology releases the drug continuously, and provides stable plasma levels over 24 hours. This trial is an open-label extension of a six-arm, double-blind, prospective, placebo-controlled, 7-week,

dose-finding study in 33 centers in Europe. The aim of this trial is to determine safety, tolerability and efficacy of long-term application in subjects with moderate to severe idiopathic RLS.
Methods: After optimal dose titration, rotigotine is administered with dose-adjustments allowed at anytime to maintain optimal treatment. Data are presented assessing the 24 months follow-up after the titration period.
Efficacy variables included IRLS score, and RLS-6 scales.
Results: A total of 295 patients entered the open-label extension trial and 191 completed the 2-years. The baseline IRLS score was 27.8 ± 5.9 and optimal dose treatment resulted in a mean reduction of 17.2 ± 9.2 points.
A similar response was observed, when the RLS-6 scales were analyzed showing reductions of -2.9 ± 2.7 and -2.4 ± 2.7 for the items »severity of RLS during the day when at rest«, and »daytime tiredness and sleepiness«, respectively.
Compared to the condition at baseline, the IRLS score item 5 »daytime tiredness/sleepiness«, item 9 »daily activities«, and item 10 »mood« were reduced by -1.4 + 1.3, -1.4 + 1.2, and -1.4 + 1.2, respectively.
The most common adverse events (>10%) were application site reactions (50% mostly mild), nasopharyngitis (12%), back pain (11%), and nausea (11%). No clinical signs and symptoms of augmentation were reported.
Conclusion: Treatment with the rotigotine transdermal system was well-tolerated and showed clinically relevant improvement in the IRLS and RLS-6 scores. All improvements were observed in the titration period and were sustained during 24 months follow-up.

0842

TOLERABILITY WITH MAINTAINED EFFICACY AFTER OVERNIGHT SWITCH FROM IMMEDIATE RELEASE (IR) ROPINIROLE TO A NOVEL EXTENDED-RELEASE FORMULATION – ROPINIROLE CR – IN RESTLESS LEGS SYNDROME

Lee D,[1] Hosford D[2]
(1) East Carolina Neurology Inc., Greenville, NC, USA, (2) GlaxoSmithKline, Research Triangle Park, NC, USA

Introduction: Many patients with Restless Legs Syndrome (RLS) experience symptoms that present in the late afternoon/early evening and continue throughout the night and they may therefore benefit from a once-daily extended-duration treatment. The tolerability and safety of an overnight switch from ropinirole IR to ropinirole CR extended release in patients with primary RLS was evaluated.
Methods: Study 101468/805 was a randomized, double-blind, three-cohort study in patients with moderate-to-severe primary RLS. Patients currently taking ropinirole IR for RLS entered one of three cohorts based on their stable dose of ropinirole IR (1, 2, or 4mg). They were then randomized to one of two dosing groups within each cohort and entered into a 4-week treatment phase. Patients in the 1mg ropinirole IR cohort (data presented) were converted to 2mg ropinirole CR. Each patient was switched overnight to ropinirole CR during the treatment phase. To allow for comparison between groups within each cohort and to maintain blinding, one dosing group underwent actual conversion to the CR formulation, while the second group underwent "dummy" conversion concurrently (maintained on ropinirole IR). Primary endpoint: incidence of post-conversion emergent adverse events (AEs) (defined as: first occurrence/new episode/increase in severity of ongoing AEs). Efficacy was assessed by the International Restless Legs Scale (IRLS).
Results: Baseline demographics/characteristics were comparable between treatment groups. Emergent AEs for any event following conversion occurred in 37% (n=17) of the post-actual and 43% (n=20) of the post-dummy conversion groups; most common emergent AEs for both groups were headache, nausea, and dizziness. No patients withdrew due to an AE (pre- and post-conversion). There was no loss of efficacy following an actual conversion to ropinirole CR, based on mean change from pre- to post-conversion in IRLS total score.
Conclusion: Overnight switching from ropinirole IR (1mg) to extended-release ropinirole CR (2mg) was generally well tolerated by patients and efficacy was maintained.
Support (optional): Study supported by GlaxoSmithKline R&D.

0843

A NOVEL EXTENDED-RELEASE FORMULATION – ROPINIROLE CR – IMPROVES QUALITY OF LIFE IN PATIENTS WITH MODERATE-TO-SEVERE PRIMARY RESTLESS LEGS SYNDROME: RESULTS FROM A 12-WEEK PIVOTAL TRIAL

Schmidt M,[1] Ziman R,[2] Calloway M[3]
(1) Ohio Sleep Medicine Institute, Dublin, OH, USA, (2) Northridge Neurological Center, Northridge, CA, USA, (3) GlaxoSmithKline, Research Triangle Park, NC, USA

Introduction: Restless Legs Syndrome (RLS) is a neurological disorder characterized by a compelling urge to move the legs and the symptoms can negatively impact patients´ health-related quality of life (HRQoL). Many patients with RLS experience symptoms that occur in the late afternoon/early evening, in addition to the nighttime. An extended-release formulation, ropinirole CR, was developed to provide coverage in patients with moderate-to-severe primary RLS experiencing this longer duration of symptoms.
Methods: Study 101468/205 was a 12-week, randomized, double-blind, placebo-controlled, parallel-group study. Patients with moderate-to-severe primary RLS experiencing symptoms in the evening, and throughout the night, were randomized to ropinirole CR (n=189), 0.5–6mg/day, or placebo (n=195), titrated as needed and tolerated, taken once daily (4pm or later), 1–2 hours before onset of usual RLS symptoms. The primary endpoint was mean change from baseline in International Restless Legs Scale (IRLS) total score at Week 12 last observation carried forward (LOCF). Secondary endpoints included mean change from baseline in the Overall Life Impact score of the patient-reported Restless Legs Syndrome Quality of Life (RLSQoL) questionnaire at Week 12 LOCF.
Results: Baseline demographics and characteristics were similar between treatment groups. Mean (SD) dose at Week 12 LOCF was 2.5 (1.9) and 3.8 (2.1) mg/day for ropinirole CR and placebo, respectively. At Week 12 LOCF, mean change in IRLS total score was significantly greater (improved) for the ropinirole CR group compared with the placebo group (adjusted mean treatment difference [AMTD]: –5.9; $p<0.001$). Similarly, mean change in RLSQoL score at Week 12 LOCF was significantly greater (improved) for ropinirole CR compared with placebo (AMTD: 9.2; $p<0.001$).
Conclusion: Treatment with ropinirole CR reduces RLS symptoms and is also associated with HRQoL benefits in patients with moderate-to-severe primary RLS.
Support (optional): Study supported by GlaxoSmithKline R&D.

0844

ROPINIROLE CR – A NOVEL EXTENDED-RELEASE FORMULATION – REDUCES OVERALL SEVERITY OF ILLNESS IN PATIENTS WITH MODERATE-TO-SEVERE PRIMARY RESTLESS LEGS SYNDROME

Schmidt M,[1] Ferguson J,[2] Earl N[3]
(1) Ohio Sleep Medicine Institute, Dublin, OH, USA, (2) Salt Lake City, UT, USA, (3) GlaxoSmithKline, Research Triangle Park, NC, USA

Introduction: Restless Legs Syndrome (RLS) is characterized by an urge to move the legs. For many patients with RLS, symptoms not only occur at night, but also in the late afternoon/early evening. An extended-release treatment formulation, ropinirole CR, was developed to provide coverage for patients with moderate-to-severe primary RLS experiencing these symptoms.
Methods: Study 101468/205 was a 12-week, double-blind study. Patients with moderate-to-severe primary RLS with evening and nighttime symptoms were randomized to ropinirole CR (n=189), 0.5–6mg/day, or placebo (n=195), titrated as needed and tolerated, taken once daily (4pm or later), 1–2 hours before usual RLS symptom onset. Primary endpoint was mean change from baseline in IRLS scale total score at Week 12 LOCF. Additional endpoints included proportion of responders (rated `very much´ or `much´ improved) on the Clinical Global Impression-Improvement (CGI-I) scale, and score on the Clinical Global Impression-Severity of Illness (CGI-S) scale, at Week 12 LOCF.
Results: Baseline demographics and characteristics were similar between groups: mean (SD) IRLS total score at baseline was 25.2 (5.0) and 25.3 (5.1) for ropinirole CR and placebo, respectively. Mean (SD) dose at Week 12 LOCF: 2.5 (1.9) and 3.8 (2.1) mg/day for ropinirole CR and placebo, respectively. At Week 12 LOCF, mean change in IRLS total score was significantly greater (improved) for the ropinirole CR group vs. placebo (adjusted mean treatment difference: –5.9; $p<0.001$). Additionally, at Week 12 LOCF, a significantly greater proportion of ropinirole-treated patients were classified as responders on the CGI-I scale vs. placebo (79% vs. 50%; adjusted odds ratio: 4.6; $p<0.001$), and more ropinirole patients were rated `normal/not at all ill´ or `borderline ill´ on the CGI-S scale (49% vs. 31%).
Conclusion: Ropinirole CR reduces the overall severity of illness and is associated with global symptom improvement in patients with moderate-to-severe primary RLS.
Support (optional): Study supported by GlaxoSmithKline R&D.

0845

PICTORIAL PHENOTYPE OF RESTLESS LEGS SYNDROME (RLS)

Mummaneni R,[1] Rye D,[2] Bliwise D[3]
(1) Emory University School of Medicine, Atlanta, GA, USA, (2) Emory, Atlanta, GA, USA, (3) Emory University, Atlanta, GA, USA

Introduction: Despite widespread recognition of RLS, many aspects of the phenotype remain unclear. In this study we employed usage of a patient-completed pictorial representation for their reported symptoms.
Methods: Patients were 73 individuals (X age = 51.8, SD = 13.6, 32 men, 41 women) meeting IRLSSG criteria for idiopathic RLS. Individuals with possible augmentation were excluded. Patients were presented with a pictorial representation of the body and asked to circle any or all lower limb sites in which they experienced their symptoms. Regions for foot, calf, and thigh were analyzed separately for left and right side and from anterior and posterior perspectives. We considered distal sites to be represented by both foot and/or lower leg, whereas proximal sites were limited to upper leg. Unilateral involvement was defined as when the number of identified sites between body sides differed by a total of at least one site.
Results: For 32 patients, involvement comprised both distal and proximal sites, whereas 36 endorsed only distal and 5 only proximal sites. Involvement of only the foot was rare (n = 2). Most patients experienced both anterior and posterior involvement (n = 53), whereas fewer were limited solely to anterior (n = 14) or posterior (n = 6) regions. Bilateral symptoms predominated (n = 69) with a small number reporting symptoms on only a single body side (n = 4).
Conclusion: The pictorial phenotype approach to characterizing RLS emphasizes the heterogeneity of presentations of this syndrome. Clinical correlates of differences in distal vs proximal location, body side, and anterior/posterior involvement remain unclear at present.

0846

OVEREXPRESSION OF MUSCLE-DERIVED NEUROTROPHIN 3 IS ASSOCIATED WITH PERIODIC LIMB MOVEMENTS IN MICE

Morrissey M,[1] Duntley S,[2] Boero J,[2] Yamada K,[3] Smittkamp S,[4] Wright D[5]
(1) Children's Hospital, Saint Louis, MO, USA, (2) Washington University in St. Louis, Saint Louis, MO, USA, (3) Washington University in St. Louis, St. Louis, MO, USA, (4) University of Kansas*, Kansas City, KS, USA, (5) University of Kansas, Kansas City, KS, USA

Introduction: Periodic limb movements (PLMS) are thought to involve the dopaminergic system and/or dysfunction of peripheral nerves. Despite increased focus on PLMS, the pathophysiology remains elusive and appropriate rodent models are lacking. We hypothesized that muscle spindle abnormalities may underlie PLMS. The transgenic mice used in this study (myo/NT-3) overexpress muscle-derived neurotrophin-3 (NT-3). Developmental overexpression of muscle-derived NT-3 results in the hypertrophy of the proprioceptive system, including increased muscle spindles and gamma motoneurons, which is mantained through adulthood. Mice overexpressing muscle spindles have a phenotype that includes repetitive limb movements.
Methods: Fourteen mice were used (6 wild-types, 8 myo/NT-3). Surgery for placement of bipolar epidural screw electrodes, and one bipolar leg EMG electrode (right quadriceps) was performed. 12-hours were scored continuously in 10-second epochs to determine Total Sleep Time (TST), Wake (W), non-rapid eye movement sleep (NREMS), and rapid eye-movement sleep (REM). Leg movements with and without an arousal were also scored. PLMS were scored if there were four consecutive movements witn an intermovement interval of 5-60 seconds.
Results: No statistical differences were detected between wild-type and myo/NT-3 mice with regard to TST, wake, NREM or REM sleep. Groups however differed significantly with regard to the frequency of PLMS ($t(1,12)= -8.987$, $p<0.001$). Myo/NT3 mice had more PLMS (mean=305) compared to wild-type mice (mean=70), with a frequency of 57.5 PLMS/hour of sleep and 13.96 PLMS/hour of sleep, respectively. Myo/NT-3 mice had more arousals associated with leg movements ($t(1,12)= -4.309$, $p < 0.001$). Myo/NT-3 mice had more PLMS with arousals (mean=126) compared to wild-types (mean=24.3), with a frequency of 25.76 arousals associated with PLMS/hour of sleep and 4.42 PLMS arousals/hour, respectively.
Conclusion: The results of this study show that myo/NT-3 transgenic mice show a phenotype consistent with frequent periodic limb movements. As in humans, the periodic limb movements are associated with significant sleep fragmentation due to frequent arousals from sleep. Further studies are needed to assess the role of an overactive proprioceptive system in the pathogenesis of periodic limb movements.

0847

PERIODIC LIMB MOVEMENT DISTRIBUTION OVER THE COURSE OF A SLEEP STUDY

Fleming P,[1] Perrott J,[2] Norris A,[3] Renda F[2]
(1) Kitchener Sleep Clinic, Ontario, Canada, (2) Ontario, Canada, (3) Kitchener Sleep Clinic, Kitchener, Ontario, Canada

Introduction: Periodic limb movements can occur any time during sleep and are characterized by four or more leg movements separated by more than five, and less than ninety seconds (Atlas Task Force, ASDA1992;15:174-184). The aim of this study was to determine if PLMs congregate or distribute themselves randomly.
Methods: A sample of 237 CPAP and non-CPAP sleep studies consisting of NPSG 420min+/- 30min (lights off 22:30+/- 30 min and lights on 05:30 +/- 30 min) were selected. Periodic limb movements associated with arousals or respiratory events were excluded. Of those 237 sleep studies, 79 subjects (n=79), were found to have PLMD >5/hr. Each study was divided into three time periods, A=22:30-00:50, B=00:50-03:10, C=03:10-5:30 and PLM activity determined for each. The percentage of PLMs occurring in each period was calculated. The mean percentage of PLMs for each time period was calculated and statistical analysis performed.
Results: For n=79, 45.9 % of total PLMs occurred in time period A, 31.0% occurred in B, and 23.0% in C. Tabulated z-value was equal to 1.644853 and calculated z-values for time periods A versus B, A versus C, and B versus C were as follows: z= 2.744447, z=4.862316 and z= 2.117868. A one-sided critical test with sample variances of 0.13148749, 0.084246654, and 0.089816 for time periods A, B and C respectively, was performed. Known variance of 0.131487 and 0.084247 was used in comparisons of A, B and C. In all cases, the null hypothesis was rejected. There is 95% confidence that time period A>B>C for periodicity of PLMs.
Conclusion: Based on the above results, it would appear that the first two-thirds of the night have more PLMs, with PLMs occurring more in time period A than in B or C, and more occurring in B than in C.

0848

RESTORATION OF NORMAL MOTOR CONTROL IN PARKINSON´S DISEASE DURING REM SLEEP

Cochen-De Cock V,[1] Vidailhet M,[2] Leu S,[2] Roze E,[2] Agid Y,[2] Willer J,[2] Derenne J,[2] Arnulf I[3]
(1) Service de Neurologie, Hôpital Purpan, Toulouse, Plaisance du Touch, AE, France, (2) AE (Europe), (3) Paris, France

Introduction: Although normal subjects do not move during REM sleep, patients with Parkinson´s disease may experience REM sleep behaviour disorder (RBD). The characteristics of the abnormal REM sleep movements in RBD have however not been studied.
Methods: We interviewed one hundred consecutive non-demented patients with Parkinson´s disease and their bed partners using a structured questionnaire assessing the presence of RBD. They rated the quality of movements, voice and facial expression during RBD as being better, equal or worse than in awake "on" levodopa condition. Night-time sleep and movements were video-monitored during polysomnography in 51 patients to evaluate the presence of bradykinesia, tremor, and hypophonia during REM sleep.
Results: Fifty-nine patients had clinical RBD with 53/59 bed partners able to evaluate them. All 53 (100%) reported an improvement of at least one component of motor control during RBD. By history, movements were improved in 87% patients (faster, 87%, stronger, 87%, smoother, 51%), speech was better in 77% patients (more intelligible, 77%, louder, 38%, better articulated, 57%), and facial expression was normalized in 47% patients. Thirty-eight percent bed partners reported that movements were "much better", even in the most disabled patients. The video-monitored purposeful movements in REM sleep were also surprisingly fast, ample, coordinated, and symmetrical, without obvious sign of parkinsonism. The movements were however jerky, violent, and often repetitive.
Conclusion: The restored motor control during REM sleep suggests a transient "levodopa-like" reestablishment of the basal ganglia loop. Alternatively, parkinsonism may disappear by REM sleep-related disjunction between pyramidal and extra-pyramidal systems. We suggest the following model: the movements during the RBD would be generated by the motor cortex and would follow the pyramidal tract bypassing the extrapyramidal system. These movements would eventually be transmitted to the lower motor neuron because of brainstem lesions interrupting the pontomedullary pathways which mediate the REM sleep atonia.
Support (optional): The Clinical Investigation Center (CIC) of Saint Antoine Hospital Paris participated to protocol design, study coordination and data collection. The trial was sponsored in part by grants from France Parkinson, Lilly Foundation and Servier. ADOREP (Association for the Development of Sleep and Respiratory Research) was the promoter of the study.

0849

RESTLESS LEGS SYNDROME DURING PREGNANCY

Galdino D, Carvalho L, Prado L, Oliveira C, Prado G
Federal University of São Paulo, São Paulo, Brazil

Introduction: Restless legs syndrome (RLS) is a movement disorder characterized by uncomfortable and unpleasant sensations in the legs that appear at rest, which induces an irresistible urge to move the legs. Pregnant women present two to three times more chances to have RLS then the general population. The symptoms bother them, but they are not mencioned to doctors at pregnant women preventive assistance. The aim of this study was to determine the prevalence of the restless legs syndrome in pregnant women by clinical interview.
Methods: We evaluated 228 normal pregnant women. The pregnancy periods goes from the first to the third trimester, at the out patients clinic of Obstetrics Discipline of UNIFESP and UNILAVRAS. A diagnostic-clinical interview for RLS was done with all participants by a treined researcher for a diagnosis of RLS.
Results: Within the 228 pregnant women interview we found 18% with RLS. There was no diffirence among the trimesters (p=0,013)
Conclusion: Pregnancy is associated with a larger predominance of RLS with the general population, these data that are valuable because the results were from an interviews and not questionnaires.

0850

THE ASSOCIATION OF ANTIDEPRESSANT USE WITH RESTLESS LEGS SYNDROME IN A VA OUTPATIENT POPULATION

Baughman K,[1] Bourguet C,[1] Ober S,[2] Steiner R[3]
(1) Northeastern Ohio Universities College of Medicine, Rootstown, OH, USA, (2) Cleveland Veterans Affairs Medical Center, Cleveland, OH, USA, (3) University of Akron, Akron, OH, USA

Introduction: Mixed evidence exists for an association between antidepressant use and Restless Legs Syndrome (RLS). While RLS patients often experience greater levels of insomnia and depression, it is unclear whether antidepressants exacerbate the symptoms of RLS. Our goal was to clarify the relationship.
Methods: Telephone interviews were conducted with 1761 patients

recruited at 12 VA primary care clinics in Ohio. Measures of RLS, insomnia, depression, smoking status, and BMI were included. Also, we obtained prescription medication data for the six months prior to the interview.
Results: Patients were aged 22 to 92. Eighty percent were male, 41% had a BMI of 30 or over, and 22% currently smoked. The prevalence of RLS symptoms at least once per week was 28% for women and 18% for men. Current antidepressant users were more likely to have RLS (25%) than non-users (19%), (chi-square = 3.84, p = .05); those using a tricyclic antidepressant were most likely to have RLS (35%). While SSRI´s as a class were not associated with RLS, those using citalopram were more likely to have RLS (34% versus 20%, chi-square = 5.50, p = .02).

A logistic regression predicting RLS, adjusting for race, age, gender, BMI, and smoking status revealed that tricyclics and SSRI´s were not significantly associated with RLS. Each 20 mg of citalopram increased the odds of RLS by a factor of 1.53 (p=0.5). This association was attenuated when controlling for insomnia and depression (OR = 1.25, p = .31).
Conclusion: The relationship between antidepressant use and RLS is likely a result of RLS patients experiencing greater levels of insomnia and depression. In multivariate analyses that control insomnia and depression, the association between RLS and antidepressant use fades.
Support (optional): Supported by DAMD17-03-1-0082 from the US Army Medical Research and Materiel Command and a grant from Pfizer Pharmaceutical Corporation.

0851

THREE-MONTH EFFECTS OF PRAMIPEXOLE ON DAYTIME SYMPTOMS IN RESTLESS LEGS SYNDROME

Ballard R,[1] Bogan R,[2] Winkelman J,[3] Koester J[4]
(1) Colorado Sleep Medicine, Denver, CO, USA, (2) SleepMed, Inc., Columbia, SC, USA, (3) Brighton, MA, USA, (4) Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany

Introduction: Because restless legs syndrome (RLS) disrupts sleep, its effects extend into daytime life, which must therefore be included in assessing any RLS therapy.
Methods: For a double-blind, controlled trial of pramipexole, 344 adult patients with RLS were randomized to receive placebo or the active dopamine agonist. During a 3-week run-in phase, the pramipexole recipients were up-titrated to a fixed 0.25, 0.50, or 0.75 mg/day. After the ensuing 12-week trial, 100-mm visual analogue scales (VASs) enabled patients to characterize the RLS severity they experienced while getting to sleep, at night, and during the day, and also their satisfaction with sleep. To assess daytime somnolence, the Epworth Sleepiness Scale (ESS) was utilized. Change from baseline to the end of the study was analyzed by an analysis of covariance model, with factors treatment, center, and baseline as covariates.
Results: All VAS ratings improved significantly more in the pramipexole group than in the placebo group. For daytime symptom severity, mean baseline scores were 29.8 for the pramipexole group and 35.7 for the placebo group. At the end of 12 weeks, the mean score in the pramipexole group fell 49% (to a score of 15.1) compared with 32% (24.0) in the placebo group. The adjusted mean difference between the groups was 6.8 mm (p = .0081), with significant differences from placebo for 0.50 mg/day (8.3 mm, p = .0095) and 0.75 mg/day (7.3 mm, p = .0191). Pramipexole recipients also reported a 33% (adjusted) greater satisfaction with sleep compared with placebo (p = .0016). The adjusted mean reduction in ESS was 22% larger for pramipexole than placebo; though this difference was not statistically significant (p = .3028).
Conclusion: Patient self-ratings linked pramipexole to improvement in sleep and in daytime RLS, with no treatment-related increase in daytime somnolence.
Support (optional): This study was supported by Boehringer Ingelheim.

0852

IMPROVED SLEEP AS RATED BY SEVERAL MEASURES IN PATIENTS RECEIVING DOUBLE-BLIND PRAMIPEXOLE FOR RESTLESS LEGS SYNDROME

Ballard R,[1] Bogan R,[2] Zee P,[3] Albrecht S,[4] Winkelman J[5]
(1) Colorado Sleep Medicine, Denver, CO, USA, (2) SleepMed, Inc., Columbia, SC, USA, (3) Northwestern University, Chicago, IL, USA, (4) Boehringer Ingelheim International GmbH, Ingelheim, Germany, (5) Brighton, MA, USA

Introduction: Sleep disruption is the main reason patients with restless legs syndrome (RLS) seek medical attention.
Methods: In three double-blind, placebo-controlled trials of pramipexole (≤0.75 mg/day) for RLS, patients initially meeting all diagnostic criteria of the International RLS Study Group were assessed by subjective sleep-rating instruments. In a three-week trial, patients rated their daily sleep quality on a 10-point scale, which was averaged over at least one week. In a six-week and a 12-week trial, patients rated their sleep satisfaction in the past week on a 100-mm visual analogue scale. All three trials asked Question 4 of the International RLS Study Group Rating Scale (IRLS): "Overall, how severe is your sleep disturbance due to your RLS symptoms?" Answers range from 0 ("none") to 4 ("very severe").
Results: Among 107 patients in the three-week trial, median subjective sleep quality improved at all pramipexole dosages. Among 335 patients in the six-week trial, the mean improvement in sleep satisfaction, adjusted for age and baseline, was 29.9 mm for pramipexole vs 13.8 for placebo (p < .0001). Among 338 patients in the 12-week trial, the sleep-satisfaction improvement was 38.4 mm for pramipexole vs 25.8 for placebo (p = .0016). Among the combined 784 patients, the mean baseline answer to IRLS Question 4 was 2.6. The mean changes for pramipexole and for placebo were -2.0 and -0.9 in the three-week trial (p = .001), -1.7 and -0.8 in the six-week trial (p < .0001), and -1.7 and -1.2 in the 12-week trial (p = .0037).
Conclusion: Across three double-blind trials of pramipexole for RLS, patients´ sleep ratings showed consistent improvement across trials and scales, including an improvement on IRLS Question 4, from a mean between "moderate" and "severe" to a mean of "none" to "mild."
Support (optional): These studies were supported by Boehringer Ingelheim.

0853

THE ROLE OF THE EXTERNAL CORTEX OF THE INFERIOR COLLICULUS IN THE REGULATION OF SLEEP, SENSORY AND MOTOR ACTIVITY

Hsieh K, Nguyen D, Siegel J, Lai Y
University of California, Los Angeles, North Hills, CA, USA

Introduction: The external cortex of the inferior colliculus (ICX) is involved in auditory, visual and sensor-motor integration. Here we report that the ICX may be involved in the regulation of sleep and the pathology of sleep-related sensory-motor disorders.
Methods: Sprague-Dawley rats weighing about 600g (n=3) were implanted with EEGs, nuchal and femoral EMGs, and a guide cannula aiming at ICX. The animals were housed in sound-attenuated chambers

with 12:12 cycles of LD after recovery from surgery. On the day of the experiment, artificial cerebrospinal fluid was infused via a microdialysis probe from ZT2 to ZT7, except between ZT4 and ZT5 during which time test drugs were infused. The animals were undisturbed during simultaneous polygraphic and video recording, while the infusion was controlled outside the chamber.
Results: Infusion of the GABA-A receptor agonist, muscimol into the ICX induced an increase in sleep without changing motor activity. In contrast, infusion of the GABA-A receptor antagonist, bicuculline (100uM and 200uM) into the ICX induced a dose-dependent decrease in sleep and hyperactivity. Upon the cessation of hyperactivity, animals showed repetitive movements in both hindlimbs at an interval of 2-5 seconds during quiet wakefulness (PLMW) but not during the brief, intermittent sleep episodes. This abnormal motor activity peaked at 2-3 hour post-infusion, gradually decreased and tapered off over a period of 20 hours. The animals frequently nibbled at the hind limb contralateral to the infusion site; this behavior may indicate the occurrence of abnormal sensations in the leg. Periodic leg movements in sleep (PLMS) were observed as the frequency of PLMW diminished.
Conclusion: Disrupted sleep, unpleasant sensations, repetitive movements in the hindlimbs and the presence of PLMS in the ICX-bicuculline infused rat, resemble symptoms seen in patients with restless leg syndrome (RLS). We suggest that a GABAergic mechanism in the ICX may be involved in the generation of RLS.
Support (optional): This work is supported by grants NS42566 and HL41370 and the Department of Veterns Affairs, VAGLAHS Sepulveda.

0854

PREVALENCE, SEVERITY AND IRON METABOLISM OF RESTLESS LEGS SYNDROME IN THE KOREAN ELDERLY POPULATION – THE KLOSHA

Yoon I,[1] Chung S,[2] Shin Y,[2] Lee S,[2] Park J,[2] Choi E,[2] Kim K[2]
(1) Department of Neuropsychiatry, Seoul National University Bundang Hospital, Seongnam, Gyeonggi, South Korea, (2) Seoul National University Bundang Hospital, South Korea

Introduction: As restless legs syndrome (RLS) is frequently observed in the elderly, and secondary causes of RLS have been known to be more common in late-onset RLS patients, we aimed to assess the prevalence and severity of RLS in elderly population, and to investigate the association of RLS with iron metabolism.
Methods: This study was conducted as a part of Korean Longitudinal Study on Health and Aging (KLoSHA), a population-based prospective cohort study in the Korean elderly aged 65 years and over. Of the 1,118 subjects, 706 agreed to participate in the study (408 women and 298 men). The diagnosis of RLS was established by two trained psychiatrists in face-to-face interviews using four minimal criteria defined by the International Restless Legs Syndrome Study Group (IRLSSG). IRLSSG Severity Scale was also conducted on subjects who were diagnosed with RLS. Blood samples were obtained for laboratory tests including iron metabolism.
Results: Among 706 subjects, 59 (42 female and 17 male) were diagnosed as RLS, and the prevalence of RLS was 8.36% (95% CI 6.32% - 10.40%). RLS was more frequent in women than men (10.3% in women, 5.7% in men, $X2 = 4.74$, $p < 0.05$). There were no significant differences in age and laboratory findings including parameters of iron metabolism between subjects with RLS and without RLS. Among the patients with RLS, there was no significant difference in age and symptom severity scores between men and women. Levels of hemoglobin ($p=0.042$) and ferritin ($p=0.034$) were significantly lower in women. Serum ferritin level was negatively correlated with the symptom severity ($r=-0.283$, $p=0.03$) of RLS.
Conclusion: RLS was more frequently observed in female than male subjects among Korean elderly population, but there were no gender differences in symptom severity and laboratory findings except hemoglobin and ferritin. Although iron deficiency was not a risk factor in RLS, patients with RLS may suffer from more severe symptoms with decreased iron storage.

0855

PLM DURING SLEEP ASSOCIATED WITH CHANGES IN THE AUTONOMIC NERVOUS SYSTEM

Palombini L,[1] Kauati A,[2] Almeida D,[3] Lopes M,[4] Poyares D,[4] Tufik S[5]
(1) Univ. Fed Sao Paulo, São Paulo, Brazil, (2) Univ.Fed. Sao Paulo, São Paulo, Brazil, (3) Univ. Fed.Sao Paulo, Sao Paulo, Brazil, (4) Univ Fed sao Paulo, Sao Paulo, Sao Paulo, Brazil, (5) Univ Fed Sao Paulo, Sao Paulo, Brazil

Introduction: Patients with periodic leg movement (PLM) may be associated with clinical instabilities. PLM can occur without arousal, and may last for long periods. However, the consequences of these events are not clear. It has been suggested that PLM may be associated with ANS abnormalities, which can be related to cardiovascular risk. The purpose of this study was to evaluate autonomic changes associated with PLM during sleep in patients.
Methods: 20 patients were evaluated with PLM > 5 events/h and respiratory disturbance index (RDI) < 5 during sleep. The HRV Standard Time and Frequency Domain were calculated for each 5-minutes period without microarousal events during SWS. A total of 40 periods of sleep were analyzed using HRV (20 periods with PLM and 20 periods without PLM).
Results: The analyses of HRV (5-minute periods) showed significant differences between periods with PLM and without PLM in the frequency domain, respectively: LF (low frequency) [4998.0 ± 4277.1 vs 1891.7 ±1351.5; $p = 0.0018$]; TP (total power) [9083.1 ± 5068.6 vs 5682.4 ± 3206.5; ; $p = 0.0060$]; LF/HF (LF normalized) [3.7375 ± 3.7284 vs 1.3385 ± 1.4069; $p = 0.0032$].
Conclusion: PLM periods during sleep were associated with increase in sympathetic activity and may be a consequence of abnormal autonomic regulation. Compared to normal periods of sleep without legs movement, 5-minutes of sleep PLM were associated with predominant increase in sympathetic tone. Long-term studies are necessary to evaluate the cardiovascular consequences of these autonomic changes.
Support (optional): Supported by AFIP/FAPESP/CEPID

0856

EXCESSIVE DAYTIME SLEEPINESS IN PATIENTS WITH PARKINSON´S SYNDROME AND SLEEP-WAKE COMPLAINTS

Poryazova R,[1] Werth E,[1] Waldvogel D,[1] Bassetti C[2]
(1) University Hospital Zurich, Switzerland, Zurich, Switzerland, (2) University Hospital Zürich, Zürich, Switzerland

Introduction: Excessive daytime sleepiness (EDS) is common in patients with Parkinson´s syndrome. Age, gender, severity of the neurodegenerative process, night-time disturbances and therapy are implicated in the pathophysiology of EDS. In a group of patients a narcolepsy-like phenotype has been suggested.
Methods: Thirty-five patients (27 male, 8 female) with Parkinson´s syndrome (22 with idiopathic Parkinson´s disease and 13 with atypical parkinsonism) underwent video-polysomnography (PSG) and multiple sleep latency test (MSLT), EDS was also subjectively assessed by Epworth sleepiness scale (ESS). The patients were referred to the sleep laboratory for different reasons, 19 because of EDS.
Results: Twenty-one patients had ESS ≥ 10, of whom 19 men. Ten

patients had mean sleep latency (MSL) in MSLT ≤ 5 minutes, of whom 9 men. Male patients had higher ESS scores (although not statistically significant) and shorter MSL in MSLT (p=0.035). Sleep onset REM (SOREM) was observed in only 2 patients (5/149 nap opportunities, 3.4%). Slight negative correlation was found between MSL and the dopamine agonist dose. The amount of REM sleep correlated positively with MSL and negatively with ESS score. Apnea/hypopnea index was slightly correlated to the ESS score. No relation was found with age, diagnosis, disease severity, self-reported depression and memory problems or other night-time parameters or disturbances.
Conclusion: In this sample of patients with Parkinson´s syndrome EDS, as expressed by ESS score and MSL in MSLT was common and was related to male sex, quantity of REM sleep, dopamine agonist dose and sleep-related breathing disturbances. As SOREM was rare narcolepsy-like phenotype seems unlikely in this group of patients.

0857

PREVALENCE OF LOW FERRITIN IN RESTLESS LEG SYNDROME PATIENTS IN AN URBAN SLEEP CLINIC

Saha R, Omran A, Maslinski P, Rowley J
Wayne State University, Detroit, MI, USA

Introduction: Restless leg syndrome is a common disorder, affecting up to 10% of the population. RLS has been associated with deficiency in iron stores and current practice guidelines recommend measuring a ferritin in all patients diagnosed with RLS. The objective was to determine the prevalence and determinants of low ferritin level in patients diagnosed with RLS.
Methods: Retrospective chart review of all patients diagnosed with RLS between October 2005 and October 2006. Charts were reviewed to determine if a ferritin level was obtained. If a ferritin level was obtained, it was recorded along with demographic information and comorbidities. Patients divided into two groups based upon a ferritin level <50 micrograms/L and the demographic characteristics of the two groups were compared.
Results: 41 patients (29 women, 12 men) were diagnosed with RLS; a ferritin level was obtained in 27 (66%) patients (21 women, 6 men). Ferritin level was low in 10 (37%) of the patients (10 women, 0 men); in this group, the mean ferritin level was 26.4±8.6 micrograms/L. Patients with low ferritin were younger (low ferritin group, 42.4±7.4 yrs v. normal ferritin group, 54.2±10.7 yrs, p=0.008), while there was a trend toward a higher percentage of women with low ferritin (100% women in low ferritin group v. 71% women in normal ferritin group, p=0.057). The women with a low ferritin had an age range of 29-50 years while the women with a normal ferritin had an age range of 50-82 years. The BMI and number of comorbidities was not different between the two groups.
Conclusion: A low ferritin level is common (37%) in RLS patients but was found only in women with age <50 years. These data indicate that obtaining a ferritin level may be necessary only in younger women with RLS.
Support (optional): n/a

0858

ASSESSMENT OF DAYTIME SOMNOLENCE ACROSS THREE DOUBLE-BLIND TRIALS OF PRAMIPEXOLE FOR RESTLESS LEGS SYNDROME

Winkelman J,[1] Bogan R,[2] Lainey E[3]
(1) Brigham and Women's Hospital Sleep HealthCenter, Newton Centre, MA, USA, (2) SleepMed, Inc., Columbia, SC, USA, (3) Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA

Introduction: Because restless legs syndrome (RLS) disrupts sleep, its detriments extend into daytime life. Hence, daytime somnolence is an important facet of the assessment of any RLS therapy.
Methods: A three-week European trial studied pramipexole at fixed doses of 0.125 to 0.75 mg/day. A six-week European trial studied optimized doses of 0.125 to 0.75 mg/day. A 12-week US trial studied fixed doses of 0.25 to 0.75 mg/day. At baseline and trial completion, all patients were assessed by the Epworth Sleepiness Scale (ESS), a self-administered questionnaire asking respondents to rate, on a scale of 0 to 3, the likelihood of falling asleep during each of eight everyday situations. A score of 10 or more is considered abnormal daytime sleepiness. All trials were double-blind and placebo-controlled, and patients met all diagnostic criteria of the International RLS Study Group. Change in ESS from baseline to study end was analyzed by ANCOVA, using baseline score and age as covariates.
Results: Across the trials, 562 pramipexole recipients and 220 placebo recipients contributed analyzable ESS data. At baseline, the mean scores were <10 in all cohorts (range: 6.0 to 8.2), signifying a mean normal degree of daytime sleepiness. At endpoint, the mean scores were slightly reduced (by 0.2 to 1.7) in all cohorts. In the subgroup of patients with abnormal daytime sleepiness (ESS ≥10) at baseline (30.2% of pramipexole and 32.7% of placebo recipients), pramipexole reduced the adjusted ESS by 1.5 points more than placebo (p = .0157). In the subgroup of patients with normal daytime sleepiness (ESS <10) at baseline, no adjusted treatment difference was observed.
Conclusion: Across three double-blind trials of pramipexole for RLS, the active agent did not increase daytime sleepiness. Among patients with abnormal daytime sleepiness at baseline, pramipexole provided significantly greater improvement in the mean ESS score than placebo.
Support (optional): These studies were supported by Boehringer Ingelheim.

0859

RESTLESS LEGS SYNDROME AND EXCESSIVE DAYTIME SLEEPINESS

Kallweit U,[1] Siccoli M,[2] Werth E,[3] Bassetti C[1]
(1) University Hospital Zurich, Zurich, Switzerland, (2) Department of Neurology, University Hospital of Zurich, zurich, Switzerland, (3) University Hospital Zurich, Switzerland, Zurich, Switzerland

Introduction: Whereas insomnia is a frequent symptom of restless legs syndrome (RLS) little is known about the prevalence and characteristics of excessive daytime sleepiness (EDS) in RLS.
Methods: We studied 30 consecutive idiopathic, non-treated RLS patients, (16 women, 14 men; mean age = 61 +/- 11 years) without associated sleep-disorders. Patient assessment included the International Restless Legs Syndrome Study Group Rating Scale (IRLS), Epworth Sleepiness Scale (ESS) and conventional polysomnography (PSG). The PLM-Index was determined by PSG. Patients with ESS >11 (n=9) were also assessed by multiple sleep latency test (MSLT). Eight sleepy patients received dopaminergic treatment and were again assessed clinically and by sleep-questionnaires after two months.
Results: We found an ESS >11 (mean 14.9 +/- 3.6) in nine (30%) and an ESS >14 (mean 18.3 +/- 2.3) in four (13%) of the 30 patients. No statistical differences in IRLS-score, PLM- Index, age, gender or body mass index (BMI) were found between sleepy and non-sleepy RLS patients.
The mean sleep latency found was 6.9 +/- 3.3 min, four (44%) of the nine patients had a mean sleep latency <5 min. In 2 of these patients one sleep-onset REM period occurred.
At follow-up the ESS was lower (mean 10.4 +/- 4.5 vs. 16.2 +/- 3.8) in five patients and same or higher in three (mean 14.3 +/- 2.1 vs. 12.3

+/- 0.5).
Conclusion: Excessive daytime sleepiness in RLS is 1) relatively common, 2) detectable by MSLT and 3) occasionally in the narcoleptic range (ESS and MSLT).

0860

ALPHA – MELANOCYTE STIMULATING HORMONE AND PERIODIC LIMB MOVEMENTS DURING SLEEP: AN ANIMAL MODEL

Koo B, Strohl K, Feng P
Case Western Reserve University, Cleveland, OH, USA

Introduction: Despite much investigation into etiology, the pathophysiology of periodic limb movements during sleep (PLMS) remains elusive. Alpha – melanocyte stimulating hormone (-MSH) as a substrate for PLMS is suggested by its diurnal variability in rat hypothalamus and stimulation of locomotion and grooming in awake rats.
Methods: Three male Long-Evans rats were implanted with electrencephalography (EEG), nuchal and anterior tibialis electromyography (EMG) and intracerebroventricular (i.c.v.) cannulae. Rats received i.c.v. injections of 6 µL saline or 0.5 µg α-MSH on separate days and EEG, video and EMG were recorded in the subsequent 24 hours. State epochs were classified as quiet wake, active wake, slow wave sleep I, slow wave sleep II or paradoxical sleep. Limb movements in sleep were identified as increased EMG and verified by video EEG. Grooming and locomotion were observed in the hour following injection. Data were analyzed for descriptive statistics and paired t- tests were used for comparison of means. P values < 0.05 were statistically significant.
Results: Saline and α-MSH groups did not differ in sleep latency, active wake, slow wave sleep I or II, paradoxical sleep, arousal index, locomotion or grooming. Analysis in the saline and α-MSH groups showed trends toward significance in limb movement indices (number of limb movements per hour sleep), 30.4 ± 0.9 vs. 38.3 ± 4.7 ($p = 0.07$) and periodic limb movement indices (number periodic limb movements per hour sleep), 15.8 ± 1.1 vs. 23.4 ± 5.8 ($p = 0.1$) and significant differences in absolute numbers of limb movements (284.7 ± 20.2 vs. 368 ± 45.9, $p = 0.02$) and time spent in quiet wake (61.8 min ± 11.5 vs. 40 ± 6.5, $p = 0.03$).
Conclusion: Rats receiving i.c.v. α-MSH had greater numbers of limb movements and less quiet wake. These preliminary data may lend support to α-MSH as a substrate for PLMS.

0861

THE PHONE INTERVIEW FOR RLS DIAGNOSTIC

Gruber T, Silva R, Carvalho L, Oliveira C, Fontes S, Masuko A, Prado L, Prado G
Federal University of Sao Paulo, Sao Paulo, Brazil

Introduction: Restless Legs Syndrome (RLS) is a common disease, with a prevalence about 10% of the general population. Its symptoms appear before bedtime, causing sleeping disorders, and consequently, a worsening of the patient quality of life. The diagnostic is clinical, based on the history presented by the patient, that relates unpleasant sensations and uncomfortable sensations in the legs, mainly at the night, and experience relief or absence of the sensations with legs movements. In spite of having described for the first time 330 years ago, this disorder is still little known in the Brazilian medical community. Our point is to evaluate the sensibility and specificity of the questionnaire "Restless Legs Syndrome's Clinical-Diagnostic Interview" (RLSCDI) used at the Johns Hopkins RLS outpatient clinic, translated and adapted to Brazilian Portuguese.
Methods: We studied 19 patients with RLS clinic diagnostic and 22 without, from Neuro-Sono Outpatients, UNIFESP, Sao Paulo, Brazil. A blind and trained researcher interviewed the patients by phone. Chi-square and Kappa test were used for statistical analysis.
Results: The questionnaire identified 15/19 patients in the group with RLS and there was no agreement between clinic diagnostic and questionnaire in 4 cases. In the group without RLS, the questionnaire identified 20/22 and there was no agreement in the other 2 cases. The agreement of RLSCDI and clinical diagnostic was high (Kappa=69%) with 83% of specificity and 88% of sensibility.
Conclusion: The Portuguese version of the RLSCDI is a good instrument to diagnose RLS, throughout phone interview in a set of Brazilian speakers.
Support (optional): UNITER-SONO

0862

ASSOCIATION OF POLYSOMNOGRAPHIC LIMB MOVEMENTS WITH SLEEPINESS AND CARDIOVASCULAR MEASURES

Weber S,[1] Finn L,[2] Winkelman J,[3] Young T[2]
(1) University of Wisconsin School of Medicine and Public Health, Madison, WI, USA, (2) University of Wisconsin-Madison, Madison, WI, USA, (3) Brighton, MA, USA

Introduction: Lower limb movements (LMs) have recently been associated with autonomic changes that may predispose patients to hypertension and cardiovascular morbidity. We analyzed data from the Wisconsin Sleep Cohort Study (WSCS) to examine the relationships between LMs and questionnaire indices of cardiovascular disease, measured hypertension, and multiple sleep latency (MSLT) test data.
Methods: The sample comprised participants from the WSCS, a longitudinal study incorporating polysomnographic studies at 4 year intervals, multiple physiological measurements, and serial questionnaires. LMs irrespective of EEG arousals were defined according to Coleman´s criteria, excluding the periodicity component. LM data were classified into categories based on index per hour of total sleep time: < 5, 5-15, 15-30, >30. Data analysis incorporated 3384 studies. 1196 MSLTs were obtained on 1111 of the subjects. Generalized estimating equations were used to model the data to account for repeated measures and models were adjusted for age, sex, BMI, and apnea hypopnea index (AHI). Odds ratios and 95% confidence intervals were calculated to estimate the association between LM categories and dependent measures.
Results: Complex statistical associations were observed between LMs, and dependent measures. LMs >15 vs. <5 were not associated with pathological MSLT levels (mean < 5 min.). However, LMs 5-15 vs. <5 were negatively associated with MSLT. No associations were revealed for cardiovascular disease. Secondary analyses employing a LMs chronicity component (LM index >30 on 3 successive polysomnograms) showed a positive association with hypertension, but only in subjects with an AHI >15.
Conclusion: This population-based study demonstrates no association between overall LMs and cardiovascular disease, and a complex association of LMs with MSLT and hypertension.
Support (optional): NIH HL062252-06

0863

HYPOCRETIN (OREXIN) AND MCH (MELANIN-CONCENTRATING HORMONE) CELL LOSS IN PARKINSON´S DISEASE

Thannickal T, Lai Y, Siegel J
University of California, Los Angeles, North Hills, CA, USA

Introduction: Excessive daytime somnolence (EDS) is a common and debilitating symptom of Parkinson´s disease(PD) and many patients show sleep-onset REM periods and hypnogogic hallucination, often preceding the motor symptoms. Either normal or reduced levels of CSF hypocretin/orexin have been reported in PD by different groups.
Methods: The hypothalamus of eleven PD (mean age 79 ± 4) and five normal (mean age 77 ± 3) brains was examined. Brains from all clinical stages (Hoehn and Yahr, 2001) of PD were studied. Sections were immunostained for Hcrt, MCH, alpha synuclein and GFAP. The substantia nigra of ten PD brains and seven normal brains were used for the study of neuromelanin pigmented cell loss. Cell number, distribution and size were determined with stereology techniques.
Results: We found an increasing loss of Hcrt and MCH cells with disease progression as measured by the Hoehn and Yahr rating scale. Hcrt and MCH cells were lost throughout the A-P extent of their hypothalamic distributions. The percentage loss of Hcrt cells was minimal in stage I (23%) and was maximal in stage V (62%). Similarly, the percentage loss of MCH cells was lowest in stage I (12%) and was highest in stage V (74%). There was a significant increase ($p = 0.0006$) in the size of neuromelanin containing cells in PD, but no difference in the size of surviving Hcrt ($p = 0.18$) and MCH ($p = 0.28$) cells relative to control.
Conclusion: The significant correlations between the loss of Hcrt and MCH neurons and the clinical stage of PD suggests a previously unappreciated relationship between hypothalamic dysfunction and the time course of the overall clinical picture of PD. The narcolepsy-like symptoms of PD may be best be treated with therapies that have proved successful in the treatment of narcolepsy.
Support (optional): Tissue specimens were obtained from the Human Brain and Spinal Fluid Resource Center, West Los Angeles Healthcare Center, Los Angeles, CA. Research supported by NS14610, HL41370, MH64109 and the Medical Research Service of the Dept. of Veterans Affairs.

0864

ROTIGOTINE TRANSDERMAL PATCH IMPROVES QUALITY OF LIFE IN RESTLESS LEG SYNDROME

Paap C,[1] Stiasny-Kolster K,[2] Garcia-Borreguero D,[3] Saletu B,[4] Schollmayer E,[5] Oertel W[5]
(1) Schwarz Pharma, Mequon, WI, USA, (2) University of Marburg, Marburg, Germany, (3) Fundacion Jimenez Diaz, Spain, (4) Medical University of Vienna, Vienna, Austria, (5) Germany

Introduction: Rotigotine, a dopamine agonist delivered via transdermal patch, was evaluated in a 7-week double-blind, placebo-controlled study in moderate to severe idiopathic Restless Legs Syndrome (RLS). Patients (N=341) were randomized to placebo or rotigotine: 0.5mg/24 h, 1mg/24 h, 2mg/24 h, 3mg/24 h, and 4mg/24 h. Quality of Life was measured using the QoL-RLS score. Safety and tolerability were evaluated by AEs, SAEs, laboratory values, ECG, and vital signs.
Methods: A statistically significant treatment difference was observed for 1mg-4mg/24 h rotigotine versus placebo, with the greatest difference (6.8 points on QoL-RLS total score) occurring in the 3mg/24 h rotigotine group. No clinically-relevant changes in vital signs, clinical chemistry, hematology, endocrine parameters or urinalysis were recorded. The most common AEs (5%) were consistent with stimulation of dopamine receptors or transdermal delivery systems: nausea, application site reaction, fatigue, and headache.
Results: In this trial, rotigotine improved moderate to severe Restless Legs Syndrome compared with placebo on the QoL-RLS total score.
Conclusion: The quality of live improved consistently on all parameters tested, demonstrating that rotigotine is efficacious, well tolerated and safe.

0865

CORRELATES OF PERIODIC LIMB MOVEMENTS OF SLEEP IN PEDIATRIC POPULATION

Bokkala S,[1] Napalinga K,[1] Cruz M,[2] Adams R,[2] Pinninti N,[3] Valencia I,[2] Legido A,[2] Kothare S[2]
(1) Drexel University School of Medicine, Philadelphia, PA, USA, (2) St. Christopher's Hospital for Children, Philadelphia, PA, USA, (3) UMDNJ-SOM, Stratford, NJ, USA

Introduction: There is paucity of literature about periodic limb movements of sleep (PLMS) in children. This study was performed to evaluate the prevalence and correlates of PLMS detected on polysomnography (PSG) in children.
Methods: Data was extracted from PSGs performed at our accredited Pediatric Sleep Center from 2003 to 2006 to identify all patients with PLMS defined as movement index >5/hour. Patients´ clinical and PSG abnormalities were reviewed and correlated with PLMS.
Results: 982 PSGs were performed during the study period. PLMS were identified in 77 patients (7.9%). The age range was 1.5-18 years (mean 8.8) with 47 boys and 30 girls. Mean BMI was 22 (14-44). In 93.5% (72 of 77) PLMS were incidental on PSG without any history of sleep disturbances. The various clinical diagnoses where PLMS was an incidental finding included uncomplicated obstructive sleep apnea (n=36)), ADHD (n=10), migraines (n=7), narcolepsy (n=7), autism spectrum disorders (n=5), epilepsy (n=5), or miscellaneous (n=10). Only in 5 patients PLMs could be suspected because of symptoms suggestive of pediatric RLS.

PLM index ranged from 5-19.2/hour (mean 8.4) and PLM arousal index ranged from 0-7/hour (mean 3). Overall, 82% of patients had associated sleep disordered breathing. Mean sleep efficiency was 80% (35 to 97), mean snoring time 45.5 (0-86), mean arousal 31/h (0 to 62), total sleep time mean of 384 min (183 to 498), of which REM sleep constituted 16.3% (0 to 26.3) and stages III and IV 24.4% (12.9 to 48).

Serum ferritin levels were available on 34 patients. In 30 of them (80%) the levels were < 50 µg/ml. Twenty-five of the patients (33%) were on various medications.
Conclusion: In this biased population, the prevalence of PLMS was 7.9%. In most (93%), PLMS was an incident PSG finding. Prospective studies are necessary to clarify the significance of incidental PLMS.

0866

SLEEP LABORATORY EVALUATION OF PATIENTS WITH RESTLESS LEGS SYNDROME AUGMENTATION

Garcia-Borreguero D, Egatz R, Larrosa O
Sleep Research Institute, Madrid, Spain

Introduction: RLS augmentation is the main long-term complication of dopaminergic treatment in RLS. This is the first study to evaluate its sleep laboratory characteristics.
Methods: Thirty previously untreated patients with idiopathic RLS were treated for 12-18 months (mean: 16.4 months) with a mean dose of 240

mg/day L-DOPA. Severity of symptoms was evaluated before and every two months during treatment by means of the International RLS scale (IRLS)1. A blind rater evaluated patients every two months regarding augmentation. Patients underwent before and after treatment a suggested immobilization test (SIT) followed by an all-night polysomnographic study.
Results: a)Clinical: The sample included 30 patients (seventeen women), with a mean age of 55.1 years (+5,2 y). IRLS score improved in the overall group from 25.6(+3.2) to 11.1(+7.6) points at the end of treatment. 14 patients were classified as presenting AUG, while 16 had no AUG.
b)Polysomnography: At baseline, AUG presented a higher index of Periodic Leg Movement of Sleep (PLMS) (37.6+ 7.3 vs. 23.2+5.7) or of Wakefulness (PLMW) than N-AUG (both $p<.05$). Further, AUG presented a marginally higher sleep latency ($p=0.06$) and percentage of stage 1 sleep ($p=0.07$) than N-AUG. Following treatment, AUG presented an increased index of PLMS, PLMW, PLM-arousal index, sleep latency, as well asa lower Total Sleep Time and sleep efficiency (all $p<0.05$).
c)SIT: PLMW-index was higher in AUG than N-AUG, but no differences were seen in sensorial discomfort index (SDI) between groups. Following treatment, AUG presented showed a higher PLMW-index and SDI.
Conclusion: Polysomnographic changes during RLS augmentation are characterized by an increased number of PLMS and sleep fragmentation, and reflect a worsening of the condition. During SIT, patients undergoing augmentation suffered a more pronounced aggravation of periodic leg movements than of sensorial discomfort, suggesting that long term treatment with L-DOPA might primarily result in motor disturbance.
Support (optional): N/A

0867

PREVALENCE OF RESTLESS LEGS SYMPTOM AND GROWING PAIN AMONG PRIMARY SCHOOL CHILDREN IN JAPAN

Oka Y,[1] Suzuki S,[2] Inoue Y[1]
(1) Japan Somnology Center, Neuropsychiatric Research Institute, Tokyo, Japan, (2) Osaka Medical College, Takatsuki, Japan

Introduction: Prevalence of restless legs syndrome (RLS) in children has not been well defined especially among the Asian population. It has been suggested that growing pain is closely related to RLS, but this correlation has also not been elucidated in Asia. The aim of the study was to investigate the prevalence of restless legs symptom and growing pain among Japanese children.
Methods: The study was conducted at a primary school located in the suburbs of the second largest city of Japan. RLS/PLMD Pediatric Screening Questionnaire (RPSQ) was given to all students of the school and was filled out by the parents or caregivers. 506 subjects (252 males, 254 females, mean age : 9.0 SD 1.8) who responded to the questionnaire properly (response rate : 86.9%) were included in the analysis. Presence of restless legs symptom or growing pain was judged when the symptom occurred more than once a week, then each prevalence was estimated.
Results: Restless legs symptom was present in 18 students (3.6%). Growing pain was seen in 36 students (7.1%), and was noted in 61.1% of students with restless legs symptom. Family history of RLS was present in 11.1% of students with restless legs symptom and 25.0% of students with growing pains, while family history of RLS was noted in 5.8% of students with neither restless legs symptom nor growing pain. 22.2% of students with restless legs symptom were reported by the parents to be hyperactive, while hyperactivity was seen in 5.8% of students without restless legs symptom.
Conclusion: Restless legs symptom was closely related to growing pain and hyperactivity. Although there may be a limitation of the questionnaire survey by the parental report, there was a strong family history of RLS among students with restless legs symptom and growing pain.

0868

CHANGE OF PERIODIC LIMB MOVEMENT INDEX AFTER CPAP TREATMENT OF OBSTRUCTIVE SLEEP APNEA EXACERBATE WITH INCREASING AGE

Oka Y,[1] Inoue Y[2]
(1) Japan Somnology Center, Neuropsychiatric Research Institute, Tokyo, Japan, (2) Japan Somnology Center, Neuropsychiatric Research Institute, Japan

Introduction: Periodic limb movement in sleep (PLMS) are often seen concurrently in patients with obstructive sleep apnea syndrome (OSAS), and it has been reported that PLM index (PLMI) increase after CPAP treatment especially in severe OSAS patients. PLMS is known to be prevalent among elderly population, but the age effect on the change of PLMI after CPAP treatment has not been identified. The aim of our study was to compare the change of PLMI after CPAP treatment among different age groups.
Methods: 330 consecutive OSAS patients (313 males, 17 females) who underwent both baseline polysomnography (PSG) and CPAP titration PSG were included in the study. Positive PLMI increase was judged when 1) PLMI was below 15/hr at baseline PSG and increased above 15/hr at CPAP titration or 2) PLMI was above 15/hr at baseline PSG and increased more than 50% at CPAP titration. Patients were divided into three groups: young (below 40 years of age, n=97), middle aged (40-60 years of age, n=175) and elderly (above 60 years of age, n=58). Severity of OSAS was determined by the AHI; severe OSAS (AHI of more than 30/hr, n=244) and mild-moderate OSAS (AHI of 10-30/hr, n=86). Percentage of patients with positive PLMI increase was compared between severe and mild-moderate OSAS, and also among the three age groups.
Results: 39 patients (11.8%) showed positive PLMI increase at CPAP titration. Percentage of patients with PLMI increase was significantly higher in severe OSAS (15.2%) than in mild-moderate OSAS (2.3%). Percentage of patients with PLMI increase was also significantly different among the young group (6.2%), the middle aged group (10.9%) and the elderly group (24.1%). Moreover, in severe OSAS, PLMI increase was most remarkable in the elderly group.
Conclusion: Increase of PLMI after CPAP treatment of OSA was more frequent in patients with severe OSAS, and there was a significant age effect on the change of PLMI.

0869

HYPERTENSION RISK AND PLMS IN RESTLESS LEGS SYNDROME

Billars L,[1] Hicks A,[2] Bliwise D,[1] Sigmundsson T,[3] Sigurdsson A,[2] Kristjansson K,[2] Gulcher J,[2] Stefansson K,[4] Rye D[1]
(1) Emory University, Atlanta, GA, USA, (2) Iceland, (3) Landspitalinn, Reykjavik, Iceland, (4) AE (Europe), Iceland

Introduction: Sleep restriction and pathological sleep inclusive of Restless Legs Syndrome (RLS) have been associated with increased risks for hypertension and cardiovascular disease. For RLS these associations remain speculative because they derive from self-report and have not yet been linked to a physiological parameter of increased

sympathetic drive as have periodic leg movements of sleep (PLMs). To advance understanding of the pathophysiology and clinical impact of RLS we examined the correlates of hypertension in an Icelandic cohort (n=861) enriched for RLS.
Methods: Subjects and family members (n=861) were recruited from an advertisement describing RLS and provided clinical data that included mean PLMs/hr collected over 2-5 nights with a validated, tri-axial accelerometer (PAM-RL, IM Systems, Baltimore, MD). We examined age (dichotomized as > 51; median = 52.4), gender, Body Mass Index (kg/m2) (> 26.0; median = 25.9) and mean PLMs as cross-sectional predictors of hypertensive status.
Results: Likelihood of hypertension increased with PLMs severity; 50% in subjects with PLMs > 30/hr. Multivariate logistic regression demonstrated that older age (OR = 4.37; 3.11-6.13) and greater BMI (OR= 1.96; 1.41-2.71) predicted hypertension status. PLMs were associated with hypertension status, independent of age and BMI; the risk being over twice as high for those with PLMs > 30/hr (OR=2.26; 1.28-3.99). In 267 subjects meeting the most stringent criteria for RLS diagnosis, hypertension status was unrelated to disease duration or severity (IRLSSG rating scale).
Conclusion: Our results confirm and extend converging lines of evidence demonstrating relationships between PLMs, increased sympathetic drive, and hypertension. Causality is difficult to establish in such a cross-sectional study. Our findings nonetheless suggest that the clinical significance of PLMs may well extend beyond debates about sleep disruption and sleepiness. Their elimination could represent an independent goal of treatment in RLS, particularly in hypertensive subjects or in those with other cardiovascular risk factors.

0870

LONGITUDINAL ASSESSMENT OF NEUROPSYCHOLOGICAL FUNCTIONS IN PATIENTS WITH IDIOPATHIC REM SLEEP BEHAVIOR DISORDER (RBD)

Farini E,[1] Fantini M,[1] Ortelli P,[2] Zucconi M,[1] Manconi M,[1] Oldani A,[1] Cappa S,[2] Ferini-Strambi L[1]
(1) Sleep Disorder Center, Università Vita-Salute San Raffaele, Milan, Milan, Italy, (2) Departement of Neurology and Neurorehabilitation, Università Vita-Salute San Raffaele, Milan, Milan, Italy

Introduction: Some neuropsychological deficits, namely a visuo-spatial constructional dysfunction and visuo-spatial learning impairment, have been observed in idiopathic RBD (Ferini-Strambi *et al.*, 2004). No study assessed the longitudinal course of these deficits. The aim of this study was to prospectically assess the neuropsychological functions in a cohort of patients with idiopathic RBD.
Methods: A total of 23 patients diagnosed with idiopathic RBD according to the ICSD-2 criteria entered the study (17 M e 6 F; mean age:68.9±7.3 yrs., mean duration of symptoms:7.7±7.3 yrs., mean education:8.6±3.4yrs). All patients underwent to a standard neurological examination including the motor scale of Unified Parkinson Disease Rating Scale (UPDRS III) and to an extensive neuropsychological evaluation assessing a broad range of cognitive functions. Following the first evaluation, patients were reassessed after an interval ranging from 21.3 to 43.6 months.
Results: After a mean period of 26.5±6.1 months, 6(26%) patients developed signs and symptoms of parkinsonism, fulfilling the diagnosis of definite PD (n=1), probable PD (n=3) and possible PD (n=2), according to Calne´s criteria. In seventeen patients RBD remains idiopathic (mean UPDRSIII score: 4.7±3.4). In the whole group, significant worsening in several neuropsychological functions was observed, namely verbal logical memory (Story Recall Test: 9.7±5.0 vs.7.6±3.7;p=0.01), visuo-spatial short term memory (Corsi Block-Tapping Task: 5.3±1.3 vs. 4.7±0.9;p=0.02) and visuo-spatial learning (Corsi Supraspan Test: 12.2±3.5 vs.9.1±2.2;p=0.04). When only RBD patients free of neurological signs were considered (idiopathic RBD, n=17), neuropsychological testing still showed significant worsening in visuo-spatial short term memory (Corsi Test:: 5.4±1.5 vs.4.8±1.0;p=0.05) and in visuo-spatial learning (Corsi Supraspan Test: 13.2±3.9 vs.8.9±2.2; p=0.03). A worsening in executive function and non-verbal reasoning (Raven Test: 31.9±5.5 vs.29.8±5.9; p=0.02) was also observed, as well as a trend toward a worsening in verbal logical memory (Story Recall Task: 9.6±5.8vs.7.7±4.1; p=0.07). No differences were found in other neuropsicological measures, such as visual selective attention (Attentive Matrices), inhibition and selective attention (Stroop Color Word Interference Test), cognitive set shifting (Trail Making Test A and B) and verbal production abilities (verbal fluency with phonemic and semantic cues).
Conclusion: Several neuropsychological functions, particularly visuo-spatial abilities, showed a significant deterioration over time in idiopathic RBD patients, regardless the eventual emergence of extrapyramidal signs. Future studies including a control group will assess the exact extent of the cognitive decline in idiopathic RBD patients.

0871

THE PHARMACOLOGICAL TREATMENT FOR UREMIC-ASSOCIATED RESTLESS LEGS SYNDROME: SYSTEMATIC REVIEW

Oliveira M,[1] Conti C,[2] Valbuza J,[3] Capobianco D,[4] Andriolo R,[5] Atallah A,[6] Carvalho L,[7] Prado L,[7] Prado G[8]
(1) Federal University of Sao Paulo, São Paulo, Brazil, (2) Federal University of Sao Paulo, Sao Paulo, Brazil, (3) Federal University of Sao Paulo - Brazil, Sao Paulo, Brazil, (4) Universidade Federal de São Paulo, Brazil, (5) Federal University of Sao Paulo - Brazil, Sao Paulo, Brazil, (6) Federal University of Sao Paulo, Brazil, (7) Federal University of Sao Paulo, Sao Paulo, Brazil, (8) Federal University of São Paulo, São paulo, Brazil

Introduction: Restless Legs Syndrome (RLS) is a sensory motor disorder characterized by a distressing urge to move the legs and sometimes also other parts of the body usually accompanied by a marked sense of discomfort or pain in the legs or other affected body part. Patients under dialisys are specially at risk for RLS with a estimated prevalence of 6.6% to 21.5%. The treatment for uremic RLS has been controvertial thus a systematic synthesis of evidence is necessary to evaluate the effectiveness and safety of treatment for uremic RLS.
Methods: Systematic review of randomized or quasi-randomized, double blind trials on treatment for uremic RLS. Outcomes: relief of restless legs symptoms marked on a validated scale, subjective sleep quality, sleep quality measured by night polysomnography and actigraphy, quality of life measured by subjective measures, adverse events associated with the treatments.
Results: Six eligible clinical trials were included. The subjective analyses of these studies showed controversial results, although the objective analyses showed in one trial that treatment group had a statistically significant improvement of periodic leg movement during time asleep (PLM). Combined analyses (metanalysis) was not done. The most commonly adverse event seen was gastrointestinal symptoms.
Conclusion: Only a few therapeutic trials in uremic patients with RLS have been published, and there is no high level scientific evidence of a specific therapeutic regimen for uremic-associated RLS, and recommendations for practice can be done based on both individual trials results on uremic and non-uremic RLS patients and physician experience yet.

0872

EFFECTS OF CIRCADIAN RHYTHMS ON (NON-)EPILEPTIC SEIZURES

De Weerd A,[1] Van Leeuwen R,[2] Grootemarsink B[2]
(1) Sleepcenter SEIN Zwolle, Netherlands, Zwolle, Overijssel, Netherlands, (2) Sleepcenter SEIN Zwolle, Zwolle, Overijssel, Netherlands

Introduction: Evidence that the occurrence of seizures is influenced by the circadian rhythm, is limited. Our aim was to describe the pattern of appearance of (pseudo) epileptic seizures over the 24 hour day.
Methods: All patients with focal seizures during a 24 hours EEG/videoregistration, seen over a period of 3 years were included. They were divided in two groups: children in the age 2 to 15 years and adults. We noted the origin and classification of the epileptic seizures and the moment of occurrence during the day. Sleepstages were determined for seizures during sleep.
Results: In 182 patients (106 children and 76 adults) we recorded 939 seizures, of which 120 pseudo epileptic. Of the 606 epileptic seizures in children, 24% occurred during sleep (12 REM, 70 I/II, 62 III/IV); of the 213 epileptic seizures in adults, 27% occurred during sleep (1 REM, 47 I/II, 10 III/IV). Pseudo-seizures were seen only during daytime. Repeated measures analysis of variance revealed that: (1) the highest prevalence of seizures (>35%) is between 14.00-20.00 hrs, (2) predilection for this time window was seen for the various seizure types and origin of the seizures, except for frontal seizures in adults which mostly occurred during the night.
Conclusion: In 182 patients (106 children and 76 adults) we recorded 939 seizures, of which 120 pseudo epileptic. Of the 606 epileptic seizures in children, 24% occurred during sleep (12 REM, 70 I/II, 62 III/IV); of the 213 epileptic seizures in adults, 27% occurred during sleep (1 REM, 47 I/II, 10 III/IV). Pseudo-seizures were seen only during daytime. Repeated measures analysis of variance revealed that: (1) the highest prevalence of seizures (>35%) is between 14.00-20.00 hrs, (2) predilection for this time window was seen for the various seizure types and origin of the seizures, except for frontal seizures in adults which mostly occurred during the night.

0873

TRAUMATIC BRAIN INJURY, FATIGUE, AND SLEEP

Aurora R,[1] Ashman T,[2] Ginsberg A,[2] Mayer D,[2] Wieber S,[2] Greenwald B[2]
(1) Mount Sinai Medical Center, Center for Sleep Medicine, New York, NY, USA, (2) Mount Sinai School of Medicine, NY, USA

Introduction: Sleep-related complaints, excessive daytime sleepiness (EDS), and fatigue are common after traumatic brain injury (TBI). The cause for EDS and fatigue in patients with TBI is likely complex and multi-factorial. Nocturnal sleep disturbance and ensuing daytime impairment may persist long after the initial event. Although self-reported sleep disturbance in patients with TBI has been previously reported, there is a paucity of objective measures of sleep quality and daytime sleepiness. The objective of this study was to characterize nocturnal sleep quality and daytime sleep tendency in TBI patients.
Methods: Patients (N=9) with a prior history of TBI were recruited for overnight polysomnography and multiple sleep latency testing (MSLT). Inclusion criteria included a BMI<30 kg/m2 and a period of at least 12 months since the injury. Assessments included the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI) and Global Fatigue Index (GFI).
Results: The study sample consisted of five men and four women. The age range was 24-53years. The average BMI was 26.2kg/m2. The median time from injury was seven years. The median ESS score was nine, the median PSQI score was 8, and the median GFI was 31. Polysomnography revealed a median sleep efficiency of 90.7%. Sleep architecture showed that the median amounts of stage 1, 2, slow wave, and REM sleep were 1.9%, 32.5%, 43.8%, and 18.0%, respectively. The median arousal index was 9.8 events/hr. Results of the MSLT showed a median time of 10.7 minutes for sleep onset. Five patients had an MSLT < 10 min. Two subjects were diagnosed with narcolepsy, one with mild sleep apnea, three had an elevated periodic leg movement index (>5/hr).
Conclusion: The results of this cross-sectional study show that TBI patients may suffer from subjective complaints of fatigue and poor nocturnal sleep but manifest relatively normal sleep architecture and daytime sleep tendency.

0874

SPECTRUM OF POLYSOMNOGRAPHIC ABNORMALITIES IN CHILDREN WITH EPILEPSY

Cruz M,[1] Valencia I,[2] Adams R,[2] Khurana D,[2] Legido A,[2] Kothare S[2]
(1) St. Christopher's Hospital for Children, Philadelphia, PA, USA, (2) St. Christopher's Hospital for Children, PA, USA

Introduction: The magnitude of sleep disorders in children with epilepsy is under-recognized. At the same time, lack of adequate sleep by itself may worsen seizure control. In addition, antiepileptic medications may alter sleep patterns. The purpose of this retrospective analysis was to evaluate various abnormalities seen on polysomnography (PSG) in a cohort of patients with epilepsy.
Methods: Retrospective analysis included 40 children with epilepsy who had PSGs performed for various sleep complaints. Analysis included sleep variables from the PSG, BMI´s, presence of developmental delay (DD), anti epileptic drugs (AED), type of epilepsy, and seizure control. These were compared to 14 controls from our sleep laboratory.
Results: There were 19 females and 21 males; mean age 9.89±4.9 years, and mean BMI of 22.5±7.7. Patients with epilepsy had a higher relative snoring time (49.6 Vs. 1.36, p=0.0001) and a higher arousal index (23.7 Vs.14.8, p=0.001) than patients from the control group. Thirty four patients (85%) had sleep disorder breathing [snoring 17 (42.5%), obstructive hypoventilation 5 (12.5%), obstructive sleep apnea 4 (20%) and upper airway resistance syndrome 3 (7.5%)], and four (10%) patients had periodic limb movement. No major sleep architectural abnormalities were observed when controlling for DD, epilepsy type, or changes in BMI (>25 or <25). It was noted that REM sleep was decreased in patients with better seizure control, (r=-0.33, p=0.046) unrelated to AED use. One patient had two brief generalized tonic seizures in non-REM sleep. There was an increase in the mean sleep time by 30 minutes with patients on AED´s.
Conclusion: Our study suggests that sleep difficulties in children with epilepsy are independent of seizure treatment, presence of DD or BMI, suggesting that epilepsy may be an independent contributing factor for sleep problems in these children.

0875

POLYSOMNOGRAPHIC ABNORMALITIES IN PATIENTS WITH ADHD WITH DIVERSE SLEEP PROBLEMS.

Cruz M,[1] Valencia I,[2] Adams R,[2] Hardison H,[2] Marks H,[2] Khurana D,[2] Legido A,[2] Kothare S[2]
(1) St. Christopher's Hospital for Children, Philadelphia, PA, USA, (2) St. Christopher's Hospital for Children, PA, USA

Introduction: Attention deficit hyperactivity disorder (ADHD) is a common childhood illness with a prevalence of 3-16%. As many as 77% of patients with ADHD may have disturbed sleep patterns including bed

time resistance. There is little experience regarding the polysomnographic (PSG) findings in these patients. The objective of this study is to assess the extent of these abnormalities in patients with ADHD who were referred to our sleep laboratory to rule out sleep disordered breathing or to assess the cause of frequent arousals out of sleep.
Methods: We retrospectively analyzed the PSG data of 33 patients (26 males, 7 females), ages (3-16 years) with the diagnosis of ADHD. The PSG data was compared to 14 normal controls from our sleep laboratory.
Results: Sixteen of the 33 patients (48%) were on medication for the ADHD. ADHD patients had decreased sleep efficiency (mean 81.7 %, range 45-99% versus 89.3 %, range 80-97% in the control group, p= 0.037). There were no major sleep architectural abnormalities except for increased arousal index (mean of 26/hr, range 0.5-40/hr versus 14/hr, range 3-23/hr in the control group p< 0.01). Wake after sleep onset (WASO) was increased (mean of 57min, average 2-277min versus 22 min, range 6-98 min in the control group p=0.01). Snoring was increased in patients with ADHD (mean 41.8% of total sleep time, range 0.0-96% versus 1.3 %, range 0.0-8% in the control group P< 0.01). Eight patients (24%) had the diagnosis of obstructive sleep apnea, 10 (30%) had periodic limb movement disorder (PLMD), 8 (24%) had Upper Airway Resistance Syndrome, 5 (15%) had obstructive hypoventilation. One patient had confusional arousals during the sleep study.
Conclusion: There were no differences in variables between patients who were receiving treatment for ADHD versus the ones who were not. Physicians should be aware that beside behavioral sleep issues, sleep disordered breathing and PLMD are prevalent in patients with ADHD.

0876

TREATING OBSTRUCTIVE SLEEP APNEA IN EPILEPSY: EXPERIENCE FROM A PILOT MULTICENTER RANDOMIZED TRIAL

Malow B,[1] Foldvary-Schaefer N,[2] Vaughn B,[3] Chervin R,[4] Selwa L,[5] Weatherwax K[5]
(1) Vanderbilt University, Nashville, TN, USA, (2) Cleveland Clinic Foundation, OH, USA, (3) University of North Carolina at Chapel Hill, NC, USA, (4) University of Michigan, Ann Arbor, MI, USA, (5) University of Michigan, MI, USA

Introduction: Treatment of obstructive sleep apnea (OSA) in patients with epilepsy appears to improve seizure control and daytime sleepiness, although studies have been small and non-controlled. The goal of this pilot study was to refine design issues prior to embarking on a Phase III Trial of treating OSA in patients with epilepsy.
Methods: Adults with refractory epilepsy (2 or more seizures per month) were enrolled into the trial if they met study criteria, including a history suggestive of OSA. After polysomnography (PSG) confirmed OSA, subjects were randomized to treatment with either therapeutic or sham continuous positive airway pressure (CPAP). Subjects were maintained on stable doses of antiepileptic medications and CPAP adherence was monitored with electronic cards.
Results: Of 43 subjects undergoing PSG, 35 met criteria for OSA, defined by an apnea-hypopnea index (AHI) of 5 or more events per hour (81% true positive rate). The first night of PSG appeared sufficient for diagnosing OSA, with only one subject having OSA on night 2 (AHI 5.8) but not on night 1 (AHI 3). Twenty-two were randomized to therapeutic CPAP (with 19 completers) and 13 to sham CPAP (all completed the trial). Adherence was similar in the therapeutic and sham groups (71.8% of nights, 4.4 hours per night) and significantly higher in adults ages 45 or older (5.4 hours, p = 0.01 by independent two-tailed t-test). Subjects, coordinators, and PIs were not able to distinguish therapeutic from sham CPAP (kappa values < 0.40). A 50% or greater reduction in seizures was observed in 32% of the subjects in the therapeutic group as compared to 15% of those in the sham group.
Conclusion: Treatment of obstructive sleep apnea in epilepsy appears promising in reducing seizure frequency, and a Phase III randomized multicenter clinical trial employing therapeutic and sham CPAP appears feasible.
Support (optional): NINDS R01 NS42698 and the General Clinical Research Centers at University of Michigan (M01 RR00042), University of North Carolina-Chapel Hill (RR00146) and Vanderbilt University (M01RR-00095).

0877

SLEEP COMPLAINTS AND SLEEP DISORDERED BREATHING IN PATIENTS WITH EPILEPSY: CLINICAL HISTORY AND POLYSOMNOGRAPHIC COMPARISON WITH NON-EPILEPSY PATIENTS PRESENTING AT A SLEEP DISORDERS CENTER. A RETROSPECTIVE STUDY.

Liebman R, Rodriguez A
New York University, New York, NY, USA

Introduction: Sleeping difficulties are common in patients with epilepsy. Specifically, several studies have found a high incidence of sleep disordered breathing, in the form of obstructive sleep apnea (OSA), and complaints of insomnia among epilepsy patients when compared to normal controls. Whether OSA and/or sleep complaints, particularly insomnia, have a higher incidence among epilepsy patients than non-epilepsy patients seen at a sleep disorders center is unknown.
Methods: A retrospective chart review was conducted on all patients age 18 years and older, seen for consultation at the New York Sleep Institute over a 5 month period. A total of 111 patients were included (39 epilepsy, 72 controls). Among these patients, eighty-one (28 epilepsy, 53 controls) had a Polysomnogram (PSG) due to suspicion of OSA. All data were derived from the initial consultation and PSG results, both of which were reported by a Board Certified Sleep Specialist.
Results: Difficulty falling asleep was a significantly more common complaint in the epilepsy group (56% epilepsy, 26% controls, p = 0.0014). Complaints of EDS, snoring, difficulty staying asleep, un-refreshing sleep and restlessness in legs were similar between the groups.

After the PSG was conducted, OSA was found to be equally prevalent in both groups (75% controls vs. 68% epilepsy). However, the control group had higher values for the AHI (31.3 controls vs. 17.5 epilepsy, p= 0.016). There was no difference in sleep latency, sleep efficiency and periodic limb movement index. BMI and most co-morbidities - hypertension was more common in the control group – were similar between the two groups.
Conclusion: While difficulty falling asleep is a more common complaint in patients with epilepsy compared to non-epilepsy controls, the rate of OSA is similar between these two groups seen at a sleep disorders center.
Support (optional): none

0878

DOES INTRAMUSCULAR INTERFERON ß-1A INFLUENCE DAYTIME SLEEPINESS AND FATIGUE IN RELAPSING REMITTING MULTIPLE SCLEROSIS (RRMS) A FOLLOW-UP INVESTIGATION DURING 24-MONTHTHERAPY

Kotterba S,[1] Sindern E,[2] Lange S,[1] Gerhard R,[1] Stueckle K[1]
(1) Bochum, Germany, (2) Friedrikenstift Hannover, Hannover, Germany

Introduction: Fatigue and daytime sleepiness are complained by up to 80% in MS patients. The Expanded Disability Status Scale (EDSS) assesses disease progression. The MS Functional Composite (MSFC) allows assessment of physical and cognitive function. The present study investigates the influence of interferon ß-1a (AVONEX[R]) on fatigue, sleepiness, physical and cognitive functions in patients with RRMS.
Methods: 42 RRMS-patients (18 men, 24 women, age: 33.3 ± 9.3 years) and 22 healthy controls (4 men, 18 women, age: 27.6 ± 5.2 years) were evaluated with the following instruments:
· EDSS
· MSFC: ambulation (timed 25 Foot Walk), arm function (9 Hole Peg Test) and cognitive function (Paced Auditory Serial Addition Test-PASAT)
· Fatigue Severity Scale (FSS by Krupp *et al.*)
· Epworth Sleepiness Scale (ESS)

Baseline investigations were completed before therapy was initiated. Patients and controls underwent follow-up testing every 6 months up to 2 years.
Results: EDSS decreased after 12 months (1.8 ± 1.0 vs. 0.7 ± 0.9, p<0.008). PASAT results improved continuously (42.7 ± 14.0 vs. 45.8 ± 12.3 (month 12), 51.6 ± 8.0 (month 24) p < 0.05).
Scores on the FSS (increased in 45%) decreased in patients towards values of controls (35.1 ± 15.1 at baseline and 30.6 + 17.4 at 24 months). ESS-scores in MS decreased in patients (6.7 ± 3.5 baseline vs. 5.5 ± 3.3, month 24). After 24 months of treatment, FSS correlated with improved ambulation (p<0.02) and arm function (p< 0.001). No significant change of all scores in controls.
Conclusion: The present study demonstrates a decrease in fatigue and sleepiness in RRMS over 24 months of AVONEX [R] therapy. As decreases in fatigue correlated with MSFC results this symptom seems to be related to demyelisation. AVONEX [R] may be an additional treatment of fatigue in MS.
Support (optional): Supported by grants from BIOGEN Idec, Germany.

0879

EEG SPECTRAL ANALYSIS IN WAKEFULNESS, REM AND NREM SLEEP FOLLOWING SPORT-RELATED CONCUSSIONS

Gosselin N,[1] Lassonde M,[2] Petit D,[1] Leclerc S,[2] Mongrain V,[1] Montplaisir J[1]
(1) Sacre-Coeur Hospital, Montreal, Quebec, Canada, (2) University of Montreal, Montreal, Quebec, Canada

Introduction: Athletes who sustain concussions generally suffer cognitive and neurobehavioral symptoms in the hours, weeks, or sometimes months, following their injury. Sleep and vigilance disorders are amongst the most reported symptoms; however, no polysomnographic study has been done in this population. The aim of this study was thus to investigate the effects of sport-related concussions on sleep architecture and on quantitative EEG (QEEG) in wakefulness, REM and NREM sleep.
Methods: Ten athletes who experienced at least one concussion during the last year (total history of 4.6 ± 2.1 concussions) and 11 non-concussed athletes were recorded for two consecutive nights in the laboratory and during a 10-minute period of wakefulness the next morning. They completed the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale. Spectral analysis (Fast Fourier transforms) of the EEG recorded during wakefulness, REM and NREM sleep was performed. Nighttime course of delta activity was also determined by using a nonlinear regression analysis on all-night NREM sleep. Group differences were measured with Student t-tests and analyses of variance.
Results: Concussed athletes reported worse sleep quality and more daytime dysfunctions than control athletes (p<0.01). These athletes had significantly more delta activity during wakefulness (p<0.01) and less alpha activity in comparison with controls (p<0.05). Their subjective sleep quality and daytime dysfunctions cannot be attributed to disturbed sleep, because no between-group difference was found on any polysomnographic variable or on sleep QEEG variables. Moreover, no group difference was obtained for the delta activity dissipation.
Conclusion: Concussions in athletes were associated with abnormal waking EEG and these anomalies may be associated with the daytime dysfunctions reported by these athletes. In spite of their subjective complaints in sleep quality, no change was observed in sleep parameters and in sleep QEEG. Sport-related concussions are thus associated with wakefulness problems rather than sleep disorders.
Support (optional): This research was supported by the Canadian Institutes of Health Research (J.M. and N.G.), by the Fonds pour la Recherche en Santé du Québec (M.L. and N.G.) and by the Natural Sciences and Engineering Research Council of Canada (V.M).

0880

ELEVATED PEM (PHASIC ELECTROMYOGRAPHIC METRIC) RATES IN RAPID EYE MOVEMENT BEHAVIOR DISORDER (REMBD) ON NIGHTS WITHOUT BEHAVIORAL ABNORMALITIES

Bliwise D,[1] Rye D[2]
(1) Emory University, Atlanta, GA, USA, (2) Emory, Atlanta, GA, USA

Introduction: Confirming the diagnosis of REMBD is challenging when pts with compelling history do not show dream enactment behaviors while undergoing polysomnography (PSG). Alternatively, PSG can be examined for elevated EMG, but diverse measurement approaches exist. We describe here the application of a PEM (Phasic Electromyographic Metric) (1) in REMBD patients.
Methods: All pts (X age 68.5, SD = 10.6; 9 men, 2 women) demonstrated histories compatible with REMBD. None met criteria for Parkinson´s Disease. All had histories of dream-enactment (X duration = 6.9 years (range 1 to 15). Only 3 used psychotropics. REM sleep occurred in 9 of the PSGs. In only 1 case did dream enactment behaviors occur during polysomnography. PEM activity was scored following criteria defined previously (1). Controls were elderly subjects of comparable age without PLMS for whom normative data have been published previously (1). PEM derived from REM and NREM separately for 5 sites: mentalis, L/R brachioradialis, and L/R anterior tibialis.
Results: PEM rates (% of 2.5 second intervals with phasic activity) for mentalis in both REM and NREM sleep were significantly higher in REMBD relative to Controls (for REM, 20.0 [11.8] vs 3.5 [4.1], t = 4.13, p < .005; for NREM, 5.3 [4.7] vs 1.7 [1.6], t = 2.50, p < .05). Exclusion of cases receiving psychotropics or with explicit dream-enactment did not influence results. Statistically significant differences were also seen for anterior tibialis and brachioradialis in both REM and NREM sleep.
Conclusion: In the absence of overt dream-enactment behaviors, PEM in REM sleep, and to lesser extent, NREM sleep characterize motor

system activation in non-PD patients. These data are compatible with a hypothesized caudal-to-rostral course of broadly defined Lewy Body Disease described neuropathologically by Braak and others.
Reference: (1) Bliwise et al, J Clin Neurophysiol 2006; 23: 59-67
Support (optional): NS-050595

0881

HYPOCRETIN-1 IS INVERSELY ASSOCIATED WITH WAKE FRAGMENTATION IN ALZHEIMER´S DISEASE

Zeitzer J,[1] Friedman L,[1] Lin L,[2] Mignot E,[1] Peskind E,[3] Yesavage J[4]
(1) Stanford University, Palo Alto, CA, USA, (2) Center for Narcolepsy, Stanford University, CA, Palo Alto, CA, USA, (3) University of Washington, Seattle, WA, USA, (4) Stanford University, Stanford, CA, USA

Introduction: Sleep disruption is commonly observed in individuals with Alzheimer´s disease (AD). The biological basis of this disruption is unknown, but may be related to the degeneration of cholinergic neurons. Hypocretin-1 is a peptide involved in the consolidation of wake and projects to many of the same cortical sites as cholinergic fibers. Because of this, we hypothesized that in AD, hypocretin-1 might compensate for the loss of cholinergic tone in AD.
Methods: Fifteen individuals diagnosed with AD had lumbar CSF collected (analyzed for hypocretin-1 concentrations) and seven days of ambulatory actigraphy data with accompanying sleep logs, completed by a caregiver. Data were analyzed for fragmentation of both daytime wake and nighttime sleep.
Results: Lumbar CSF hypocretin-1 concentrations were 417 ± 44.2 pg/mL. There was a linear correlation between the number of daily naps and hypocretin-1 concentrations ($r=-0.64$, $p<0.05$), as well as between the total amount of daily nap time and hypocretin-1 concentrations ($r=0.62$, $p<0.05$). The average nap length was not associated with hypocretin-1 concentrations ($r=0.004$, $p=0.99$). There were no correlations between hypocretin-1 concentrations and any of our measures of nocturnal sleep fragmentation (r-values between -0.3 and 0.37, p-values>0.15, n=14). The daily amplitude of actigraphy data was negatively correlated with the number of naps ($r=-0.84$, $p<0.001$) and the total time spent napping ($r=0.77$, $p<0.001$), and positively correlated with hypocretin-1 concentrations ($r=0.63$, $p<0.05$).
Conclusion: Although lumbar CSF concentrations of hypocretin-1 were in the normal range in AD, they were inversely correlated with fragmentation of daytime wakefulness. Thus, the greater the fragmentation (i.e., more naps), the lower the hypocretin-1 concentrations. It may be that individuals with naturally higher levels of hypocretin-1 may be better able to compensate for the loss of cholinergic fibers and maintain a greater consolidation of daytime wakefulness.
Support (optional): P30 AG 17824, P50 AG05136, and NIH 23724 [NIH]; Medical Research Service of the Veterans Affairs Palo Alto Health Care System; Howard Hughes Medical Institute; Department of Veterans Affairs Sierra-Pacific and VA Northwest Network Mental Illness Research, Education, and Clinical Centers.

0882

NEUROLOGICAL SYNDROMES DETECTED FIRST IN AN OUTPATIENT SLEEP CLINIC

Fahed G,[1] Koo B,[2] Strohl K[1]
(1) Case Western Reserve University, Cleveland, OH, USA, (2) OK, USA

Introduction: Sleep problems and disorders are associated with many neurologic disorders, and often it is a neurologic diagnosis that results in a sleep referral. How often the reverse phenomenon, namely frequency and types of previously undiagnosed neurological problems or syndromes surfacing during the evaluation for sleep disorders, is unknown.
Methods: A case series review of 40 consecutive first-visit evaluations by residents and fellows of patients referred to a general sleep outpatient clinic were performed for evidence of new neurological syndrome detected by the examining physicians.
Results: All subjects were adult males; mean age 59.2 years. Presenting features for referral to sleep clinic were: hypersomnolence, sleep apnea, movement disorders, and nocturnal choking. The majority (85%) of the referrals were for evaluation of obstructive sleep apnea, the remaining being insomnia and sleep movement symptoms; all but one were referred from primary care; and in this series none had previously undergone formal evaluation for or had a diagnosis of a neurological disorder. After the initial examination, 4 patients (10%) were considered to have a previously undetected primary neurological disorder: dementia (two patients: both referred for insomnia), Parkinsonism (referred for REM-behavior disorder), and epilepsy (referred for parasomnia). These suspected syndromes were confirmed by a board-certified neurologist who is also a sleep specialist. Patients were then referred for specialty management. In addition we noted a non-uniform reporting of neurological examinations across all reviewed charts.
Conclusion: This small survey suggests that sleep clinicians and trainees should evaluate all patients for neurological syndromes. We believe that if a neurological diagnosis can be detected earlier, it would improve patient outcome. We propose that a focused history and physical examination for dementia, movement disorders, and possibly headache be a part of the routine reporting of a sleep disorder evaluation.
Support (optional): University Hospitals of Cleveland
Cleveland, OH

0883

TIME COURSE PREVALENCE OF SLEEP DISTURBANCES AND MOOD ALTERATIONS AFTER MILD TRAUMATIC BRAIN INJURY: A PRELIMINARY REPORT

Chaput G,[1] Lavigne G,[1] Paquet J,[2] Manzini C,[2] GiguèRe J,[2] Demers A,[2] Denis R[2]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) Hôpital du Sacré-Coeur de Montréal, Quebec, Canada

Introduction: Acute and persistent symptoms such as sleep disturbances, headaches, mood and cognitive alterations can appear following a mild traumatic head injury (MTBI). This retrospective study consisted of reviewing patient charts to determine the prevalence and time course of these symptoms.
Methods: Charts from 175 patients diagnosed with MTBI (by JF.G.) were reviewed for assessment of presence or absence of symptoms via the Rivermead Post-Concussion Symptom Assessment Questionnaire and self-report. Population characteristics were: 68.6% males vs. 31.4% female subjects with mean age of 48.9 (min 16 – max 93). Symptoms were assessed at two different time course intervals (interval 1 = mean 10.7 days (response rate: 75%) vs. interval 2 = mean 6.3 weeks (response rate: 56%) and controlled for presence pre-trauma symptoms. Chi square were calculated.
Results: For time intervals 1 and 2, complaints of sleep disturbances were reported by 11.1% and 34.7% ($p= 0.0001$) of patients; headaches 46.6% and 40.6% ($p= 0.37$); feeling depressed or teary-eyed 9.5% and 20.4% ($p= 0.02$); irritability 5.6% and 20.2% ($p= 0.089$); and subjective reduced ability to concentrate 18.8% and 31.3% ($p= 0.03$), respectively. The co-existence of sleep and headache symptoms was found to be

7.2% (x2:0.5) at time 1 and 19.6% at time 2 (x2:0.004). Sleep and headache complaints were present in only 1 and 4 patients prior to trauma, respectively.
Conclusion: There was a two to three time fold increase in the prevalence of sleep disturbances and mood alterations from time courses 1 to 2. Complaints of headache showed no significant change in prevalence in studied time intervals. Patients whom reported headaches were 3 times more likely to report concomitant sleep disturbances. We are currently reviewing charts of over 500 patients with assessment of one year follow-up.
Support (optional): (Supported by CIHR/Pain M2C Training grant and Trauma hospital funds)

0884

PREVALENCE AND PREDICTORS OF EXCESSIVE DAYTIME SLEEPINESS IN EPILEPSY

Foldvary-Schaefer N,[1] Bedford T,[2] Zahand Z,[3] Ginal S,[3] Podmore P[3]
(1) Cleveland, OH, USA, (2) Cleveland Clinic Foundation, Cleveland, OH, USA, (3) Cleveland Clinic Foundation, OH, USA

Introduction: Epilepsy is a common disorder affecting approximately 1% of the population and excessive daytime sleepiness (EDS) is the most common complaint among those affected. No study has compared subjective measures of EDS (self-report and the Epworth Sleepiness Scale, ESS) to the gold standard multiple sleep latency test (MSLT) or determined the impact of seizures and antiepileptic drugs (AEDs) on EDS in epilepsy patients with variable degrees of seizure control.
Methods: This is a cross-sectional study of adults with epilepsy presenting to a tertiary care clinic from April 2004 to September 2006. 111 subjects participated, representing 10% of the clinic population. Subjects completed a series of questionnaires and underwent an overnight PSG and MSLT. Mean monthly seizure frequency (SZ) for the 6 months prior to enrollment was used as a measure of seizure severity.
Results: Complete data were available for 92 cases (71.7% female). Mean age was 39.8 years (95%CI: 36.97, 42.59). Mean number of AEDs was 1.54 (95%CI: 1.39, 1.70). Mean SZ was 4.99 (95%CI: 3.12, 6.85). EDS was confirmed by self-report, ESS, and MSLT in 71.7, 37, and 62% of subjects, respectively. A model incorporating ESS, AHI, and SZ represented by the equation MSL=10.26904 + 0.02828(AHI) + 0.06355(SZ) – 0.32543(ESS) was predictive of MSL (p=0.04332). Self-reported EDS, age, gender, BMI, and number of AEDs were not significant predictors.
Conclusion: By all measures, EDS exceeds that previously reported in the epilepsy population. Self-reported EDS is not a reliable predictor of the MSLT, while the ESS is the best predictor of those studied. A model incorporating ESS, AHI, and SZ as predictors of MSL is proposed, suggesting that epilepsy severity and co morbid sleep apnea are important variables when assessing EDS in epilepsy patients.

0885

NOCTURNAL SEIZURES/PAROXYSMAL EVENTS AS REPORTED BY PATIENTS REFERRED TO A SLEEP CLINIC FOR DIFFERENTIAL DIAGNOSIS.

Silvestri R,[1] Arico' I,[2] Mento G,[2] Condurso R,[2] Gervasi G,[3] Pisani L[2]
(1) Sleep Medicine Center Messina Italy, Messina, Sicily, Italy, (2) Sleep Medicine Center Messina Medical School, Italy, (3) Sleep Medicine Center, Messina Medical School, Italy

Introduction: To assess the frequency, features, comorbidities and therapeuthic response of different nocturnal seizures reported to an outpatient Sleep Clinic over the last 6 monthes.
The reason for nocturnal seizures being rarely reported as primary diagnosis in a Sleep Center could depend on several factors: infrequent nocturnal expression, unclear differential diagnosis (DD) between seizures and sleep disorders, suspected role for comorbid SD (OSAS, PLMs, bruxism).
Methods: 21 patients (15 M, 6 F, mean age 35) seen over the last year at our Sleep Clinic with a referral of nocturnal paroxysmal episodes of probable ictal origin, underwent 1 or more nights of complete video-PSG with extended EEG montage. Recordings were read by 2 blind polysomnographists with EEG/epilepsy expertise. We did not include those patients whose episodes by history had clear-cut features of parasomnias or REM Behavior Disorders.
Results: 4/21 pts were known epileptics. Alleged nocturnal episodes were GTCS in 10, hypermotor seizures/paroxysmal arousals in 8, sensory-visceral episodes in 3. Typical events were recorded only in 7. In the remaining 12 pts. IEDs were right sided in 5, left in 5, rolandic bilateral in 2, mainly frontal in 5, posterior temporal in 8. Most frequent co-morbid SD were sleep breathing disorder (SDB, 5 pts), sleep related movement disorders (SRMD, 5 pts), ADHD (3 pts), cerebrovascular disorders (3 pts). Sleep was characteristically superficial and fragmented with high arousal and low sleep efficiency. A diagnosis for nocturnal epileptic seizures was reached in 13/21 pts. Other events had a DD of GERD, SRMD or panic attacks. In 8 pts AED monotherapy was started (LEV or TPM) with good therapeutic response.
Conclusion: GTCS and partial motor seizures/paroxysmal arousals were the most frequent type of seizures. Ictal events were infrequently detected and seldom contributory during diagnostic video-PSG. Co-morbidity with neurologic and SD is often the case and represents a confounding factor for DD. Nocturnal paroxysmal episodes show a good response to AED monotherapy expecially in young subjects independently of etiology.

0886

REM SLEEP DISTURBANCES IN HUNTINGTON DISEASE

Arnulf I,[1] Nielsen J,[2] Schiefer J,[3] Wild E,[4] Jennum P,[4] Konofal E,[5] Oudiette D,[6] Tabrizi S,[4] Durr A[7]
(1) Pitie-Salpetriere Hospital and Pierre and Marie Curie University, Paris, France, (2) Copenhagen University, Denmark, (3) University Hospital RWTH Aachen, Germany, (4) Institute of Neurology, Queen Square, London, United Kingdom, (5) University Pierre et Marie Curie Paris 6, Paris, France, (6) Pierre and marie Curie University, France, (7) Pitié-Salpetriere hospital and Pierre and marie Curie University, France

Introduction: Hypocretin deficiency, leading to daytime sleepiness and shortened REM sleep latency in narcolepsy, has recently been identified in the brains of patients with Huntington disease (HD) and in a transgenic animal model of HD. Daytime sleepiness and abnormal REM sleep have not been evaluated in patients with HD.
Methods: 25 patients with HD underwent clinical interview, night-time video/sleep monitoring, and daytime multiple sleep latency tests. Their results were compared with those of patients with narcolepsy and controls matched for age and sex.
Results: Two-thirds of patients with HD were insomniac, a complaint tending to increase with disease severity. Compared with controls, patients with HD (including pre-manifest carriers) had lower sleep efficiency, and delayed (164±85 min) and shortened (14±6% of total sleep time) REM sleep. Three patients (12%) with HD had REM sleep behavior disorders. In contrast to narcoleptic patients, patients with HD had no cataplexy, hypnagogic hallucinations and sleep paralysis, and no more daytime sleepiness than controls. The mean daytime sleep latencies were longer in the HD group (14.3±5.9 min) than in the narcolepsy group (4.3±3.1 min), and were abnormally low (<8 min) in 16% patients with HD versus 88% patients with narcolepsy. No patient

with HD had multiple sleep onset REM periods.
Conclusion: In HD, the absence of narcolepsy but occasional REM sleep behavior disorders and frequently reduced REM sleep suggest that mutant huntingtin exerts an effect on pontine REM sleep executive systems. REM sleep dysfunction, occurring early in the course of disease, may represent a marker of disease progression.

0887

STROKE PREVALENCE ACCORDING TO SEASONAL AND CIRCADIAN VARIATION IN A TROPICAL COUNTRY.

Ribeiro J, Fukujima M, Aguiar A, Marin L, Santos W, Carvalho L, Prado L, Prado G
Federal University of Sao Paulo, Sao Paulo, Brazil

Introduction: Several studies have shown seasonal and circadian variation on stroke onset with a moderate to high prevalence during the night or sleep period, but it is not known if there are differences among tropical and winter countries. Our aim is to analyze if seasons have influence on ischemic stroke onset concerning to seasons days of the week, and circadian variation, and also on stroke severity.
Methods: We retrospectively studied data collected from 185 ischemic stroke patients (86 men, 99 women, aged 30 to 92 years, mean age=62.9) from the Sao Paulo Hospital out-patient clinic, Sao Paulo, Brazil. All patients were randomly selected from other ongoing trial, so they had data collected systematically.
Results: There were 43 stroke occurrence in spring, 68 in summer, 29 in fall, and 45 in winter. From those strokes occurred in fall-winter, 28 (37.8%) presented its onset during sleep, and 46 (62.2%) when awoke. From those in spring-summer, 42 (37.8%) had onset during sleep, and 69 (62.2%) when awaked. Barthel Index was similar in both fall-winter group (mean 79.2) and spring-summer group (mean=80.1). Canadian Neurological Scale was also similar in both groups (fall-winter mean value 8.2; spring-summer mean value 8.2). In spite of apparent predominance of stroke onset on Mondays (41 patients, 22%), Kolmogorov-Smirnov test showed uniform distribution on the seven days of the week (p=0.175). Time of stroke onset was obtained in 81% of fall-winter group and in 80% of spring-summer group. It was divided into 6-hourly intervals. Kolmogorov-Smirnov test showed uniform distribution for the stroke onset time (p=0.964); Qui-square test showed no difference between seasonal groups (p=0.581).
Conclusion: It seems that tropical countries, where there are small changes in temperatures, do not have significant seasonal or circadian variation on stroke onset, neither on stroke severity. These results may have important clinical implications in ischemic stroke prevention.
Support (optional): UNITER-SONO

0888

RISK FACTORS FOR STROKE DURING SLEEP

Santos W,[1] Ribeiro J,[2] Marin L,[1] Carvalho L,[1] Prado L,[1] Fukujima M,[1] Prado G[1]
(1) Federal University of Sao Paulo, Sao Paulo, Brazil, (2) Federal University of Sao Paulo, Sao Paulo, Brazil

Introduction: The prevalence of heart attack during the night and early morning is already recognized, and it is suspected that stroke can also be more prevalent during that period. The aim of this study was to evaluate if risk factors for stroke during sleep are different from those associated to stroke while awaken.
Methods: We studied 576 patients with ischemic stroke, where 202 with stroke onset during sleep and 374 while the patients were awaken. All the selected patients were submitted to transesphageal echocardiogram, brain computed tomography and carotid Doppler. The patients selected to the study had no cardiac disease.
Results: Third five percent of the strokes occurred during sleep. There were no differences between the groups concerning to all analyzed risk factors. The risk factors analyzed were hypertension with a prevalence of 79% in the patients who had the stroke awaken (A group) and 82% in the sleep (S group) without statistical differences (p= 0.72). Diabetes mellitus with 26%in the A group and 29% in the S group(p=0.43).Previous cerebrovascular disease was present in 24% of A and in 22% of S group (p=0.57). The presence of coronary artery disease was 14% in the A and 12% S group(p=0.49). The habit of smoking was present in 36% of both groups (p=0.91).The alcoholism in the group A 14% and in S was 17%(p=0.37). The body mass index greater than 30 was present in 15% of A and in 18 of S group (p=0.28).
Conclusion: There was no particular risk factor for stroke during sleep. Conventional risk factors should be controlled to prevent stroke, but no specific factor for stroke during sleep were detected. Stroke has been associated to arrhythmias and sleep apnea, but in this study patients with any cardiac disease were excluded previously, and they do not have sleep analyzed before stroke.
Support (optional): UNITER-SONO

0889

DONEPEZIL IMPROVES SLEEP APNEA IN ALZHEIMER´S DISEASE: A DOUBLE-BLIND PLACEBO-CONTROLLED STUDY

Moraes W,[1] Poyares D,[1] Sukys-Claudino L,[2] Guilleminault C,[3] Tufik S[2]
(1) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil, (2) Univ Fed Sao Paulo, Sao Paulo, Brazil, (3) Stanford University, Stanford, CA, USA

Introduction: The aim of this study was to examine the effects of donepezil on sleep apnea and oxygen desaturation in patients with Alzheimer´s disease.
Methods: Randomized, double-blind, placebo-controlled design. Twenty-three patients with mild to moderate Alzheimer´s disease, allocated to two groups, donepezil-treated (n=11) and placebo-treated (n=12). Patients were administered donepezil or placebo. Polysomnography and cognitive evaluation using ADAS-cog subscale were performed at baseline and after 3 months. Cognitive and sleep data were analyzed using ANOVA.
Results: Sleep apnea and oxygen saturation improved significantly after donepezil treatment compared to baseline and placebo (p<0.01). REM sleep duration increased after donepezil treatment. REM sleep increase and sleep apnea improvement correlated with cognitive improvement rate.
Conclusion: Donepezil treatment improved apnea-hypopnea index and oxygen saturation in patients with Alzheimer´s disease. Treatment also increased REM sleep duration. Cognitive improvement did not correlate with REM sleep increase and sleep apnea improvement.
Support (optional): AFIP, FAPESP/CEPID

0890

SLEEP-DISORDERED BREATHING AND SLEEPINESS IN PATIENTS WITH ARNOLD-CHIARI TYPE I MALFORMATIONS

Watson N,[1] Noonan C,[2] Goldberg J,[3] Ellenbogen R,[4] Maravilla K,[5] Buchwald D[2]
(1) Department of Neurology, University of Washington, Seattle, WA, USA, (2) Department of Medicine, University of Washington, Seattle, WA, USA, (3) Department of Biostatistics, University of Washington, WA, USA, (4) Department of Neurosurgery, University of Washington, Seattle, WA, USA, (5) Department of Radiology, University of Washington, Seattle, WA, USA

Introduction: Arnold-Chiari Type I (AC-I) malformations are congenital anomalies of the hindbrain characterized by a downward elongation of the brainstem and cerebellum into the foramen magnum and upper spinal canal. The resulting compression can adversely affect brainstem functions such as respiration, particularly during sleep. We sought to better understand the association between AC-I malformations and sleep-disordered breathing.
Methods: Arnold-Chiari Type I malformation patients and healthy controls were subjectively assessed for evidence of sleep-disordered breathing and sleepiness with the Berlin Questionnaire (BQ) and Epworth Sleepiness Scale (ESS). Also ascertained was the presence of nocturnal choking, gasping, or shortness of breath, morning headaches, heartburn, or sore throat, and habitual sleep duration and sleep latency. Fisher´s exact test was used for non-continuous variables and student´s t-test for continuous variables.
Results: Eighteen female AC-I patients (mean age 36 years) and 35 healthy female controls (mean age 39 years) completed the BQ, ESS, and other subjective questionnaires. Arnold-Chiari Type I patients were more likely to be considered "high risk" for sleep-disordered breathing on the BQ than healthy controls (69% vs. 20%; p=0.001) and more likely to be sleepy on the ESS (10.2 vs. 5.5; p=0.001). Nocturnal choking or gasping (p=0.001) and shortness of breath (p=0.002) were also more common in the AC-I group. Headaches (p=0.002), heartburn (p=0.03), and sore throat (p=0.007) were all more common upon awakening in the AC-I group. Patients with AC-I malformations reported habitually sleeping fewer hours (6.3 vs. 7.6; p=0.002) with longer sleep latencies (61.4 vs. 18.6 minutes; p=0.004) than the healthy control group.
Conclusion: Patients with AC-I malformations are at higher risk of sleep-disordered breathing and sleepier than healthy controls. They also sleep fewer hours and take longer to fall asleep. These findings suggest an association between brainstem compression in AC-I patients and impaired nocturnal respiration and sleep regulation.
Support (optional): NIH/NIAID RO1 AR 47678-01A1

0891

PRELIMINAR OBSERVATIONS ON SLEEP, MEMORY AND ATTENTION IN PATIENTS WITH MIASTENIA GRAVIS.

Sanchez-EscandóN O,[1] Arana-Lechuga Y,[2] Teran-PéRez G,[2] Castillo C,[2] Gonzalez R,[2] Burgos J,[1] Velazquez-Moctezuma J[2]
(1) National Institute of Neurology and Neurosurgery "Manuel Velasco Suárez", D.F, AA, Mexico, (2) Autonomy Metropolitan University, D.F, Mexico

Introduction: Myasthenia Gravis (MG) is an autoimmune disorder, caused by the destruction of postsynaptic acetylcholine receptors in the neuromuscular junction. MG is considered peripheral nervous system pathology; nevertheless there is evidence of MG participation in central processes specifically in REM sleep and endogenous sensory mechanisms of memory and attention
Methods: It was evaluate sleep architecture, attention and memory, in ten patients with MG.
Results: About sleep architecture there was find several abnormalities in sleep stage distribution: decrease in slow wave sleep (13.9% of total sleep time), REM sleep (14.4% of total sleep time) and REM sleep latency (71.5 min since sleep initiate) there was also an increase in light sleep (71.7% of total sleep time) and in movements during sleep. Memory evaluation was made with Barcelona test. 60% of patients presented percentile less than 30 in memory, similarities and abstraction functions. The attention was evaluated with P300, where none of the patients presented abnormal latencies, but it was seen a marked trend to appear in normal limit top.
Conclusion: The alterations in REM sleep suggest a possible influence in the integration of this sleep stage that can owe to a cholinergic dysfunction in CNS. Thought there wasn´t an abnormal memory and attention value, it was seen a tendency to decline cognitive functions specifically in memory and abstraction. These results suggest some influence of MG in CNS.

0892

SLEEP EFFICIENCY AND MEMORY RETURN FOLLOWING TRAUMATIC BRAIN INJURY

Makley M,[1] Johnson-Greene L,[2] Spiro J,[3] Kreuz A,[4] Green E,[2] Corcoran M,[2] Rao V[3]
(1) University of Maryland School of Medicine, Baltimore, MD, USA, (2) University of Maryland Neurology, Baltimore, MD, USA, (3) Johns Hopkins School of Medicine, Baltimore, MD, USA, (4) Villa Julie College, Baltimore, MD, USA

Introduction: In the United States traumatic brain injury (TBI) results in the annual hospitalization of approximately 230,000 people. Many of the more severe cases are subsequently admitted to a rehabilitation hospital. A previous study from our group using nursing observation logs found 68% of patients with Closed Head Injury (CHI) had disrupted nighttime sleep on a rehabilitation unit. In the present study, we sought to confirm these findings using actigraphy. We also wanted to look at the correlation of sleep efficiency with duration of post traumatic amnesia (PTA).
Methods: 9 CHI patients were enrolled. Mechanism of injury included motor vehicle accident (6), fall (2), and blunt assault (1). An actigraph [ActiTrac;IM Systems], was placed on each subject´s wrist within 72 hours of admission to the rehabilitation unit and recorded for the duration of their stay. A minimum of 7 days of continuous actigraphy data was obtained on all subjects. PTA was measured concomitantly using the Orientation Log (O-LOG).
Results: 78% of subjects had mean week-1 sleep efficiency scores of <65%. Patients admitted without PTA (n=3) had higher week -1 sleep efficiency scores than those with ongoing amnesia (p=.032). Sleep efficiency was positively correlated with O-LOG score (P=.001) and significantly predicted clearance of PTA (p=.009).
Conclusion: This pilot data confirms our earlier study that showed disrupted sleep is a major problem for patients with TBI on a rehabilitation unit. Previous investigators have proposed that sleep may be important for memory consolidation. In our study there is a significant correlation with an improvement in sleep efficiency and the resolution of the amnestic syndrome that is the hallmark of TBI. We feel actigraphy is uniquely suited to study the sleep patterns of the emerging TBI patient and our results warrant a larger study looking at the relationship of sleep and memory in this population.
Support (optional): This research was supported in part by a grant from the Kernan Hospital Endowment Board as well as The Institute for

Rehabilitation Studies at Kernan.

0893

EVOLUTION OF NEUROLOGICAL, NEUROPSYCHOLOGICAL AND SLEEP-WAKE DISTURBANCES IN PARAMEDIAN THALAMIC STROKE

Hermann D,[1] Siccoli M,[1] Brugger P,[2] Wachter K,[2] Mathis J,[3] Achermann P,[4] Bassetti C[5]
(1) Department of Neurology, University Hospital of Zurich, Zurich, Switzerland, (2) Department of Neurology, Neuropsychology Unit, University Hospital of Zurich, Zurich, Switzerland, (3) Department of Neurology, University Hospital of Bern (Inselspital), Bern, Switzerland, (4) Department of Pharmacology and Toxicology, University of Zürich, Zurich, Switzerland, (5) Department of Neurology, University Hospital Zürich, Zürich, Switzerland

Introduction: The long-term consequences of paramedian thalamic stroke are poorly known. The aim of this study was to characterize the evolution of neurological, neuropsychological and sleep-wake disturbances in this stroke syndrome.
Methods: Forty-six consecutive patients, aged 48.4±16.6 years, were studied. Fourteen had bilateral, 16 left-sided and 16 right-sided lesions. Assessment included neurological examinations, estimation of sleep needs (subjectively and by actigraphy), formal neuropsychological tests (n=27), and polysomnographies (n=31). Functional outcome was followed up over more than one year in 31 patients with the modified Rankin Scale and the Barthel index.
Results: Vertical gaze palsy (76% of patients), mild gait ataxia (67%), deficits of attention (63%), fluency and error control (67%) and learning (52%), as well as behavioral functions (74%) were common in the acute stroke phase. Outcome was excellent with right-sided infarcts but incomplete with bilateral and left-sided lesions related mainly to persistent frontal lobe-related and cognitive deficits. Initially, hypersomnia (increased sleep needs) was present in all patients, in association with increased stage 1 sleep, reduced stage 2 sleep, and reduced sleep spindles. Within one year, hypersomnia improved in patients with bilateral and almost disappeared with unilateral lesions. Sleep architecture remained abnormal, with the exception of some improvement of sleep spindles.
Conclusion: The evolution of paramedian thalamic stroke is characterized by improvement of hypersomnia and neurological deficits and the persistence of often disabling frontal lobe-related and cognitive deficits (mainly after bilateral and left-sided infarcts) and sleep architecture changes.

0894

SYMPTOMS OF SLEEP APNEA AND DAYTIME SLEEPINESS ARE HIGHER IN AFRICAN AMERICANS THAN CAUCASIAN AMERICANS WITH STROKE

Alattar M, Wedsworth J, Sen S, Vaughn B
University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Introduction: We compared the prevalence of symptoms of sleep apnea and daytime sleepiness between Caucasian Americans (CA) and African Americans (AA) with stroke. AA have higher risk of stroke and more severe strokes than CA (Gillum RF 1988). Strokes tend to occur at younger age in AA. Hypertension, diabetes and socioeconomic factors may partially explain the difference. AA with sleep disordered breathing are more likely to present at younger age than CA (Redline S 1997).
Methods: We surveyed168 patients who were admitted to University of North Carolina´s stroke center with documented acute strokes (157 ischemic, 11 hemorrhagic) for symptoms of sleep disorders. Age, gender, sleep apnea portion of the Sleep Disorders Questionnaire (SDQ-SA) and Epworth Sleepiness Scale (ESS) were obtained. The T-test is used for the statistical analysis ($p < 0.05$).
Results: Our cohort had 117 CA (60 Females, 57 Males) and 51 AA (18 Females, 33 Males). Average age for CA was 66 and AA was 58. Average SDQ-SA for CA was 33 (sd 9) and AA was 36 (sd 7); $p < 0.013$. Average ESS for CA was 7 (sd 4) and AA was 9; $p < 0.43$. These racial differences could not be accounted for by gender or smoking.
Conclusion: These findings demonstrate significant differences of the symptoms of sleep apnea and daytime sleepiness between CA and AA in the stroke population. The higher SDQ-SA between the races cannot be accounted for by the gender or smoking differences. Further exploration of the etiology that accounts for the discrepancy of stroke risks between CA and AA populations is needed.

0895

FUNCTIONAL ANATOMY AND TREATMENT OF RLS/PLMS EMERGING AFTER SPINAL CORD LESIONS

Trotti L, Rye D
Emory University, Atlanta, GA, USA

Introduction: Restless Legs Syndrome (RLS) and Periodic Leg Movements of sleep (PLMs) can occur secondary to spinal cord disease. The functional anatomy of "spinal" RLS/PLMs has not been clearly delineated and treatment efficacy is poorly defined.

Methods: Four patients with spinal cord disease were questioned regarding RLS symptoms and PLMs analyzed by actigraphy using a validated, tri-axial accelerometer (PAM-RL, IM Systems, Baltimore). Efficacy of pharmacological intervention was assessed with actigraphy repeated for 2-5 consecutive nights after pramipexole (n=2) or gabapentin (n=1).
Results: Subject #1 suffered an anterior spinal artery infarct with flaccid hemiparesis, loss of spinothalamic tract function, and severe PLMs (91.2/hr) without RLS. Subject #2 had a Brown-Sequard syndrome secondary to a thoracic cord lymphoma and PLMs (28.4/hr) lacking RLS. Subject #3 experienced spinal cord ischemia following aortic aneurysm surgery, lower motor neuron weakness, loss of dorsal column more than spinothalamic function, and PLMs (33.5/hr) in conjunction with RLS. Subject #4 developed neuromyelitis optica with transverse myelitis, pyramidal weakness, impaired dorsal column integrity with sparing of the spinothalamic function, and PLMs (30.0/hr) in conjunction with RLS.

Subjects #2 and #4 were treated with pramipexole (0.25mg) with reduction in PLMs to 6.5/hr and 2.6/hr, respectively. Subject #3´s post-treatment PLMs diminished to 13.1/hr with 1500mg gabapentin. Subjective RLS symptoms and sleep complaints resolved in parallel with PLMs decrements in Subjects #3 and #4. Subject #1 appreciated improvement with 0.25mg pramipexole.
Conclusion: Our experience is the first to suggest that the sensory "urge" attending RLS ascends to the brain via the spinothalamic tract in line with recent findings concerning the neurobiology of "itch". We also demonstrate that treatments effective in primary, idiopathic RLS appear efficacious in treating RLS and PLMs that emerge after injury to supraspinal descending pathways or to the spinal grey matter.

0896

SLEEP SYMPTOMS IN FRONTAL LOBE EPILEPSY

Lee E,[1] So E,[2] Colligan R,[2] Rummans T,[2] Trenerry M,[2] Maurer M,[2] Pankratz V[3]
(1) Royal Ottawa Mental Health Center, Ottawa, Ontario, Canada, (2) MN, USA, (3) Mayo Foundation for Medical Education and Research, MN, USA

Introduction: Frontal Lobe Epilepsy (FLE) accounts for 20-30% of surgically treated focal epilepsies, making it the second largest group of localization related epilepsies after temporal lobe epilepsy. Often such symptoms may occur in sleep, but there is a paucity of data in this area. The aim of this study was to evaluate the frequency of sleep disturbances in a sample of FLE patients.
Methods: This protocol received IRB approval to examine the medical records of 85 patients who underwent surgical treatment at the Mayo Clinic in Rochester, Minnesota, for intractable FLE and consented to have their records retrospectively reviewed. FLE was diagnosed by epileptologists using closed circuit television and prolonged EEG monitoring. Sleep symptoms were abstracted through a thorough review of each patient´s chart and categorized as ictal if symptoms were clearly related to a seizure, or interictal if symptoms did not clearly occur during a seizure. Additional data regarding medication and substance use were also abstracted to determine associations to sleep symptoms.
Results: Sleep disturbances were common in these FLE patients, with 60.2% (51/85) demonstrating sleep symptoms preoperatively (36/85 ictal, 25/85 interictal, 10/85 with both). The most frequent symptoms included paroxysmal nocturnal arousals (25/85, 29.4%), excessive daytime sleepiness (6/85, 7.0%), sleep/nocturnal wandering (4/85, 4.7%), somniloquy (4/85, 7.0%), and sleep apnea (2/85, 3.5%). Several others had nonspecific sleep disturbances (13/85, 15.3%). Sleep symptoms were also significantly associated with caffeine (p=0.022) and tobacco (p=0.04) use. Postoperatively, sleep disturbances were significantly less frequent with only 33/85 patients having sleep symptoms (p=0.005).
Conclusion: Sleep symptoms in FLE are common. Caffeine and tobacco use may play a significant role in promoting sleep disturbances, possibly because these patients may be using these substances to compensate for being on sedating antiepileptic medications. Although prolonged EEGs were performed, results are limited by lack of polysomnogram data.

0897

SLEEP STRIDOR AND HYPOPNEA CAUSED BY VAGUS NERVE STIMULATION

St. Louis E
University of Iowa, Iowa City, IA, USA

Introduction: Vagus Nerve Stimulation (VNS) therapy is an approved therapy for refractory partial onset-seizures in adolescents and adults. VNS therapy has been previously recognized to be associated with development of sleep disordered breathing, but no previous cases of stridorous respiration have been reported.
Methods: Case report from a tertiary care epilepsy program and sleep laboratory.
Results: A 23 year-old woman without previous history of sleep complaints or excessive daytime sleepiness underwent VNS implantation for medically-refractory partial epilepsy. During the first six months of VNS therapy at device output currents of 0.5 milliamps and below, she reported no symptoms of sleep-disordered breathing. Due to continued seizure activity her device output current was further titrated to 0.75 milliamps, upon which the patient and her family reported emergence of snoring and mild daytime sleepiness. A polysomnogram demonstrated primary snoring with apnea-hypopnea index of 0. Upon further subsequent VNS titration to 1.0 milliamps, the patient's family reported an alarming and peculiar "wheezy" respiratory pattern during sleep which recurred cyclically every few minutes throughout the night. Reduction of VNS pulse width and signal frequency parameter settings did not alter the respiratory pattern, and a cassette tape audio recording made by the family sounded consistent with stridor. Repeat polysomnography with concurrent VNS adjustment documented cyclic stridorous respirations associated with mild hypopneas, but no arousals or desaturation, which halted completely during VNS deactivation and recurred when VNS was resumed at 1.0 milliamp output current setting. Sequential reduction of VNS output current back to 0.5 milliamps completely obviated audible stridor and hypopnea and greatly improved snoring.
Conclusion: VNS therapy caused fully reversible stridor and hypopnea confirmed by polysomnography in our patient, expanding the known spectrum of sleep-disordered breathing associated with VNS. VNS parameter adjustment during polysomnography may improve the quality and quantity of stridorous respirations and hypopnea associated with VNS.
Support (optional): The Nathan and Beth Tross Research Fund for Epilepsy and Cognitive Neuroscience, The University of Iowa, and NIH K12 #510 17 3220 04000 11812015.

0898

DAYTIME SLEEPINESS SCALES IN ALZHEIMER'S DISEASE

Singer C,[1] Nanda F[2]
(1) University of Vermont, Burlington, VT, USA, (2) University of Vermont, VT, USA

Introduction: Daytime sleepiness is common in Alzheimer´s disease (AD). There are no validated instruments to rate sleepiness in AD or dementia patients. The Sleep Disorders Inventory (SDI) is a validated rating scale of sleep disturbance in dementia patients (Tractenberg RE *et al.*, 2003). SDI covers a wide range of sleep disturbance symptoms usually reported by AD patients but has only one question addressing daytime sleepiness. Epworth Sleepiness Scale (ESS) is a gold-standard rating scale for sleepiness, but may have reduced validity in dementia patients. As part of a small intervention trial with modafinil, we compared the SDI-sleepiness item to the eight question ESS and actigraph-scored daytime sleep.
Methods: Daytime sleepiness was scored by SDI and ESS by family caregivers blinded to treatment condition. Scores were compared to actigraph Daytime Total Sleep Time (DTST) during 0800-2000 over three weeks´ tx with modafinil 200mg (M200) and four-week placebo wash-out in 16 AD patients.
Results: The Spearman´s correlation coefficients between SDI-sleepiness and ESS scores were significant (P<.05) at different time-points (r M200=0.60 and r wash-out=0.74). SDI-sleepiness and ESS scores showed significant correlation with the actigraph DTST (P<.05). One subject however, scored zero on SDI despite high ESS scores and DTST.
Conclusion: SDI and ESS showed fairly high correlation in this study, and external validity with actigraph-scored daytime sleep. Nevertheless, the one question of SDI relevant to sleepiness may miss daytime sleepiness detected by more specific questions of ESS or objective sleep daytime sleep measures.
Support (optional): Investigator-initiated clinical trial grant from Cephalon Pharmaceuticals.

0899

POSTPARTUM SLEEP FOR MOTHERS WHO EXPERIENCED CESAREAN DELIVERY COMPARED TO VAGINAL DELIVERY

Lee S,[1] Lee K[2]
(1) Georgia State University, Alpharetta, GA, USA, (2) University of California, San Francisco, San Francisco, CA, USA

Introduction: Sleep disturbance is prevalent in childbearing mothers with a healthy newborn baby. The characteristics of the postpartum nocturnal sleep patterns for those mothers with a healthy infant at home include less total sleep time, more wake time during the night, less stage 2 sleep and more slow wave deep sleep. In addition, postpartum fatigue severity has been found to be associated with fragmented sleep patterns. To date, objective sleep measures of mothers during their first week of their postpartum recovery are rare. The purpose of this report is to describe the nature of sleep and fatigue for mothers during first week of postpartum recovery from labor and delivery while their infants remained hospitalized in intensive care. Sleep and fatigue after cesarean delivery while still hospitalized was compared to sleep and fatigue after vaginal delivery and discharged to home.
Methods: 21 first-week postpartum mothers participated in this cross-sectional descriptive study (six after cesarean delivery and 15 after vaginal delivery). Three sets of data were collected: 1) infants´ medical records and mothers´ demographic data; 2) General Sleep Disturbance Scale, Numerical Rating Scale-Fatigue; and 3) objective sleep data from wrist actigraphy that included total sleep time (TST) and wake after sleep onset (WASO).
Results: All of the mothers experienced sleep problems after their infants were admitted to the ICU. Actigraphy records showed mothers after cesarean birth averaged only about 4 hours TST with 34% WASO, compared to 6.5 hours TST and 14% WASO for mothers after vaginal delivery. The cesarean delivery mothers experienced higher morning fatigue severity compared to vaginal delivery mothers.
Conclusion: Sleep disturbances and fatigue need to be further investigated to better understand the relationship to type of delivery and maternal health outcomes. Intervention is needed to promote sleep for new mothers during postpartum recovery.
Support (optional): The first author was supported by NINR T32NR 07088 and by the Graduate Diversion at University of California, San Francisco.

0900

PREVALENCE OF SLEEP DISORDERS IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOUS

Cruz M,[1] Chawla A,[2] Adams R,[3] Martucci C,[3] Coleman C,[3] Grant M,[3] Fathalla B,[3] Goldsmith D,[3] Kothare S[3]
(1) St. Christopher's Hospital for Children, Philadelphia, PA, USA, (2) Tulane University, LA, USA, (3) St. Christopher's Hospital for Children, PA, USA

Introduction: The magnitude of sleep disorders in children with Systemic Lupus Erythematous (SLE) is under-recognized. The purpose of this prospective study was to evaluate various sleep abnormalities observed in a cohort of patients with SLE using a standardized sleep questionnaire.
Methods: Twenty randomly selected patients from a predominantly minority population with SLE were prospectively enrolled to complete a standardized 35-item Children´s Sleep Habits Questionnaire (CSHQ; Owens et al). Scores obtained were compared to the controls in CSHQ population group and also to 70 controls from a minority population at our center. Subset analysis included 8 areas of assessment: Bedtime Resistance, Sleep Onset Delay, Sleep Duration, Sleep Anxiety, Night Waking, Parasomnias, Sleep Disordered Breathing and Daytime Sleepiness. A SLEDAI score was also included in the analysis to assess the severity of SLE.
Results: There were 16 females and 4 males; mean age 17.3 ± 2.9 years. When compared to CSHQ´s control population, the scores obtained in patients with SLE were significantly higher in 6 of the 8 subgroups ($p < 0.05$), except for sleep anxiety and night waking, using pair t-Test analysis. When compared with the minority population control group, patients with SLE showed scores significantly higher in 6 of the 8 areas ($p < 0.05$), but in the normal range for Sleep Onset Delay and in Parasomnias using pair t-Test analysis. The severity of SLE measured using SLEDAI and depression did not correlate with the sleep disturbances using Pearson´s correlation analysis.
Conclusion: Our preliminary results from a small cohort of children with SLE showed increased incidence of sleep disorders including excessive daytime sleepiness, sleep disordered breathing, bedtime resistance, and sleep duration as assessed using a standardized questionnaire. This will need to be further explored using objective analysis via performing polysomnography and multiple sleep latency tests.

0901

SLEEP EFFICIENCY AND DAYTIME SLEEPINESS IN PATIENTS WITH COMPLAINTS OF DEPRESSION AND CHRONIC PAIN

Zanette M
University Services, West Chester, PA, USA

Introduction: Research has shown that patients with complaints of depression and chronic pain also have sleep complaints including fragmented and un-refreshing sleep. This study examines subjective complaints of depression and chronic pain among men and women and the impact these complaints have on sleep efficiency and daytime sleepiness in the absence of other significant sleep disorders.
Methods: 84 patient charts were reviewed (35 males) with mean age 43 ±12.2. Patients had a history and physical, a polysomnogram, and completed the Epworth Sleepiness Scale (ESS). Patients were excluded from this study if they had clinical findings including OSA, RLS, PLMD, idiopathic hypersomnia, insomnia, or narcolepsy. In addition, patients who had significant uncontrolled medical conditions were excluded. Patients were categorized into one of four complaint groups based on their subjective reports (1. no complaints 2. complaints of depression 3. complaints of chronic pain 4. complaints of depression plus chronic pain). Chronic pain was considered chronic back pain, chronic neck pain, or fibromyalgia.
Results: 71% of women had a complaint as opposed to 45.7% of men ($p=.0081$). There was a significant difference in mean ESS scores between the group with no complaints (6.95±4.46) and the group with complaints of chronic pain (11.54±6.29) ($F=3.32$, $p=0.0240$). There were no significant differences among the groups in mean sleep efficiency.
Conclusion: Subjective complaints of chronic pain alone increased subjective daytime sleep propensity but did not affect the objective measure of sleep efficiency at night. This did not hold true if the patient complained of chronic pain plus depression. Subjective complaints of depression alone did not have an impact on either measure. Women were more likely than men to make complaints in all three groups.

0902

POOR SLEEP QUALITY IN PATIENTS WITH ADVANCED LUNG CANCER

Dean G,[1] Gooneratne N,[2] Rogers A[3]
(1) University at Buffalo, Buffalo, NY, USA, (2) University of Pennsylvania, Philadelphia, PA, USA, (3) University of Pennsylvania School of Nursing, Columbia, MD, USA

Introduction: Patients with lung cancer experience a variety of distressing symptoms that adversely affect their quality of life. Sleep disruption is one complaint that has received little attention. The purpose of this study was to determine the prevalence, pattern and perceived causes of sleep disruption in patients with advanced lung cancer.
Methods: Eligible participants were recruited from the Lung Cancer Clinic at the Philadelphia VA Medical Center. The Pittsburgh Sleep Quality Index (PSQI), demographic, disease and treatment information were collected from eligible participants while awaiting clinic appointments.
Results: Among 21 participants, the mean age was 62.5 years (SD=9.3, Range=47-75), with 95% male, and 77% African American. The majority of participants were diagnosed with nonsmall cell lung cancer (86%) and 59% received both chemotherapy and radiotherapy. Participants reported spending 7.9 (SD=1.9) hours in bed, but only 5.8 (SD=1.9) hours asleep; they thus had a markedly low sleep efficiency of 74% (SD=24%). Mean sleep latency was 44 (SD=37) minutes. More than half of the participants reported the following causes of trouble sleeping: nocturia (85%), experiencing pain (67%) and dyspnea (52%). Mean overall global sleep quality was 9.8 (SD=4.7) with 72% of the sample above the clinically significant cut-off score of five. The majority of participants (65%) rated their overall sleep quality as very good or fairly good, but all of their component scores indicated poor sleep quality except for one-daytime dysfunction.
Conclusion: These preliminary data suggest that a substantial number of patients with advanced lung cancer experience sleep disruption. Lung cancer patients may be unique in their underestimation of their sleep problems. Further investigation is warranted to examine the nature and impact of sleep problems in this population.

0903

COGNITION AND SLEEP IN WOMEN WITH BREAST CANCER: PRELIMINARY OBSERVATIONS

Ancoli-Israel S,[1] Palmer B,[1] Lawton S,[1] Natajaran L,[1] Parker B,[1] Mills P,[2] Cornejo M,[1] Pressman M,[1] Sadler G[2]
(1) University of California, San Diego, San Diego, CA, USA, (2) University of California, San Diego, La Jolla, CA, USA

Introduction: Treated breast cancer patients complain of cognitive dysfunction during and for some years after chemotherapy. This phenomenon has been termed "chemobrain." Treated breast cancer patients also complain of difficulties with sleep. Yet whether chemobrain is related just to the chemotherapy only or is secondary to sleep problems, has not been fully explored. We present preliminary data from an on-going study that addresses this question.
Methods: 13 women diagnosed with stage I-III breast cancer undergoing adjuvant anthracycline-based chemotherapy and 8 age- and SES-matched women with no history of any cancer participated. A neuropsychological (NP) test battery and the Pittsburgh Sleep Quality Index was administered and actigraph was worn for 72 hours pre-treatment (Time 0 or T0) and after four cycles of chemotherapy (Time 1 or T1). Each control woman was matched to and tested at the same time points (T0 and T1) as a patient.
Results: No differences were observed between patients and controls at T0. During T1, compared to controls, patients spent more time napping (11% vs. 3% of the day; p=0.045) and had higher PSQI total scores (11.0 vs. 4.4; p=0.004). At T1 compared to T0, there was a greater change in NP scores in patients (who showed a small decline) than in controls (who had increased scores, possible due to a practice effect)(p=0.069).
Conclusion: Although the sample size is still small, findings suggest that, when compared to controls, breast cancer patients undergoing chemotherapy show a decline in cognitive function as well as a decline in sleep quality. Additional data are being collected to help understand the relationship between these variables in patients undergoing chemotherapy so that intervention strategies to minimize chemobrain can be explored.
Support (optional): NCI CA112035, CBCRP 11IB-0034, CBCRP 11GB0049, NIH M01 RR00827 and the research service of the VASDHS.

0904

HEADACHE SEVERITY AND SLEEP DYSFUNCTION

Grieser E, Tatum J, Taylor D, Bramoweth A, Gardner C, Williams J, Zimmerman M, Roane B
University of North Texas, Denton, TX, USA

Introduction: Studies have shown a substantial sleep/headache relationship, suggesting that one-half to one-third of headache sufferers have chronic sleep difficulties; headache is often precipitated by sleep disorders such as bruxism and sleep apnea. (Kelman & Rains, 2005). In addition, management of sleep disorders may improve or resolve headache, and behavioral sleep regulation strategies are compatible with primary headache treatment (Rains & Poceta 2006). Few studies have addressed which parameters of sleep are most related to increased headache severity.
Methods: Undergraduate students (N=367) who were enrolled in psychology classes completed a health survey that included questions about their headache severity and sleep habits in exchange for extra credit. This sample was 69% female, with the following ethnic distribution: Caucasian=65.5%; African American=15%; Hispanic American =8.8%; Asian/Pacific Islander = 6.5%; Other/missing = 3.5%.
Results: The primary measure analyzed was the Pittsburgh Sleep Quality Index (PSQI). Preliminary analyses of the sleep data show that as headache severity increased, overall sleep quality as measured by the total PSQI score decreased (p<.01). Post hoc analyses of the individual parameters of sleep showed that increased headache severity was associated with poorer self-reported sleep quality (p<.05), increased sleep onset latency (p<.05), increased sleep aid medication usage (p<.05), increased daytime sleepiness (p<.05), and decreased motivation (P<.01).
Conclusion: Data show significant relationships between severity of headache and many parameters of disordered sleep. Future studies should focus on effects of treating either problem (e.g., headaches or sleep problems) on the other comorbid disorder. We will present more data and further analyses at the conference.

0905

ASSOCIATION OF USUAL SLEEP DURATION WITH ATHEROGENIC DYSLIPIDEMIA

Kaneita Y,[1] Uchiyama M,[2] Yoshiike N,[3] Ohida T,[4] Nakajima H[4]
(1) Nihon University Tokyo, Itabashi-ku, Tokyo, Japan, (2) Nihon University School of Medicine, Tokyo, Japan, (3) National Institute of Health and Nutrition, Tokyo, Japan, (4) Nihon University Tokyo, Tokyo, Japan

Introduction: It has been increasingly recognized that sleep habits are potential risk factors for diabetes mellitus, obesity, hypertension, and coronary heart disease. The association between atherogenic dyslipidemia and sleep duration is still not well understood. We examined the associations of serum triglyceride and high density lipoprotein (HDL) cholesterol levels with sleep duration.
Methods: The present study analyzed data from the National Health and Nutrition Survey that was conducted in November 2003 by the Japanese Ministry of Health, Labour and Welfare. This survey was conducted on residents from districts selected randomly from all over Japan. The subjects included in the statistical analysis were 1,666 men and 2,329 women aged 20 years or more. Logistic regression analyses were performed by gender in order to examine the associations between sleep duration and high triglycerides, and sleep duration and low HDL cholesterol. These analyses were adjusted for the following items: age, blood pressure, body mass index, plasma glucose level, smoking habit, alcohol consumption, dietary habits, and psychological stress.
Results: Among women, significant associations were observed between sleep duration and both high triglycerides and low HDL cholesterol. The adjusted odds ratios for high triglycerides and low HDL cholesterol in subjects who slept less than or more than 6–7 hours per night were higher than for subjects who slept for 6-7 hours. Among men, no significant associations were observed between sleep duration and high triglycerides and low HDL cholesterol.
Conclusion: Among women, both short and long sleep durations are associated with an increased prevalence of atherogenic dyslipidemia. It is important to implement preventive measures against atherogenic dyslipidemia based on knowledge of its association with sleep duration.

0906

REDUCED RENAL FUNCTION AND SLEEP APNEA IN COMMUNITY-DWELLING ELDERLY MEN

Canales M,[1] Taylor B,[2] Ishani A,[3] Mehra R,[4] Steffes M,[1] Stone K,[5] Susan R,[6] Ensrud K[2]
(1) University of Minnesota, Minneapolis, MN, USA, (2) Minneapolis-VAMC, MN, USA, (3) Minneapolis VAMC, Minneapolis, MN, USA, (4) Case Western Reserve University, Cleveland, OH, USA, (5) California Pacific Medical Center (CPMC), San Francisco, CA, USA, (6) Case Western Reserve University School of Medicine, OH, USA

Introduction: Non-traditional risk factors, including sleep disordered breathing (SDB), may contribute to the increased risk of cardiovascular disease and death in chronic kidney disease (CKD). However, the association between mild to moderate reductions in renal function and likelihood of SDB is uncertain.
Methods: We studied 508 community-dwelling men over 65 enrolled at the Minnesota site for the Outcomes of Sleep Disorders in Older Men (MrOS Sleep) study who had serum cystatin-C and creatinine measured coincident with polysomnography. CKD was defined as estimated glomerular filtration rate < 60 ml/min/1.73m2 using Cockcroft-Gault(CG), Modification of Diet in Renal Disease(MDRD) and Mayo Clinic formulae. Sleep apnea was defined by a respiratory disturbance index (RDI) >= 15 events/hour at >= 4% desaturation.
Results: Mean age (SD) was 76.0 (5.3) years; 95% were white. Mean cystatin-C (SD) was 1.21 0.30) mg/L and mean creatinine (SD) was 1.09 (0.23) mg/dL. Median RDI was 7.0 events/hour (range 0-73). Mean RDI (95% CI) by cystatin-C quartile was as follows: 8.7 (6.4-11.0) for Q1(< 1.00mg/L); 10.4 (8.2-12.6) for Q2(1.00-1.14mg/L); 13.5 (11.3-15.7) for Q3(1.15-1.34mg/L); 11.5 (9.3-13.7) for Q4(>1.34mg/L) (p for trend=0.03). This association persisted after adjustment for age and race (p for trend=0.06), but not after adjustment for BMI (p for trend=0.56). CKD as defined by the Mayo Clinic formula, but not the CG or MDRD formulae (p>0.3 for both), was associated with a 2.0-fold increase in prevalence of sleep apnea (95% CI 1.04-3.65, p=0.04), despite adjustment for age, race, BMI, hypertension, cardiovascular disease and diabetes.
Conclusion: In this cohort, the relationship between reduced renal function as measured by higher cystatin-C and higher mean RDI was largely explained by greater BMI at higher cystatin-C levels. However, CKD defined by the Mayo Clinic formula was independently associated with a higher prevalence of sleep apnea.
Support (optional): The Osteoporotic Fractures in Men (MrOS) Study is supported by National Institutes of Health funding. The following institutes provide support: the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute on Aging (NIA), and the National Cancer Institute (NCI), under the following grant numbers: U01 AR45580, U01 AR45614, U01 AR45632, U01 AR45647, U01 AR45654, U01 AR45583, U01 AG18197 and M01 RR000334. The National Heart, Lung, and Blood Institute (NHLBI) provides funding for the MrOS Sleep ancillary study "Outcomes of Sleep Disorders in Older Men" under the following grant numbers: R01 HL071194, R01 HL070848, R01HL070847, R01 HL070842, R01 HL070841, R01 HL070837, R01 HL070838, and R01 HL070839.

0907

HISTORICAL FEATURES OF SLEEP DISORDERED BREATHING ARE NOT ASSOCIATED WITH ALBUMINURIA IN AFRICAN-AMERICAN PARTICIPANTS OF THE JACKSON HEART STUDY

Fulop T,[1] Hickson D,[1] Rack M,[2] Wyatt S,[1] Schmidt D,[3] Miller R,[1] Bhagat R,[4] Ajelabi A,[4] Taylor H[1]
(1) University of Mississippi Medical Center, Jackson, MS, USA, (2) Somnus Sleep Clinic, Flowood, MS, USA, (3) School of Medicine, University of Mississippi Medical Center, Jackson, MS, USA, (4) G.V. Sonny Montgomery Veterans Administration Medical Center, Jackson, MS, USA

Introduction: Sleep disordered breathing (SDB) is associated with obesity, hypertension and cardiovascular disease, potentially contributing to African-American health disparities. Less clear is the association of SDB to renal or urinary abnormalities. We hypothesized that SDB may have an independent association with albuminuria in the Jackson Heart Study (JHS).
Methods: The JHS is a prospective cohort study of 5,302 African-Americans designed to identify risk factors for cardiovascular disease. All participants responded to extensive questionnaires, underwent physical exam, and provided blood and urine samples. Random urine albumin and creatinine concentrations were measured in mg/dl and a ratio of >/= 0.03 was considered abnormal, or presence of albuminuria. Five specific questions queried the clinical likelihood of SDB, composing total Sleep Quality Score (SQS), which was dichotomized as none-mild or moderate-severe. Pearson correlation and Mantel-Haenszel chi-square analyses assessed the correlation and association, respectively, between SQS and the presence/absence of albuminuria. Multivariate logistic regression models were formulated in stepwise hierarchical fashion, sequentially incorporating SQS; age and gender; blood pressure and body mass index (BMI); alcohol use and smoking; and chronic medical diseases (diabetes, hypertension, and cardiovascular disease).
Results: 2553 participants with valid spot urine protein and creatinine measurements were included in this analysis. SQS scores had little correlation with albuminuria (R = 0.008, p=0.706). SQS dichotomized according to severity did not associate with albuminuria in either the

unadjusted (p=0.706) or final adjusted (p=0.634) models. Major predictors of albuminuria were age (p=0.001), BMI (p=0.003), blood pressure and diabetes (p<0.000 for each) and hypertension (p=0.006).
Conclusion: SDB, as assessed by sleep questionnaire, was not associated with albuminuria. The disproportionate burden of kidney disease in African-Americans needs further investigations.
Support (optional): This research was supported by NIH contracts N01-HC-95170, N01-HC-95171, and N01-HC-95172 that were provided by the National Heart, Lung, and Blood Institute and the National Center for Minority Health and Health Disparities.

0908

SLEEP IN A TRANSLATIONAL RESEARCH IN ACTION FOR DIABETES COHORT WITH LONG-TERM TYPE 2 DIABETES

Taub L,[1] Redeker N[2]
(1) University of Medicine and Dentistry of New Jersey, Newark, NJ, USA, (2) Newark, NJ, USA

Introduction: Little is known about sleep in community dwelling persons with long-term type 2 diabetes that do not seek help for sleep complaints. The purpose of this pilot was to describe sleep and correlates of sleep in patients recruited from the N.J. TRIAD study.
Methods: We recruited 27 persons with diabetes (M age = 61.04 +/- 7.20 years; 13/43.3% men, 14/46.7% women; M months diagnosed with diabetes = 166.22 +/- 96.32; M Hgb A1c = 7.72 +/- 1.44; M BMI = 31.71 +/- 6.92; M nocturia episodes = 1.48 +/- 1.91. Three days of Actigraphy data and sleep diaries were obtained. Participants completed the Epworth Sleepiness Scale (ESS), Multidimensional Assessment of Fatigue Scale (MAF), Center for Epidemiologic Studies of Depression Scale (CESD), and SF-36 Bodily Pain Subscale (BPS). Diagnosis of diabetes was self-reported and verified by clinical records obtained in the parent TRIAD study.
Results: Mean 3-day sleep time was 345.55 +/- 83.73 min. and efficiency was M = 79.45%+/- 9.82. Mean fatigue score was 21.28 +/- 14.53; CESD M = 12.25 +/- 9.68; ESS M = 8.66 +/- 3.72; and BPS M 63.03 +/- 29.69. Age was associated with sleep duration (r = .49, p = 0.05). Depression and fatigue were negatively associated with sleep efficiency (r = -.41, p = 0.05 and r = -.55, p = 0.01), respectively. There were no relationships between gender, CESD, ESS, MAF, or BPS and sleep duration or between gender, BMI, AIc, sleepiness or bodily pain and either of the sleep variables.
Conclusion: The TRIAD cohort on average is obese, in fair glycemic control, and has more bodily pain than the general population, but is not depressed, fatigued nor excessively sleepy during the day. Older adults had shorter sleep duration and sleep efficiency was associated with both depression and fatigue.
Support (optional): This study was funded by the UMDNJ Foundation and the UMDNJ School of Nursing.

0909

EFFECT OF BRIGHT LIGHT THERAPY ON SLEEP QUALITY IN WOMEN UNDERGOING CHEMOTHERAPY: PRELIMINARY RESULTS

Rissling M,[1] Trofimenko V,[2] Natajaran L,[3] Liu L,[2] Lawton S,[2] Cornejo M,[2] Chuang J,[2] Pressman M,[2] Ancoli-Israel S[2]
(1) SDSU/UCSD Joint Doctoral Program in Clinical Psychology, San Diego, CA, USA, (2) Dept of Psychiatry, University of California, San Diego, La Jolla, CA, USA, (3) Dept of Community and Family Medicine, University of California, San Diego, San Diego, CA, USA

Introduction: Chemotherapy induces disturbed sleep in a large percent of women with breast cancer. Evidence has shown that bright light therapy can improve sleep in other populations. We present preliminary data from an on-going study that addresses whether morning bright light would improve the quality of sleep in women with breast cancer undergoing chemotherapy.
Methods: Ten women (mean age=51.2 yrs, SD=9.0, range=35-70 yrs) diagnosed with stage I–III breast cancer, scheduled to receive at least four cycles of adjuvant anthracycline-based chemotherapy participated. Participants were randomized into one of two treatment groups: bright white light (BWL; n = 7) or dim red light (DRL; n = 4). Both groups were instructed to self-administer light therapy (Litebook Co, LTD) for 30 minutes upon awakening every morning at their normal wakeup time throughout four cycles of chemotherapy. Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI) at baseline (pre-chemotherapy) and during the last week of cycle four (C4).
Results: PSQI sleep latency subscale for BWL was reduced from 2.6 (SD=3.0, range=0-5) at baseline to 1.9 (SD=2.3, range=0-6) at C4 for a mean decrease of 0.7, while for DRL, mean sleep latency increased from 2.7 (SD=2.5, range=0-5) at baseline to 3.0 (SD=3.0, range=0-6) at C4 for a mean change of -0.3. PSQI total score for BWL decreased from 12.0 (SD=4.7, range=7-19) at baseline to 10.9 (SD=4.2, range=5-16) at C4 a mean decrease of 1.1 while for DRL it decreased from 8.3 (SD=3.1, range=5-11) at baseline to 7.7 (SD=5.1, range=2-12) at C4 a mean decrease of 0.6.
Conclusion: Preliminary results suggest that bright white light may improve sleep quality and decrease sleep latency in women with breast cancer undergoing chemotherapy. Additional data will reveal if these effects are significant.
Support (optional): CBCRP 11IB-0034, NCI CA112035-01A and the research service of the VASDHS.

0910

IS APNEA AN EXCLUSIONARY CRITERION FOR CHRONIC FATIGUE SYNDROME? NO!

Creti L,[1] Rizzo D,[1] Bailes S,[1] Baltzan M,[2] Fichten C,[3] Libman E[1]
(1) Sir Mortimer B. Davis - Jewish General Hopital - Montreal, Montreal, Quebec, Canada, (2) Mount Sinai Hospital, Montreal, Quebec, Canada, (3) Dawson College, Montreal, Quebec, Canada

Introduction: Chronic Fatigue Syndrome (CFS) is an illness characterized by disabling fatigue of at least 6 months. The pathophysiology and etiology of CFS is poorly understood and no single diagnostic test can confirm its presence. Traditionally, an individual cannot be diagnosed with CFS if sleep apnea is present: this is an exclusion criterion. We contend that this exclusion criterion is inappropriate.
Methods: We evaluated 68 individuals who had been diagnosed with CFS with respect to fatigue, sleepiness, insomnia and psychological distress. No participant had ever been evaluated prior to our study in a sleep lab. Subsequent to overnight polysomnography, 45 were found to have sleep apnea; twenty-three were not. We offered CPAP treatment to individuals with apnea and examined changes pre and three months post CPAP treatment. We examined the findings for individuals who either fully complied with treatment or did not do so. Of interest for the present submission is the variable of fatigue, the core symptom of CFS.
Results: Results show that Compliant subjects were more fatigued pre treatment than non-compliant subjects; both compliant and noncompliant participants improved over time. After treatment, fatigue scores for all participants with apnea resembled those of individuals with CFS but no apnea.
Conclusion:
Since the treatment itself did not appear to have any differential effect, these data suggest that sleep apnea is a comorbidity of CFS rather than

an exclusionary criterion in the diagnosis.

0911

THE COGNITIVE BEHAVIORAL MODEL OF INSOMNIA AND SLEEP IN CHRONIC PAIN.

Ashworth P,[1] Davidson K,[2] Espie C[3]
(1) Gloucestershire Hospitals NHS Foundation Trust, UK, Gloucester, United Kingdom, (2) Psychological Medicine, University of Glasgow, United Kingdom, (3) University of Glasgow Sleep Research Laboratory, United Kingdom

Introduction: Insomnia is common amongst people with persistent pain. Cognitive behavioural models of insomnia propose that insomnia is underpinned by dysfunctional beliefs about sleep, which are endorsed more strongly by people with primary insomnia when compared to good sleepers. Dysfunctional beliefs about sleep have not been examined in chronic pain samples.
Methods: The relationship between pain, sleep, and dysfunctional beliefs about sleep were explored in a cross sectional design.160 people with chronic benign pain completed a postal questionnaire. Measures included pain severity, disability, pain related anxiety, depression, sleep quality (Pittsburgh Sleep Quality Index) and beliefs about sleep (Dysfunctional Beliefs and Attitudes about Sleep Questionnaire - 16-item version). Using a screening questionnaire the sample was split into three subgroups: good sleepers (n=32), insomnia (n=73), and "other poor sleepers" who met screening questions for other sleep disorders such as restless legs syndrome, sleep apnoea and parasomnias (n=51).
Results: The insomnia group reported higher levels of nighttime pain (p=0.001), disability (p=.016) depression (p=0.001), pain related anxiety (p=0.020) and more dysfunctional beliefs about sleep (p=0.025) than good sleepers. The "other poor sleepers", displayed similar levels of functioning to the insomnia group, and also endorsed more dysfunctional beliefs about sleep than the good sleepers. Hierarchical regression analysis was used to examine the roles of pain, depression, pain related anxiety and dysfunctional beliefs about sleep in predicting concurrent sleep quality. After the inclusion of pain and depression, only the addition of information about dysfunctional beliefs about sleep improved the regression model.
Conclusion: As predicted by the cognitive model of insomnia, people with chronic pain and insomnia display more dysfunctional beliefs about sleep than good sleepers. However poor sleepers with other sleep disorders also displayed similar patterns of beliefs. This raises the possibility that dysfunctional beliefs about sleep are an epiphenomenon of poor sleep.

0912

GENDER DIFFERENCES IN SLEEP, SLEEP DISORDERED BREATHING, AND DAYTIME SYMPTOMS IN STABLE HEART FAILURE

Redeker N,[1] Campbell D,[2] Qureshi R[2]
(1) University of Medicine and Dentistry of New Jersey, Newark, NJ, USA, (2) University of Medicine and Dentistry of New Jersey, NJ, USA

Introduction: Disturbed sleep is common in heart failure (HF). The purpose is to evaluate gender differences in sleep and sleep disordered breathing and their contributions to daytime symptoms in stable HF.
Methods: We recruited 119 stable Class II-IV HF patients (n = 36 women, M age = 56.53 +/- 16.27 years) (n = 83 men, M age = 60.37 +/- 16.86 years). Portable home polysomnography was obtained (Safiro, Compumedics, Inc.). Data were scored with Rechtschaffen & Kales and AASM criteria. Participants completed the Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, and Multidimensional Assessment of Fatigue Questionnaire.
Results: There were no statistically significant gender differences in age, NY class, ejection fraction, or comorbidity. Women had higher BMI (M = 33.37+/- 9.72 vs. M = 29.78 +/- = 7.24), depression (p = .008),and fatigue (p < .001), but were no more sleepy than men. There were no statistically significant differences in self-reported sleep, PSG-recorded nocturnal sleep time, efficiency, latency, arousals, or oxygen desaturation. Women had less Stage 1 (M = 17.62 +/- 6.36 vs. M = 21.91 +/- 8.04) and more Stage 3/4 (M = 7.80 +/- 6.27 vs. 4.61 +/- 5.06) sleep and lower apnea hypopnea index (M = 15.42 +/- 15.26 vs. 23.61 +/- 20.51). Gender, comorbidity, and sleep quality explained 33% of the variance in depression; gender and sleep quality explained 32% of the variance in fatigue; and sleep quality explained 14%of the variance in sleepiness. None of the PSG variables explained significant variance in daytime symptoms.
Conclusion: Although women with stable HF are more fatigued and depressed than men, these differences are not associated with sleep disordered breathing or objective attributes sleep attributes. Despite higher levels of sleep disordered breathing, men do not report more sleepiness.
Support (optional): NIH/NINR 5R01NR08022

0913

EFFECT OF CHRONIC SLEEP RESTRICTION AND EXERCISE TRAINING ON METASTASIS IN MICE

Zielinski M,[1] Davis J,[2] Wyatt, Jr. W,[2] Montagu D,[2] Youngstedt S[3]
(1) University of South Carolina, Columbia, SC, USA, (2) University of South Carolina, SC, USA, (3) Columbia, SC, USA

Introduction: Epidemiological evidence indicates that long and short sleep are associated with increased risk of cancer. However, there has been limited experimental investigation of this topic. Physical activity may reduce the risk or progression of certain cancers. Our aim was to determine the effects of chronic sleep restriction and exercise training on experimental tumor metastasis in mice.
Methods: Thirty-five male mice were maintained on 12:12 hr light:dark cycle and randomly assigned to 8-wk treatments in a 2X2 SLEEP (sleep restriction vs. normal sleep) by ACTIVITY (exercise vs. sedentary control) design. Sleep restricted mice were placed on a slow rotating disk (1 rev/min) for 15 hr/d beginning 3 hrs before dark onset. In other mice, electroencephalographic data indicated a ~40% reduction in sleep time/day using this protocol. Mice in normal sleep groups were placed on a locked disk. Exercised mice ran on a treadmill moderately; sedentary groups were subjected to the noise of the treadmill. After the 8-wk treatment, mice were injected with syngeneic B16 melanoma cells and 2 wks later lungs were excised and lung tumor foci were counted.
Results: ANOVA revealed a significant main SLEEP treatment effect ($p<0.001$). Tumor foci numbers were less in sleep restricted groups vs. normal sleep groups. A significant SLEEP by ACTIVITY interaction was exhibited ($p<0.01$). Exercise significantly decreased tumor loci in the normal sleep mice group ($p<0.05$), but not in the sleep restricted mice. No significant main ACTIVITY treatment effect was found. Skin lesions were observed in all of the sleep restricted, but none of the normal sleep mice.
Conclusion: Chronic sleep restriction reduced B16 lung tumor metastasis in mice. However, skin lesions elicited by sleep restriction could have pathological implications. Exercise training reduced tumor metastasis, but only in the normal sleep group.
Support (optional): Gatorade Sports Science Institute Grant

0914

GASTROESOPHAGEAL REFLUX IN CHRONIC SLEEP MAINTENANCE INSOMNIA

Vaughn B,[1] Madanick R,[2] Heidt-Davis P,[1] Alattar M,[2] Shaheen N[1]
(1) University of North Carolina at Chapel Hill, Chapel Hill, NC, USA, (2) University of North Carolina at Chapel Hill, NC, USA

Introduction: Insomnia may be exacerbated by a wide range of etiologies. Yet, little is known regarding the connection between "asymptomatic" GERD and insomnia.
Methods: To evaluate this potential relationship, we recruited 31 subjects with the history of chronic sleep maintenance insomnia (lasting over 6 months) with no identifiable cause, BMI < 30, no ongoing reflux therapy and no history of snoring. Subjects completed the GERD Symptom Assessment Scale (GSAS) and underwent simultaneous standard overnight polysomnography (PSG) and 24-hour dual-channel wired pH study off acid-suppressing medications. The subjects who were verified to have low sleep efficiency and apnea hypopnea index under 10 events /hour were given rabeprazole 20 mg BID for 2 weeks and underwent a second overnight sleep and pH study.
Results: Twenty subjects meet criteria for inclusion and seventeen completed both overnight studies. Sixteen subjects had adequate data for analysis. Baseline GSAS showed none or only trivial scores (none above 8 out of 45). Four subjects demonstrated Johnston-Demeester scores over 10 on the first study. Following treatment, three of the four increased their sleep efficiency above 86% whereas four of the twelve non GERD subjects showed normalization of sleep efficiency. Two of the four had a decrease in spontaneous arousals index of 10 events per hour compared to three of the twelve non GERD subjects demonstrated decrease. Repeated measures analysis showed significant improvement in spontaneous arousal index between the first and second study for the whole group ($p<0.0035$).
Conclusion: These preliminary results demonstrate that a significant subgroup of individuals may express insomnia as their subjective complaint of reflux and that these same individuals may improve objectively with treatment of their reflux. Larger study groups are needed to estimate the prevalence, but clinicians should consider reflux as a potential contributing factor for chronic sleep maintenance insomnia.
Support (optional): This study was financially supportted by Pricara/Essai Janssen

0915

GASTROESOPHAGEAL REFLUX DURING SLEEP IN PATIENTS WITH UNEXPLAINED SLEEP COMPLAINTS

Orr W,[1] Goodrich S,[1] Fernstrom P,[2] Hasselgren G[2]
(1) Lynn Health Science Institute, Oklahoma City, OK, USA, (2) AstraZeneca, Molndal, Sweden

Introduction: Sleep complaints are commonly noted among patients with gastroesophageal reflux disease. Studies have shown that treating nighttime heartburn improves subjective sleep reports. Complicated reflux disease has been noted to occur in individuals who are relatively asymptomatic with regard to heartburn, but since gastroesophageal reflux (GER) during sleep has been shown to cause sleep fragmentation the question arises as to whether sleep complaints may be a marker of "silent" sleep related GER. We studied patients with documented sleep disturbance without symptoms of heartburn, and a group of normal controls.
Methods: 55 subjects with documented sleep disturbance and 40 controls without symptoms of sleep disorders or heartburn were studied for two nights via polysomnographic evaluations that included distal esophageal pH recordings. Subjects kept a sleep log for two weeks and the sleep disturbance group had to have at least 6 nights of reported unrefreshed sleep to qualify, while the normals had to have at least 10 nights of satisfactory sleep. The two nights in the sleep laboratory were separated by at least one week.
Results: The sleep disturbance group had significantly lower sleep efficiency and longer sleep onset latency ($p < .01$). Of the sleep complaint group, 33% had at least one reflux event during the two sleep nights, which was not significantly different from the control group (32%). The average duration of reflux events was 40 minutes in the sleep disturbance group, and 17 minutes in the controls ($p > .05$). Acid contact time was significantly greater (4.4% versus .59%) in the sleep disturbance versus control groups ($p < .05$).
Conclusion: 1. A substantial proportion of individuals with unexplained sleep complaints may have significant sleep related GER. 2. An otherwise unexplained sleep disturbance may be an important marker for the presence of significant sleep related GER.
Support (optional): This study was supported by a grant from AstraZeneca.

0916

POOR PRE-CHEMOTHERAPY SLEEP PREDICTS DEPRESSIVE SYMPTOMS AND QUALITY OF LIFE DURING TREATMENT IN BREAST CANCER PATIENTS

Liu L,[1] Parker B,[2] Natarajan L,[2] Fiorentino L,[1] He F,[2] Johnson S,[1] Mills P,[3] Palmer B,[1] Ancoli-Israel S[1]
(1) University of California, San Diego, San Diego, CA, USA, (2) University of California, San Diego, CA, USA, (3) University of California, San Diego, La Jolla, CA, USA

Introduction: Sleep disturbances and depressive symptoms are common in breast cancer patients. Quality of life (QOL) is one of the most important concerns of cancer survivors. Sleep disturbances are correlated with depression and QOL. We hypothesize that breast cancer patients with poor pre-chemotherapy sleep have more symptoms during treatment.
Methods: Eighty-one women (mean age=51.3 years, SD=9.7, range 34-79) with newly diagnosed stage I-IIIA breast cancer were examined. All participants were scheduled to receive at least 4 cycles of chemotherapy. Sleep was measured with the Actillume wrist actigraph recorder (Ambulatory Monitoring, Inc, Ardlsey New York). The percent of total sleep time (%TST) was calculated. Depressive symptoms were assessed using the Center for Epidemiologic Studies-Depression (CES-D). QOL was assessed using the Functional Assessment of Cancer Therapy-Breast (FACT-B) and the Functional Outcomes of Sleep Questionnaire (FOSQ). Data were collected before (baseline) and during cycle 1 and cycle 4 treatments. Differences between those with mean %TST below the group mean (< 74.7%; Group 1; n=41) and those with %TST equal or above the group mean (> 74.7%, Group 2; n=40) were assessed using mixed-effects models. All analyses were performed using version 9 of SAS (SAS Institute Inc 2003).
Results: At baseline, there were no significant differences between the two groups in the total CES-D, FACT-B and FOSQ scores. There were significant group by time effects in the total CES-D score (p=0.037), total FACT-B score (p=0.0025), and total FOSQ score (p=0.034), with those with lower pre-treatment %TST experiencing more depressive symptoms and poorer QOL during chemotherapy.
Conclusion: Breast cancer patients with less sleep before chemotherapy suffer from more depressive symptoms and worse QOL during treatment. Improving the pre-treatment sleep might improve patients´ mood and QOL during chemotherapy.
Support (optional): Supported by NCI CA85264, NCI CA112035,

CBCRP 11IB-0034, CBCRP 11GB0049, NIH M01 RR00827 and the research service of the VASDHS.

0917

THE EFFECT OF SLEEP ON GASTROESOPHAGEAL REFLUX: IS SLEEP PROTECTIVE?

Orr W,[1] Goodrich S,[1] Fernstrom P,[2] Hasselgren G[2]
(1) Lynn Health Science Institute, Oklahoma City, OK, USA, (2) AstraZeneca, Molndal, Sweden

Introduction: It has been reported that gastroesophageal reflux (GER) occurring during the sleeping interval generally occurs in the first third of the night. Previous studies have reported GER predominately during stage 2 sleep, but there was not assessment of GER which accounted for the different time distribution of sleep stages. Since the distribution of rapid eye movement (REM) and non-REM (NREM) sleep is substantially different throughout the sleeping interval, we have hypothesized that REM sleep, which occurs predominantly during the last third of the sleeping interval, may be protective against GER. We have evaluated the occurrence of GER during REM and NREM sleep.
Methods: We have studied 55 subjects without heartburn but with sleep complaints and 40 normal asymptomatic individuals for two nights of polysomnographic recording that included pH recordings from the distal esophagus. Each reflux event was determined to be associated with REM sleep, NREM sleep, or wakefulness (WASO). All data from the 95 subjects were combined for these analyses.
Results: 26 subjects had GER on at least one night. 68 reflux events were identified. There were 29 events noted to occur during NREM sleep and 7 events noted to occur during REM sleep. When events per hour of each sleep stage were analyzed, there was no significant difference between REM and NREM. There was a significant increase of reflux events during WASO compared to sleep ($p < .01$).
Conclusion: 1. GER is not affected by sleep stage. 2. Sleep itself appears to provide a protective effect against GER.
Support (optional): This study was supported by a grant from AstraZeneca.

0918

EXAMINING RELATIONSHIPS AMONG FATIGUE, SLEEP, CIRCADIAN RHYTHMS, AND QUALITY OF LIFE DURING ADJUVANT BREAST CANCER CHEMOTHERAPY TREATMENTS

Berger A,[1] Fischer P,[2] Farr L,[2] Kuhn B[1]
(1) University of Nebraska Medical Center, Omaha, NE, USA, (2) University of Nebraska Medical Center, NE, USA

Introduction: This study evaluates relationships among fatigue, sleep, circadian rhythms, and Quality of Life (QOL) within a randomized control trial designed to modify fatigue.
Methods: Subjects (N=204) were randomized to the behavioral sleep intervention (BSI) or a healthy eating control group. They were post-operative for Stage I/II/IIIA breast cancer, receiving four or more anthracycline-based chemotherapy treatments (Tx) mean age 52.2 yrs (range 29-83). Most were married(73%), employed[μ=28.0 hrs(19.4)], and had some college(75%). Measurements were collected two days prior to, during, and 30 days after the last Tx, including: fatigue (Piper Fatigue Scale, PFS), subjective sleep (Pittsburgh Sleep Quality Index, PSQI); objective sleep and circadian rhythms (wrist actigraphy); and QOL (SF-36v2).
Results: Prior to Tx, there were no group differences on any variables; including total PFS [μ=2.69(2.4)], total PSQI [μ=6.98(6.0)], and eight QOL subscales. Correlations were significant in both groups between total PFS with total and most subscales of the PSQI and all subscales of the SF-36v2 ($p < .01$-$.001$). There were no significant correlations between PFS and actigraphy variables. During intervention, correlations remained highly significant in both groups between PFS, PSQI and SF-36v2 scores; there also were significant negative correlations in the BSI group between PFS and circadian rhythms. There were no significant differences over time between groups on subjective measures, however circadian rhythms in the BSI group trended toward significance ($p<.09$). After treatment, there were continued associations between PFS, PSQI, all SF-36v2 scores in both groups, and fatigue and circadian rhythms in the BSI group.
Conclusion: Higher fatigue was consistently related to poorer sleep and QOL. Lower fatigue was consistently related to higher circadian rhythms in the BSI group. Changes occurred during treatment; most values didn't return to baseline by 30 days. Results will be compared to long-term results of the BSI on reducing fatigue and maintaining sleep and QOL.
Support (optional): Funded by NIH, 5R01NR007762-05

0919

SLEEP, BREATHING, AND NEUROBEHAVIOR IN COPD: PILOT STUDY

Reishtein J,[1] Kuna S,[2] Weaver T[2]
(1) Drexel University, Philadelphia, PA, USA, (2) University of Pennsylvania, Philadelphia, PA, USA

Introduction: Deficits in neurobehavior have been shown in COPD, possibly associated with the poor sleep and oxygen desaturations experienced by patients. There has been limited exploration of these associations. We present preliminary data describing the association between pulmonary parameters and sleep quality, and the impact of sleep quality on neurobehavior.
Methods: Subjects with COPD (FEV1 < 60% predicted for gender, age, and height) were recruited from a pulmonology clinic during routine visits. For one week, subjects wore an ambulatory pulse oximeter (one day) and accelerometer, and completed a sleep diary. All subjects completed the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), a 4 word memory recall test, a psychomotor vigilance task (PVT), a computerized digit-symbol substitution test (DSST), and a finger tapping test.
Results: Nine subjects (mean age 65.0 ± 7.29 years, FEV1 45.50 ± 13.06% predicted, and FEV1/FVC 51.13 ± 15.83) have been studied. Sleep quality is below normal, with PSQI global scores ranging from 5 to 11 (mean 7.78 ± 2.11). PSQI correlated moderately with number of minutes during sleep SO2 < 88% ($r = .45$), but minimally with baseline SO2 or the SO2 nadir. Additionally, PSQI had a moderate correlation with FEV1% predicted ($r = -.44$), but small correlation with FEV1/FVC ($r = -.27$). Sleep quality also demonstrated small to moderate correlations with neurobehavioral measures, including short term memory ($r = -.36$), PVT (reaction time $r = .69$, trend $p = .08$; lapses $r = .59$), finger tapping ($r = -.46$), and executive function (DSST $r = -.24$;
Conclusion: Although we present a small sample size (data collection is ongoing), this preliminary data suggests that pulmonary parameters are related to sleep quality, which impacts neurobehavioral performance. The nature of this relationship will be delineated in the modeling of these variables using a larger sample.
Support (optional): NHLBI T32-HL07953; Hartford Center for Geriatric Nursing Excellence Frank Morgan Jones Fund grant for pilot study, University of Pennsylvania

0920

SLEEP SYMPTOMS OF MEXICAN AMERICAN VETERANS WITH AND WITHOUT DIABETES

Baldwin C,[1] Bell I,[2] Silva Torres G,[3] Mays M,[3] Quan S[2]
(1) Arizona State University, Phoenix, AZ, USA, (2) University of Arizona, Tucson, AZ, USA, (3) Arizona State University, AZ, USA

Introduction: Rates of diabetes in Mexican Americans are twice those of non-Hispanic whites (NHW), yet little is known about sleep and medical problems of Mexican Americans.
Methods: Male Mexican American veterans 54-85 years old (n=109) with and without physician diagnosed Type 2 diabetes completed the Sleep Heart Health Study Sleep Habits and Centers for Epidemiological Studies—Depression (CES-D) questionnaires. Demographic, health and anthropometric data were also obtained. Analyses included Chi-square for nominal variables, ANOVA for continuous variables. Significance was set at $p<0.05$.
Results: Thirty-two percent of Mexican American veterans had MD-diagnosed diabetes. Veterans with diabetes were significantly more likely to have elevated BMI (30 SD 5 versus 27 SD 3, $p<0.01$), and higher CES-D scores (16 SD 11 versus 10 SD 8, $p<0.01$) compared to Mexican American veterans without diabetes. Diabetic Mexican Americans were nearly four times more likely to self-report restless legs syndrome (RLS) compared to non-diabetic Mexican Americans (OR=3.9; CI: 1.5-10.3). Diabetics also reported higher rates of snoring (79% to 54%, $p<0.05$) and were significantly more likely to have physician-diagnosed obstructive sleep apnea (OSA) (13% to 2%, $p<0.05$). There were no differences between diabetic and non-diabetic Mexican Americans on other demographic and health variables, including age, education, smoking pack years, or blood pressure. Diabetic and non-diabetic Mexican Americans did not differ for other sleep symptoms, including insomnia, insufficient sleep, or daytime sleepiness; however, rates for these sleep symptoms were higher for diabetic compared to non-diabetic Mexican American veterans.
Conclusion: Findings suggest that Mexican American veterans with Type 2 diabetes are at greater risk for RLS, significantly more likely to snore, and to have OSA. The RLS might be linked to diabetes-related peripheral neuropathy. Associations between RLS and depression have been reported in NHW patients. Future studies need to examine these relationships with larger samples of Mexican American men and women.
Support (optional): This work was supported by a Southern Arizona VA Health Care System Minority Vascular Center grant (Drs. Baldwin and Bell) and, in part, by NHLBI cooperative agreement supplement U01HL53938-07S1 (Dr. Baldwin).

0921

ASSOCIATION OF SLEEP DURATION WITH HEMOGLOBIN A1C AND FASTING PLASMA GLUCOSE

Nakajima H,[1] Kaneita Y,[1] Ohida T,[1] Takahashi I,[2] Umeda T,[2] Sugawara N,[2] Nakaji S[2]
(1) Nihon University, Itabashi-ku, Tokyo, Japan, (2) Hirosaki University, Hirosaki, Japan

Introduction: It has been increasingly recognized that sleep habits are potential risk factors for diabetes mellitus. The association between hemoglobin A1c or fasting plasma glucose, and sleep duration is still not well understood. We examined the associations of hemoglobin A1c and fasting plasma glucose with sleep duration.
Methods: Subjects of this study were residents in a rural community of Japanese Tohoku provinces. The subjects included in the statistical analysis were 406 men and 656 women aged 20 years or more. Data of sleep habits were collected by a self-reported questionnaire. Hemoglobin A1c and fasting plasma glucose level were included in blood tests. Logistic regression analyses were performed in order to examine the associations between sleep duration and hemoglobin A1c level, and sleep duration and fasting plasma glucose level. These analyses were adjusted for the following items: sex, age, blood pressure, body mass index, plasma triglyceride level, insomnia symptoms, and use of hypnotic medication.
Results: Significant associations were observed between sleep duration and both high hemoglobin A1c (6.5% or more) and high fasting plasma glucose (126 mg/dl or more). The adjusted odds ratios for high hemoglobin A1c in subjects who slept less than or more than 6–8 hours per night were higher than for subjects who slept for 6-8 hours.
Conclusion: Both short and long sleep durations are associated with an increased prevalence of high hemoglobin A1c. It is important to implement preventive measures against diabetes mellitus based on knowledge of its association with sleep duration.

0922

COGNITIVE BEHAVIORAL PAIN MANAGEMENT PROGRAMME HAS LITTLE IMPACT ON SLEEP OF PEOPLE IN PAIN.

Ashworth P,[1] Burke B,[2] McCracken L[3]
(1) Gloucestershire Hospitals NHS Foundation Trust, Gloucester, United Kingdom, (2) Gloucestershire Hospitals NHS Foundation Trust, United Kingdom, (3) Royal National Hospital for Rheumatic Diseases, Bath, UK, United Kingdom

Introduction: Poor sleep is commonly reported by people with chronic pain. A cognitive behavioral Pain Management Programme (PMP) might be expected to impact on sleep. Elements of the programme include stress management, relaxation, exercise, and pacing, as well as the specific sessions targeting sleep hygiene, beds, and advice about managing sleep related medication. The impact of such interventions on sleep has not been examined using validated measures of sleep.
Methods: 42 outpatients completed a postal questionnaire before and after attending the PMP. There was no control group. Measures included pain severity, pain related disability, pain related anxiety, depression, sleep quality (Pittsburgh Sleep Quality Index) and beliefs about sleep (Dysfunctional Beliefs and Attitudes about Sleep Questionnaire - 16 item version).
Results: After PMP there was improvement in some ratings of daytime (but not nighttime) pain, pain related disability ($p=0.05$) pain related anxiety ($p<0.05$), depression ($p<0.001$). Sleep quality (PSQI) improved ($p<0.05$). The improvement in PSQI global score was associated with improvement on the PSQI subscales of sleep onset latency, use of sleeping medication and daytime dysfunction. The mean reduction in sleep onset latency was 8.06 minutes. The remaining subscales of the PSQI (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance) showed no significant change. Beliefs about sleep showed no significant change. Multiple regression analysis indicates that change in sleep quality is associated with change in disability.
Conclusion: The PMP had the expected impact on pain, disability and mood. Whilst ratings of some aspects of sleep quality improved, reported sleep patterns showed little change. The results reflect the challenge of improving sleep amongst people with chronic pain. Cognitive behavioural interventions for insomnia have been successful in people with chronic pain (Currie et al 2000, Edinger et al 2005). The integration of the two approaches might improve outcomes.

0923

PREVALENCE OF SLEEP APNEA IN TYPE 1 DIABETES PATIENTS

Porto-Silva C,[1] Rolim L,[2] Poyares D,[3] Tufik S,[4] Silva A,[3] Dib S[3]
(1) UNIFESP, São Paulo, Sao Paulo, Brazil, (2) Sao Paulo, Brazil, (3) SP, (4) Univ Fed Sao Paulo, Sao Paulo, Sao Paulo, Brazil

Introduction: The observation of sleep-disordered breathing (SDB) in diabetic patients has deserved the attention of researchers in the last two decades. Some authors have already correlated the occurance of sleep apnea with diabetes chronic complications. Our aim was to compare the prevalence of SDB in type 1 diabetic patients and controls without diabetes, all young and nonobese.
Methods: We studied 25 type 1 diabetic patients and 22 healthy individuals, paired by age, sex and BMI. All subjects were submitted to the Epworth Somnolence Score (ESS) and to a polysomnography according to the recommendations of the ASDA. The statistical analysis was made by chi-square and t-tests. A probability value of 0.05 was considered significant.
Results: The mean age of the diabetic group was 27 years-old (±7.2), while the control group was 23.2 (±3.9). In the diabetic group there were 15 women and 10 men, and the control group was divided in 13 women and 9 men. The mean BMI was 23 kg/m2 (±2.7) for the DM1 group and 21.8 kg/m2 (±2.1)for the non-DM1. The ESS showed statistical difference between both groups (p=0.004). The sleep architecture didn´t reveal significant differences (p>0.05). We observed that 28% of the diabetic patients presented more than 5 apneas/hypopneas per hour, in contrast to 4.5% of the non-diabetics, leading to a statistical significant difference between the groups (p=0.03). Although not statistically significant (p=0.14), we observed that the diabetic patients have a tendency to present central apneas (3 DM1 vs 0 Non-DM1).
Conclusion: The type 1 diabetic group showed significant higher prevalence of obstructive apneas compared to the control group. Also, the diabetic patients presented more daytime sleepness than the control individuals. Finally, our data suggest that, even though they present breathing disorders, young patients with the diagnosis of type 1 diabetes don´t have significant changes in the sleep architecture.

0924

NOCTURNAL PULSE OXIMETRY PATTERNS AMONG LATE-STAGE LUNG, BREAST AND COLORECTAL CANCER PATIENTS

Vena C,[1] Bliwise D,[2] Ribiero M,[3] Harris W,[3] Kohles-Baker M,[2] Parker K[1]
(1) Emory University, Atlanta, GA, USA, (2) Emory University, GA, USA, (3) Atlanta Veterans Administration Medical Center/Winship Cancer Institute, GA, USA

Introduction: Pulse oximetry is often used to screen for sleep disordered breathing (SDB). We performed an analysis of nocturnal pulse oximetry in cancer patients to examine patterns and associated features.
Methods: The sample included 71 outpatients (28 lung, 15 colorectal, 28 breast) with a mean age of 53.86±8.82 years. Thirty eight subjects (53.5%) were female and 54.9% were African-American. All subjects underwent 48-hours of pulse oximetry in conjunction with ambulatory polysomnography as part of a larger study of pain, opioids and sleep. Subjects were assessed for high hypoxic burden (>20% total sleep time [TST] with SaO2 <90%) and for Oxygen Desaturation Index (ODI) (number of SaO2 drops of ≥ 4% for at least 10 seconds per sleep hour). Threshold for ODI was defined as >10/hour of sleep. Data were averaged over the 2 nocturnal recordings. Association of oximetry patterns to demographic, clinical, and treatment variables was examined by non-parametric correlations and logistic regression.
Results: While the breast cancer group differed relative to gender (p<.001), younger age (p=.002), and higher BMI (p=.005), there were no other significant group differences relative to demographic, clinical, or treatment factors. Atypical oximetry patterns were identified in 45.1% of subjects (12.7% hypoxic burden; 39.4% high ODI). Correlates of oximetry differed among cancer groups. Hypoxic burden was associated with a lower BMI and functional status (p=.02) in the lung group and a higher BMI and number of morphine equivalents (MEQ) taken during the recording period (p=.005) in the breast group. No correlates were identified in the colorectal group. A higher BMI was associated with ODI in all groups, however, MEQ also contributed significantly to ODI in the colorectal (p=.002) and breast (p=.001) groups.
Conclusion: These data suggest that a substantial number of cancer patients may experience SDB secondary to the disease process and/or treatments, as well as known clinical risk factors.
Support (optional): National Institute of Nursing Research RO1 NR008124 and P20 NR07798: PI, Kathy P. Parker, PhD

0925

SLEEP IMPROVEMENT IN CHRONIC OSTEOARTHRITIS PAIN PATIENTS WITH MORNING DOSING OF ONCE-A-DAY EXTENDED RELEASE MORPHINE SULFATE

Rosenthal M,[1] Moore P,[1] Groves E,[2] Schlosser L,[2] Dziewanowska Z,[2] Negro-Vilar A[2]
(1) California Clinical Trials, San Diego, CA, USA, (2) Ligand Pharmaceuticals, San Diego, CA, USA

Introduction: A-MQD (AVINZA®) is an oral, once-a-day, extended-release morphine capsule approved for treatment of chronic, moderate-to-severe pain. Osteoarthritis pain patients taking A-MQD reported improved sleep quality (Caldwell et al 2002); moreso when dosed in the morning compared to evening. This study investigated the effect on PSG measures of morning dosing of A-MQD in a population of chronic osteoarthritic pain patients complaining of sleep difficulties.
Methods: This was a single center, placebo lead-in, open label study of 30mg or 60mg A-MQD. Thirty-four patients (26 to 75 y.o.) complaining of sleep difficulties and chronic pain secondary to a diagnosis of osteoarthritis of the hip or knee, stable on previous pain medication (only intermittent opiates allowed), were enrolled. Patients underwent three PSG recordings: at screening on current pain medication, at the end of single-blind placebo run-in, and at the end of treatment. Neurocognitive testing, as well as self-assessments of mood, sleep and sleepiness were obtained at these timepoints. After placebo run-in, patients received A-MQD 30 mg/day for 6 days. At Day 6, patients who met the criteria for incomplete pain relief had their dose increased to 60 mg/day. Treatment continued for another 8 days at the new dose level (14 days for a subgroup at 60 mg/day).
Results: Sleep was strikingly impaired on prior pain therapy. On A-MQD, sleep maintenance tended to improve as demonstrated by increased TST and sleep efficiency and decreased WASO and NAW compared to placebo baseline. Some increases in stage 2 and 3/4 sleep were seen compared to placebo baseline. Subjective ratings of sleep quality and subjective sleep time were significantly improved with treatment, as were pain scores and ratings of medication acceptance and pain relief.
Conclusion: A-MQD is an effective treatment for pain and improves both objective and subjective sleep parameters in patients with chronic osteoarthritic pain.
Support (optional): Sponsored by Ligand Pharmaceuticals, Inc.

0926

SLEEP DISTURBANCE IN MENOPAUSE

Freedman R,[1] Roehrs T[2]
(1) Wayne State University, Detroit, MI, USA, (2) Henry Ford Hospital Detroit, Detroit, MI, USA

Introduction: Although most epidemiologic studies have found increased reports
of disturbed sleep at menopause, this has not been confirmed by laboratory sleep studies. Moreover, the effects of menopausal hot flashes upon sleep are not clear. Here, we sought to determine the sources of sleep complaints in peri- and postmenopausal women reporting disturbed sleep.
Methods: 102 women, of ages 44 – 56 years, who reported disturbed sleep were recruited though newspaper advertisements. They were given the Pittsburgh Sleep Quality Index (PSQI) and the Hamilton Anxiety and Depression scales. Those using illicit drugs or medications that would affect hot flashes or the sleep EEG were screened out. Results were analyzed by multiple regression.
Results: 56% of the women demonstrated hot flashes in the laboratory. 53% of the women had apnea, periodic leg movements or both. The best predictors of objective sleep quality (laboratory sleep efficiency) were apneas, periodic leg movements, and arousals ($R2 = .44$, $P < .0001$). The best predictors of subjective sleep quality (PSQI Global Score) were Hamilton Anxiety score and number of hot flashes in the first half of the night ($R2 = .19$, $P < .001$).
Conclusion: Primary sleep disorders: apnea and restless legs syndrome, are common in this population. Amelioration of hot flashes may reduce some complaints of poor sleep, but will not necessarily alleviate underlying primary sleep disorders. Since these can result in significant morbidity and mortality, they require careful attention in peri- and postmenopausal women.
Support (optional): Supported: R01-MH63089 to RRF

0927

EFFECT OF BRIGHT LIGHT THERAPY ON SLEEP TIME IN WOMEN UNDERGOING CHEMOTHERAPY: PRELIMINARY RESULTS

Trofimenko V,[1] Rissling M,[2] Liu L,[3] Natajaran L,[4] Lawton S,[3] He F,[5] Cornejo M,[3] Ancoli-Israel S[3]
(1) Dept of Psychiatry, University of California, San Diego, San Diego, CA, USA, (2) SDSU/UCSD Joint Doctoral Program in Clinical Psychology, San Diego, CA, USA, (3) Dept. of Psychiatry, University of California, San Diego, La Jolla, CA, USA, (4) Dept Community and Family Medicine, University of California, San Diego, San Diego, CA, USA, (5) University of California, San Diego, La Jolla, CA, USA

Introduction: Studies have shown that women with breast cancer undergoing chemotherapy report disturbed sleep. Studies have also suggested that these women have very little bright light exposure, yet it is known that bright light can improve sleep. We present preliminary data from an on-going study that addresses whether bright light improves sleep in women with breast cancer undergoing chemotherapy.
Methods: Eleven women (mean age=50.3 yrs, SD=8.4, range: 35-70 yrs) diagnosed with stage I–III breast cancer, scheduled to receive at least 4 cycles of adjuvant anthracycline-based chemotherapy participated. Participants were randomized into one of two treatment groups: bright white light (BWL; n = 7) or dim red light (DRL; n = 4). Both groups were instructed to self-administer light therapy (Litebook Co, LTD) for 30 minutes every morning throughout 4 cycles of chemotherapy. Actigraphy (Ambulatory Monitoring, Inc. and Respironics) was used to record sleep/wake activity for 72-hours at baseline (pre-chemotherapy) and during the last week of cycle 4 (C4).
Results: In the BWL group, TST increased by 28 minutes (SD=69), while WASO stayed approximately the same. In the DRL group TST decreased by 32 minutes (SD=30), while WASO increased by 27 minutes (SD=39).
Conclusion: Preliminary results suggest that bright white light may be having a positive effect on sleep; however, additional data are needed to demonstrate the possible significance of these effects.
Support (optional): CBCRP 11IB-0034, NCI CA112035-01A and the research service of the VASDHS.

0928

ACTIGRAPHY IN MONOZYGOTIC TWINS DISCORDANT FOR CHRONIC FATIGUE SYNDROME

Watson N,[1] Jacobsen C,[2] McCurry S,[3] Buchwald D,[2] Afari N[4]
(1) Department of Neurology, University of Washington, Seattle, WA, USA, (2) Department of Medicine, University of Washington, Seattle, WA, USA, (3) Department of Psychosocial and Community Health, University of Washington, Seattle, WA, USA, (4) Department of Psychiatry, University of California, San Diego, San Diego, CA, USA

Introduction: Chronic Fatigue Syndrome (CFS) is a heterogeneous disorder of excessive fatigue of 6 months duration. Although subjective unrefreshing sleep is a defining symptom of CFS, studies confirming objective differences in sleep quality have been lacking. We used a co-twin control study design to compare objective (actigraphy) and subjective (sleep diary) sleep indices in monozygotic twins discordant for CFS.
Methods: Thirteen pairs of monozygotic twins (mean age 44 years, 12 female pairs) discordant for CFS completed 14 consecutive nights of actigraphy and sleep diaries. Diary reports included estimates of sleep latency, nocturnal awakenings, total sleep time, sleep quality, and subjective rest upon awakening. Data were analyzed using a random effects regression model comparing fatigued twins to their non-fatigued co-twins. This approach accounted for the strong genetic influence on sleep.
Results: Actigraphy revealed that, on average, fatigued twins were in bed longer (504 vs. 441 minutes, $p=0.02$) and slept longer (495 vs. 435 minutes, $p=0.02$) than their non-fatigued co-twins. However, sleep latency ($p=0.85$), sleep efficiency ($p=0.44$), wake after sleep onset ($p=0.66$), and sleep fragmentation index ($p=0.39$) did not differ between the twins. On sleep diaries, fatigued twins endorsed significantly longer sleep latencies ($p=0.01$), greater nocturnal awakenings ($p=0.01$), worse sleep ($p=0.01$) and feeling worse upon awakening ($p<0.001$) than their non-fatigued co-twins. Subjective total sleep time was not different ($p=0.24$).
Conclusion: Fatigued twins spent more time in bed and slept longer than their non-fatigued co-twins, with no subjective difference in sleep time and similar objectively measured sleep efficiencies and latencies. Fatigued twins reported worse sleep quality and feeling worse upon awakening than their non-fatigued co-twins. The longer sleep times may reflect the fatigued twins´ attempts to resolve their chronic daily fatigue.
Support (optional): NIH NIAID U19AI38429-05

0929

ASSOCIATIONS OF PHYSICAL ACTIVITY, DEPRESSION, AND SLEEP DURATION WITH CORONARY HEART DISEASE

Jean-Louis G,[1] Zizi F,[1] Bijoux C,[2] Dim R,[2] Mckenzie D,[2] Shaheen S,[2] Clark L[2]
(1) State University of New York Health Science Center at Brooklyn, Brooklyn, NY, USA, (2) State University of New York Health Science Center at Brooklyn, NY, USA

Introduction: This study examined the independent associations of physical activity, depression, and sleep duration with coronary heart disease (CHD).
Methods: A total of 29,818 adults representative of the civilian U.S. population (mean age = 48 ± 18 yrs; range: 18-85) participated in the 2005 National Health Interview Survey (NHIS). The NHIS is a cross-sectional household interview survey, which uses a multistage area probability sampling technique. The sample included Whites (85%) and Blacks (15%) of both genders: men = 44% and women = 56%. Trained interviewers from U.S. Census Bureau conducted face-to-face interviews soliciting information about physician-diagnosed chronic conditions and sociodemographic data. Respondents estimated habitual sleep duration and rated physical activity. Depressed moods experienced in the past 30 days were assessed.
Results: Of the sample, 35% reported functional limitation due to chronic conditions: hypertension (28%), heart disease (8%), cancer (8%), diabetes (9%), and arthritis (23%). The rate of CHD among Whites and Blacks was 5.2% and 4%, respectively; among men and women, rates were 6.2% and 4.1%, respectively. Results of Fisher´s exact tests indicated respondents with CHD were more likely to report short (≤ 5 hrs) or long (≥9 hrs) sleep duration [26% vs. 16%; $\chi^2 = 72$, $p<0.0001$] than their counterparts. They were less likely to engage in physical activity, anchored either by ability to walk ¼ mile [43% vs. 83%; $\chi^2 = 1101$, $p<0.0001$] or ability to climb 10 steps [53% vs. 86%; $\chi^2 = 895$, $p<0.0001$]. ANOVA results indicated that they were more depressed [$F = 163$, $p<0.0001$]. According to logistic regression results, of those three factors physical activity was the strongest predictor of CHD [Wald = 195, $p<0.0001$].
Conclusion: Physical activity, depression, and sleep are associated with coronary heart disease, but physical activity was the best predictor even after adjustment for sociodemographic factors and health characteristics.
Support (optional): This research was supported by funds from NIH (1R24MD001090).

0930

POWER SPECTRAL ANALYSIS OF NONREM SLEEP IN CHRONIC PAIN PATIENTS

Jungquist C,[1] Pigeon W,[1] Perlis M,[2] Swan J,[3] Leonard M,[3] Howard E,[3] Odhiambo S[3]
(1) University of Rochester, Rochester, NY, USA, (2) NY, USA, (3) University of Rochester, NY, USA

Introduction: The sleep of chronic pain patients has often been characterized as including excessive alpha activity. A small number of studies have also noted power spectral changes in other EEG frequency bands, although the results have been mixed. The current study assesses multiple frequency bands during the NREM sleep in chronic pain patients.
Methods: From a sample of 44 chronic back pain patients (CPP) with chronic insomnia, 18 subjects were matched to a sample of 18 good sleepers (GS) on BMI (group means: 24.6 vs. 23.9), age (41.9 vs. 37.6), and gender (5 males per group). PSG data were obtained from the first night of sleep. Data from frontal and central leads were subjected to power spectral analysis using Stellate Harmonie software. Power spectral data for delta, theta, alpha, sigma, beta-1, beta-2, gamma, and omega frequencies were assessed in terms of relative power for the first 4 NREM cycles. Epochs scored as stage wake or with arousals were excluded. Two-tailed, independent sample t-tests were performed to compare group means for each frequency band and each site.
Results: There were no significant differences in sleep architecture between the CPPs and GSs. Of the sleep continuity findings, CPPs had significantly more WASO (p=.05). Power spectral measures revealed that CPPs had significantly less delta activity (p=.001) and significantly more theta (p=.001), beta1 (p=.002), and beta2 (p=.04) activity than GSs. These differences were more pronounced in frontal leads and diminished over successive NREM cycles, such that by Cycle 4 only delta (p= .001) and beta1 (p= .01) differences remained significant. Finally, although there was a trend for increased alpha in CPPs in each cycle and at each site, none of these differences reached significance.
Conclusion: Despite nonsignificant differences in sleep architecture, CPPs exhibit significantly less delta, more theta and beta activity than GSs. Given prior work showing an increase in alpha activity in chronic pain samples, our lack of such a finding is surprising. Decreased delta and increased beta activity are consistent with findings from primary insomnia samples. Further studies are needed to investigate whether the effects observed may be ascribed to the use of pain medications, the lack of pain during PSG, and/or to the presence of insomnia.
Support (optional): NIH NS049789; NIH NR009080; UR School of Nursing data management team

0931

OBJECTIVE AND SUBJECTIVE POSTPARTUM SLEEP DISTURBANCE AND DEPRESSIVE SYMPTOMS

Clegg M, Gould C, Montgomery-Downs H
West Virginia University, Morgantown, WV, USA

Introduction: Fatigue, sleep disruption, and mood disturbances are common following childbirth. Few studies have included objective measures of maternal sleep or napping. The purpose of the current analyses was to investigate relations between subjective and objective postpartum sleep measures and depressive symptoms.
Methods: Beginning at 8 weeks postpartum, daily palm-based sleep quality ratings (scale:0-100) were collected. Mothers completed the Edinburgh Postnatal Depression Scale (EPDS) and Beck Depression Inventory (BDI) on postpartum weeks 10 and 11, respectively, concerning their symptoms during the previous week. Total sleep time (TST) and sleep efficiency were calculated from actigraphy and included napping periods.
Results: The first 17 participants in a larger study were 28.7 (SD±4.7) years, 88% Caucasian and 47% primiparous. BDI (M=6.5,SD±3.3) at postpartum week 10 was negatively correlated with sleep efficiency during the preceding week ($r=-.563$;$p<0.05$). EPDS (M=4.0,SD±2.6) at postpartum week 11 was positively correlated with self-reported sleep quality during the preceding week ($r=.587$;$p<0.05$). BDI and EPDS were not significantly correlated with each other (p=0.07) or TST. There were no significant parity effects for objective or subjective sleep measures, BDI, or EPDS.
Conclusion: Findings suggest that the BDI may be most useful when analyzing objective sleep measures, while the EPDS may be more effective when utilizing subjective sleep measures. It is possible that counterintuitive results relating higher scores on the EPDS to higher subjective measures of sleep quality may be attributed to inaccurate self-analysis of sleep quality for mothers scoring higher on the EPDS, or perhaps the finding is due to the sub-clinical level of depressive symptoms among the sample. One goal of the larger study is to determine whether sleep-related questions on the BDI influence its relationship with objective sleep measures.

0932

THE EFFECTS OF AGE AND WORK STATUS ON SLEEP DURING PREGNANCY

Gardiner A, Gay C, Lee K
University of California, San Francisco, San Francisco, CA, USA

Introduction: The mean age of first-time mothers has increased by nearly 4 years since 1970, and a growing number of women are delaying motherhood until after they have established careers. Few studies have investigated the influence of maternal age and work status on sleep during pregnancy.
Methods: A sample of 229 women was assessed in their last month of pregnancy. Wrist actigraphy and sleep diaries were used to measure sleep over 48 hours. The General Sleep Disturbance Scale was used to assess perceptions of sleep and daytime function. The women were grouped by age (<25, 25-34, or 35+ yrs).
Results: The age groups differed in time in bed (TIB; p<.001), total sleep time (TST; p=.043), wake after sleep onset (WASO; p=.036) and time of waking (p=.005). Those <25 had the longest TIB (548±77 mins), longest TST (430±93 mins), most WASO (18.8%±14.5%), and latest wake time (08:28±1:34), while those 25-34 had the least WASO (14.6%±11.0%), and those 35+ had the shortest TIB (492±68 mins), shortest TST (394±72 mins) and earliest wake time (07:40±1:24). Older women reported more problems with sleep maintenance (p=.004) and too little sleep (p=.029). The age groups differed in work status, with 4% of women <25, 45% of women 25-34, and 48% of women 35+ working at the time of assessment. Regardless of age, working women had earlier bed and wake times, less daytime sleep, and less WASO.
Conclusion: Women starting a family later in life are more likely to have established careers and more restricted sleep schedules. The older women in this sample were more likely to be working late in pregnancy, spent less time in bed, and obtained less sleep, although their sleep was more consolidated than that of younger women. Older women´s subjective experience of insufficient and disrupted sleep has implications for the growing group of older childbearing women.
Support (optional): NIH Grant #R01 NR05345, KA Lee, P.I.

0933

POLYSOMNOGRAM IN SLEEP APNEA AND PULMONARY HYPERTENSION

Ricaurte B,[1] Minai O,[2] Golish J,[3] Kaw R,[4] Mansoor M[5]
(1) Cleveland Clinic Foundation, westlake, OH, USA, (2) Cleveland Clinic Foundation, OH, USA, (3) Cleveland Clinic, Cleveland, OH, USA, (4) Cleveland Clinic Foundation, Cleveland, OH, USA, (5) New York College of Osteopathic Medicine, NC, USA

Introduction: Although, sleep disordered breathing (SDB) is an established etiology of pulmonary hypertension (PHT) associated with hypoxemia, this relationship has been understudied with moderate observational studies and few interventional studies and data has been inconsistent.
Since the more severe forms of (PHT) are not uncovered until late in their coarse, high level of suspicion is required when evaluating SDB. The objective of this study is to evaluate polysomnogram (PSG) variables to predict PHT in patients referred for evaluation of SDB. This Observation will help increase the awareness of sleep specialist of coexistent PHT that has an impact on cardiovascular morbidity and mortality.
Methods: This is a retrospective, descriptive study of all patients underwent right heart catheter (RHC) and PSG at the Cleveland Clinic Foundation between 2000-2005. A total of 112 complete data was available.
It was divided into 3 groups: without pulmonary hypertension (no PHT=29.5%), pulmonary arterial hypertension (PAH=24%), and pulmonary venous hypertension (PVH=46.5%)
SDB: Apnea hypopnea index (AHI) > 5
Data from: RHC, PSG, 2 D echocardiogram and pulmonary function tests were included.
Descriptive statistical analysis was used to compare between groups by using student t-test.
Results: Patients who underwent RHC and PSG:
Prevalence of PHT was 70.5% and PHT among SDB (AHI > 5) was 67.4
Analysis of PSG variables: we found that irrespective of AHI, nocturnal desaturation was the only significant factor to predict pulmonary arterial hypertension, with no significant difference among confounding factors: Age, Body mass index, LVEF, FEV1
Nocturnal Desaturation was 33% in patients with pulmonary hypertension in comparison to 11% in patients with no pulmonary hypertension.
Other PSG variables were not significantly different.
Conclusion: Nocturnal desaturation is the most significaant predictor of pulmonary arterial hypertension in PSG variables regardless of severity of respiratory events.
We need prospective studies to test this observation on the short and long term
and to Investigate the degree and chronicity of Nocturnal desaturation that may lead to irreversible pulmonary hypertension.

0934

THE RELATIONSHIP BETWEEN SLEEP DISTURBANCES AND PAIN, MOOD, AND DISEASE ACTIVITY IN POSTMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

Bourguignon C, Taylor A
University of Virginia, Charlottesville, VA, USA

Introduction: Sleep disturbances have been linked to pain, mood, and disease activity in adults with rheumatoid arthritis (RA). However, less is known about sleep disturbances in postmenopausal women with RA.
Methods: Women provided subjective ratings of pain (NRS 0-10 and McGill Pain Questionnaire – Short Form), depression (CESD), negative affect (PANAS), arthritis helplessness (Arthritis Helplessness Index), and sleep disturbances (Pittsburgh Sleep Quality Index, and General Sleep Disturbance Scale). Objective sleep disturbances were measured by wrist actigraphy. Actigraphs were worn for 3 consecutive nights and sleep parameters were averaged over the 3 nights.
Results: The sample consisted of 44 postmenopausal women with RA. These women had a mean age of 60.8 (SD=7.7) years, with 13.3 (2.9) years of education, and with a mean duration of RA of 10.7 (11.4) years. The NRS mean for average pain was 4.7 (1.6) and for worst pain 6.4 (1.9). The mean CESD score was 12.0 (7.8), with 36.6% of women scoring above the cutoff of 16 indicating clinical depression. Actigraphy indicated that women slept a mean of 6.7 (1.7) hours, with a mean of 24.1 (23.9) minutes of sleep latency, and a low sleep efficiency mean of 78.2% (18.1). Women´s estimates of subjective sleep parameters closely approximated the objective actigraphy results. Moderate correlations were found between sleep disturbances and pain, mood, and RA disease activity. As pain, helplessness, negative affect, and RA disease activity increased, sleep efficiency decreased. Increases in pain and helplessness were associated with increased sleep latency.
Conclusion: The mean sleep efficiency for postmenopausal women with RA was low, indicating that the majority of these women had some sleep disturbance. Those women with higher levels of pain, arthritis

helplessness, negative affect, and disease activity had more sleep disturbances. Women had moderate pain levels in spite of taking medications for RA.
Support (optional): This study was supported by Grant Numbers 1 R21 AT 01469-02 and 5-K30-AT000060 from the National Center for Complementary and Alternative Medicine (NCCAM). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCCAM, NIH.

0935

CLINICAL ASSOCIATIONS OF COMPLEX SLEEP APNEA IN THE SLEEP HEART HEALTH STUDY

Pogach M,[1] Weiss M,[1] Mietus J,[1] Peng C,[1] Gottlieb D,[2] Goldberger A,[1] Thomas R[1]
(1) Beth Israel Deaconess Medical Center, Boston, MA, USA, (2) Boston University, Boston, MA, USA

Introduction: Complex sleep apnea (complex SA) is a newly recognized subset of SA, characterized by induction, by the application of positive airway pressure (PAP), of central apneas and periodic breathing in those with apparent obstructive SA on the diagnostic polysomnogram (PSG). Using a continuous single lead ECG, heart rate variability and respiratory modulation of R wave amplitude are mathematically combined to generate sleep spectrograms. Preliminary data (unpublished) shows that a distinct spectrographic phenotype of unstable cardiopulmonary oscillations marked by narrow-band elevated low frequency coupling (NB-eLFC) detects chemoreflex modulation or mediation of SA, and that this marker predicts PAP failure (i.e., detects complex SA on the diagnostic PSG).
Methods: To assess the prevalence and association of complex SA in the population, we applied the ECG-based spectrographic technique to the Sleep Heart Health Study (SHHS) database.
Results: A minimum of 17 minutes of eLFCNB was present in 957 of 3989 analyzed subjects (24%) by the spectrographic method, while a central apnea index of 5 or greater was observed in 89 (2.2%) by conventional scoring. Restricting the analysis to the 2499 subjects with RDI-4% >5, complex SA defined by the presence of eLFCNB was present in 37% of subjects. Groups could not be readily distinguished by the central apnea index (1.7 ± 4.5 vs. 0.5 ± 1.5). Subjects with the eLFCNB phenotype had more severe sleep apnea (AHI: 22.9 ± 18 vs. 13.7 ± 10.9; $p < 0.001$), were predominantly males, and had increased odds ratios, both adjusted for BMI and age and unadjusted, for hypertension (18.5 [6.9-49.9]; 3.4 [1.3-9.2]), pacemaker use, COPD/emphysema, and ischemic vascular disease (including myocardial infarction and stroke).
Conclusion: In this cross-sectional analysis of the SHHS, those with suggestive evidence of chemoreflex mediation or modulation of SA had greater disease severity and higher odds ratios for hypertension and cardiovascular disease.
Support (optional): This research was funded by NIH and by the Periodic Breathing Foundation.

0936

DEPRESSION, PAIN, AND LIFE STRESS PREDICT SLEEP DISTURBANCE IN WOMEN WITH METASTATIC BREAST CANCER

Palesh O,[1] Collie K,[2] Koopman C,[3] Perlis M,[4] Butler L,[5] Carlson R,[5] Spiegel D[5]
(1) University of Rochester, Rochester, NY, USA, (2) University of Rochester, CA, USA, (3) Stanford University, Palo Alto, CA, USA, (4) Pittsford, NY, USA, (5) Stanford University, Stanford, CA, USA

Introduction: The present study examined the associations between depression, pain, life stress and sleep disturbance in a sample of women with metastatic breast cancer who participated in a group therapy intervention trial.
Methods: Ninety-three women with metastatic breast cancer participated in a large intervention trial examining the effect of the group therapy on their symptoms. They completed measures of depression, pain, life stress, and sleep disturbance at baseline, 4, 8 and 12 months.
Results: Higher levels of depression at baseline predicted problems with getting up in the morning, waking up during the night, and daytime sleepiness. Increased depression over the course of 12 months was associated with fewer hours of sleep, more problems with waking up during the night and more daytime sleepiness. Higher levels of pain at baseline predicted more problems initiating sleep. Increases in pain predicted more difficulty initiating and maintaining sleep. Greater life stress at baseline predicted more problems initiating sleep and more daytime sleepiness.
Conclusion: While it is not possible to know what represents "cause and effect" these data suggest that the sleep disturbance commonly observed in women with breast cancer may be multiply determined and that the various forms of sleep disturbance (you may want to list these) may each derive from specific co-morbidities (e.g., depression predisposes the individual to increased sleep maintenance problems while pain predisposes the individual to sleep onset problems).
Support (optional): 5R25CA102618-03 (PI Morrow) 1R01CA118567-01A1 (PI David Spiegel)

0937

AN EPIDEMIOLOGICAL SURVEY OF EXCESSIVE DAYTIME SLEEPINESS IN PRADER-WILLI SYNDROME (PWS).

Kheirandish-Gozal L, Gozal D
University of Louisville, Louisville, KY, USA

Introduction: Prader-Willi syndrome (PWS) is a multisystemic disorder caused by the loss of expression of paternally transcribed genes within chromosome 15q11-q13. Most cases are due to paternal deletion of this region with the remaining cases resulting from maternal uniparental disomy (UPD) and imprinting defects. In recent years, it has become apparent that sleep disturbances are frequently reported in patients with PWS, and may include central and obstructive sleep apnea, altered sleep architecture with sleep-onset REM, and excessive daytime sleepiness (EDS). However, the prevalence of EDS in PWS is unknown.
Methods: A questionnaire on PWS and sleep related issues was mailed with the assistance of the PWS Association (USA) to all their registered members. Habitual snoring (HS) was defined as loud snoring occurring >3 times/week. EDS was evaluated using 8 questions (0-4), with a maximum total score of 32. The mean score in 10 normal adolescent or adult subjects without EDS was 7±1, while the mean score for 10 narcolepsy patients was 24±2. Thus, EDS was defined as a score >15.
Results: Of the 1253 mailed questionnaires, 372 were received, and contained complete datasets (29.7%). In addition, 163 questionnaires were returned, but had to be excluded for either unwillingness to participate, or due to incomplete information (13%). Of the responders, PWS diagnosis was based on genetic testing in 193, while 164 were diagnosed using chromosomal analysis, and a clinical diagnosis was performed in the remainder. Mean age was 16.1±10.8 years, 336 were white Caucasian (90.3%), and 174 were male (46.8%). 205 subjects received GH therapy (55.1%). HS was reported in 127 PWS subjects (34.1%). EDS scores>15 were found in 254 PWS subjects (68.2%), with a mean EDS score of 17.5±4.0. Genotype-phenotype correlation assessments revealed no differences in the frequency of either EDS or

HS among PWS with deletion or maternal uniparental disomy gene findings. GH therapy did not modify the frequency of EDS, but was associated with reduced HS (p<0.02; OR: 1.74; CI: 1.10-2.75).
Conclusion: Habitual snoring and EDS are exceedingly common features in PWS patients, and appear to be unrelated to the nature of the genetic defect. GH does not modify EDS, but is associated with a reduced frequency of HS, suggesting diminished risk for SDB.
Support (optional): The Children´s Foundation Endowment for Sleep Research, and the Commonwealth of Kentucky Challenge for Excellence Trust Fund

0938

THE ASSOCIATION BETWEEN NOVEL PSG (POLYSOMNOGRAPHY) DERIVED FEATURES AND HYPERTENSION

Jamasebi R, Redline S, Loparo K
Case Western Reserve University, Cleveland, OH, USA

Introduction: Previous studies suggest that SDB (Sleep Disorder Breathing) is associated with a broad range of health outcomes including hypertension, cardiovascular disease, impaired glucose tolerance and mortality. Prior analyses using traditional PSG indices as exposure measures have identified only modest associations with hypertension. We now investigate the role of novel PSG-derived measures that can quantify temporal patterns of sleep and evaluate their utility as predictors of hypertension.
Methods: Analyses were based on a sub-sample of subjects from the Cleveland Family Study, selected to comprise two groups (n=46, each) with disparate hypertension status: (1) Hypertensive (HTN) group with mean Diastolic Blood Pressure (mDBP) >= 90 or mean Systolic Blood Pressure (mSBP) >= 140, (2) Non-Hypertensive (Non-HTN) group with mDBP < 70 and mSBP < 110 and not on hypertension medication. Novel measures that quantify temporal patterns of sleep stages and the regularity or periodicity of the arousal event process are derived and compared to traditional measures.
Results: Among traditional predictors, AHI has the highest Odds Ratio (unadjusted and age, gender, race, BMI adjusted OR=2.36 (95% CI: 1.48, 3.75, p=0.0003) and 1.18, (95% CI: .76, 1.84, p=0.46), respectively). The best predictor among the novel measures is derived from the arousal events with unadjusted and adjusted ORs of 1.36 (95% CI: 1.08, 1.71) and 2.08 (95% CI: 1.19, 3.64), respectively. The Spearman correlations for this measure with BMI, age, AHI and AI are 0.06, 0.12, 0.4547 and 0.7369, respectively.
Conclusion: Of the novel measures, an index that quantified the temporal patterns of arousal events predicted HTN status. Unlike the AHI or Arousal index this measure was not strongly correlated with age or BMI. As such, this measure may provide unique information on temporal patterns of sleep disruption that are associated with hypertension.
Support (optional): HL 45380

0939

FETAL MOVEMENT IS SUPPRESSED DURING MATERNAL SLEEP IN PREECLAMPSIA

Edwards N, Blyton D, Sullivan C
University of Sydney, Sydney, New South Wales, Australia

Introduction: Quality and quantity of fetal movements are robust indicators of fetal well-being. Fetal outcome is often compromised in women with preeclampsia, with increased prevalence of growth restriction and reduced Apgar scores at birth. Preeclamptic women have frequent upper airway obstruction during sleep that is temporally linked to maternal hypertension and reduced maternal cardiac output. Our hypothesis was that maternal sleep would be associated with alterations in fetal movement profiles.
Methods: We performed full polysomnography and fetal movement detection during nocturnal sleep in 20 women with severe preeclampsia (age 29 ± 6 years, gestation 34 ± 4 weeks) and 18 normal pregnant women (age 30 ± 3 years, gestation 34 ± 2 weeks).
Results: Partial upper airway obstruction during sleep occurred ubiquitously in women with preeclampsia, although this was not reflected in the rate of arterial oxyhaemoglobin desaturation (oxygen desaturation index ≥ 4% was 4 ± 0.7 per hour of maternal sleep in control subjects and 5 ± 0.8 per hour in preeclamptic subjects). Fetal movement during maternal sleep in preeclamptic women was considerably suppressed (55 ± 6 per hour of maternal sleep in preeclamptic women and 116 ± 10 per hour in controls, $p < 0.001$). This was exacerbated during maternal REM sleep (while the number of fetal movements per hour of maternal REM sleep increased in control subjects to 180 ± 24, the number decreased in preeclamptic subjects to just 35 ± 5, $p < 0.001$).
Conclusion: This study suggests that fetal movement is suppressed during maternal sleep in preeclampsia. This is almost certainly a result of maternal partial upper airway obstruction that leads to maternal hemodynamic compromise. One important implication of this finding is that maternal hemodynamic compromise associated with sleep in women with preeclampsia may be associated with poorer neuro-developmental outcomes in the fetus.

0940

CENTRAL AND OBSTRUCTIVE SLEEP RELATED BREATHING DISORDERS IN PATIENTS WITH SYSTOLIC CARDIAC DYSFUNCTION

Hirshkowitz M,[1] Sharafkhaneh H,[2] Tang J,[3] Sharafkhaneh A[3]
(1) Houston, TX, USA, (2) Baylor College of Medicine, TX, USA, (3) TX, USA

Introduction: The present study was designed to explore the occurrence and type of sleep related breathing disorders (SRBD) in subjects with systolic cardiac dysfunction compared to routine sleep clinic patients.
Methods: In the present analysis, we compared sleep cardiopulmonary recorder (Stardust, made by Respironics) results from patients with systolic cardiac dysfunction (SCD) to sequentially recorded clinic patients controls (CTL). We recruited subjects in the SCD group echo-lab patients with left ventricular ejection fractions below 40%. Subjects provided written informed consent. Data were scored blindly with respect to group.
Results: We compared 30 SCD with 30 CTL subjects. SCD patients were slightly older (59 vs. 53 years for SCD vs. CTL, respectively) but overall apnea+hypopnea index did not differ (32 vs.34 events per hour, respectively). We calculated a central apnea index (CAI) and an obstructive apnea index (OAI) for each subjects. OAI included both obstructive and mixed apnea episodes. SCD patients had a slightly CAI:OAI ratio (6:10 vs. 3:14, respectively). Overall, the number of subjects with AHI of 15 or more was identical for the two groups (26 of 30 subjects); however CAI exceeded OAI in 5 SCD subjects but in none of the controls.
Conclusion: These data indicate that SRBDs are very common in patients with systolic cardiac dysfunction. Overall, selecting patients with low ejection fraction produced equivalent positive test results to patients selected by routine SRBD triage (loud snoring with frequent nocturnal awakening, arousals from sleep with choking or gasping, and excessive daytime sleepiness). While central apnea was more common in patients with systolic cardiac dysfunction than in routine sleep clinic

patients, the majority had significant levels of obstructive sleep apnea.
Support (optional): Authors wish to than Respironics, Inc and The Veterans Affairs Medical Center for supporting this research program.

0941

EFFECT OF ETHNICITY ON SLEEP AMONG HIV INFECTED PATIENTS

Song Y,[1] Gay C,[1] Davis H,[2] Coggins T,[1] Kelly R,[1] Lee K[1]
(1) University of California, San Francisco, San Francisco, CA, USA, (2) San Francisco State University, San Francisco, CA, USA

Introduction: Sleep disturbance is a common symptom in HIV disease. Among various factors related to sleep, little attention has been given to ethnic differences. The purpose of this study is to examine the effect of ethnicity on sleep among adults with HIV.
Methods: As part of a large longitudinal study of sleep in adults with HIV infection, 72 hours of wrist actigraphy was used to estimate total sleep time (TST) and wake after sleep onset (WASO). ANOVA was used to detect sleep differences by ethnicity, and multiple regression analysis was performed to evaluate contributions of ethnicity to TST and WASO. Ethnicity, gender, age, education, household income, CD4 count, BMI, neck circumference, and blood pressure were included as predictors of TST and WASO.
Results: Among the 176 HIV-infected adults (73 black, 68 white, 35 others), TST averaged about 60 minutes greater for Whites than Blacks ($p=0.001$) and WASO was about 7% less for Whites compared to Blacks ($p=0.004$). Neck circumference and education were also significant correlates of TST and WASO. However, only ethnicity ($p<0.05$) and education ($p<0.01$) were significant predictors of TST and WASO in the regression models.
Conclusion: Ethnicity and education level were better predictors of sleep disturbance and sleep restriction than many other well-known sleep-related influences (such as neck circumference, gender, age, or BMI). Prior to developing specific interventions for this population, further research is needed to determine whether these ethnic differences are genetic, environmental, or cultural. Level of education should be considered when developing more efficient patient education about sleep promotion and sleep hygiene among adults with HIV to reduce their sleep-related problems.
Support (optional): NIH Grant # R01 MH074358, KA Lee, P.I.

0942

UNIQUE REM REBOUND FOLLOWING SLEEP RESTRICTION IN FIBROMYALGIA PATIENTS IS NOT RELATED TO A PRIOR HISTORY OF DEPRESSION

Burger A,[1] Stout R,[1] Gillis M,[2] Burduvali E,[2] Lumley M,[1] Roehrs T,[1] Roth T[3]
(1) Wayne State University, Detroit, MI, USA, (2) Henry Ford Hospital Detroit, MI, USA, (3) Detroit, MI, USA

Introduction: Patients with fibromyalgia (FM) report increased difficulties with nighttime sleep which may reflect hyperarousal in FM. Previously we reported a unique REM rebound following sleep restriction compared with rheumatoid arthritis (RA) patients and healthy controls. We sought to confirm this result in a larger sample and test the relation between REM rebound and a prior history of depression given the high co-morbidity of depression and FM.
Methods: Eighteen FM, 13 RA, and 12 healthy, controls (NC) without co-morbid current major depression slept in the lab for 4 nights of PSG: Night 1 = lab adaptation (8 hours TIB), Night 2 = baseline (8 hours TIB), Night 3 = sleep restriction (4 hours TIB), and Night 4 = recovery (8 hours TIB). Participants were administered the SCID-II to assess current and/or a prior history of Major Depression.
Results: There were no differences between groups on Nights 2 and 3 in total sleep time (TST) or REM %. On night 4 there were no significant group differences in TST. However, on Night 4, FMS patients had significantly more REM % (FMS = 25%, RA = 18%, NC = 17%). In post-hoc comparisons of REM %, FM patients differed significantly from RA ($p = .01$) and NC ($p = .01$). Finally, for FM patients, Night 4 REM % was significantly elevated relative to their own Night 2 values ($p < .001$) The confirmed REM rebound effect in FM patients was not related to a prior history of depression (Prior history = 26%, no prior history = 25%).
Conclusion: These data support a REM rebound after 1 night sleep restriction in FM patients but not in RA or NC. The fact that FMS patients are hypersensitive to the loss of REM sleep is not related to having a prior history of depression.

0943

RESTLESS LEGS SYNDROME IN SCLERODERMA PATIENTS

Canepa R, Carvalho L, Prado L, Varella M, Mazuko A, Pucinelli M, Feldman D, Andrade L, Prado G
Federal University of Sao Paulo, Sao Paulo, Brazil

Introduction: Restless Legs Syndrome (RLS) is a neurological disorder associated to dopamine and iron metabolism problems. The patients have unpleasant sensations in the lower limbs with dysesthesia resulting in an urge to move the legs, mostly at night. Scleroderma is a rare progressive systemic sclerosis of unknown etiology, characterized by endothelial lesions and fibrosis of the skin and other organs. In a previous study we suggested that scleroderma patients were more allowed having RLS, but at that time we did not exclude from analysis patients with scleroderma and associated rheumatic condition. The objective of this study is to verify the prevalence of RLS in "pure" scleroderma patients compared to osteoarthrits patients.
Methods: 90 consecutive patients with scleroderma and 90 with osteoarthrits for control group will be evaluated for RLS symptoms. The PS group must not have other co morbidities. All patients were interviewed for RLS.
Results: Until this moment, 43 scleroderma patients (49±10 years old) and 14 osteoarthrits (62±7years old) had been evaluated. In the scleroderma group 10/33 (23%) patients presented RLS symptoms and 3/14 (21%) in the osteoarthrits group ($p=0.8$). Because of the difference of ages in the two groups, we evaluated more 32 health persons (without osteoarthrits or scleroderma) paired by age with the two groups. The scleroderma group had more RLS patients than the health persons (10 in scleroderma group, zero in health group, $p=0.02$), and there was no difference between osteoarthrits group (3 RLS patients) and health group (zero RLS patients), $p=0.2$.
Conclusion: Our preliminary data showed that RLS is equally prevalent in the scleroderma and osteoarthrits groups.
Support (optional): UNITER-SONO

0944

SLEEP, PAIN, AND USE OF METHADONE AND OPIATES AMONG HIV-POSITIVE ADULTS

Davis H,[1] Gay C,[2] Coggins T,[2] Kelly R,[2] Aouizerat B,[2] Portillo C,[2] Lee K[2]
(1) San Francisco State University, San Francisco, CA, USA, (2) University of California, San Francisco, San Francisco, CA, USA

Introduction: We examined HIV+ adults who reported pain in the last week and compared the objective and subjective sleep of those using methadone or opiates to a group not using pain medication. Given the pharmaceutical effects of methadone and opiates, we hypothesized that

subjects using methadone would have better sleep than those using opiates or those using neither methadone nor opiates.
Methods: As part of a descriptive study of sleep in 201 HIV-infected adults, data were collected on 89 subjects who reported pain in the last week. Urine toxicology was used to determine drug use, and those using illicit drugs were excluded. Wrist actigraphy was used to measure total sleep time (TST), wake after sleep onset (WASO), and circadian activity rhythm (acrophase and amplitude). Participants also completed the Pittsburgh Sleep Quality Index (PSQI).
Results: Results to date are presented for 53 men, 31 women, and 5 transgender adults, primarily Caucasian (40%) and African American (35%). The mean age was 45±8 years and mean CD4 cell count was 442±282 (range = 3 to 1246). Subjects using opiates (n=25) had significantly (p<.05) more TST (404±92 minutes) than those using methadone (n=15; 308±135), but neither those using opiates nor methadone differed from those using neither drug (n=52; 367±103). In addition, those using methadone had significantly (p<.05) more WASO (35.9%±22.8) than those using either opiates (18.9%±12.6) or neither drug (20.1%±15.3). Those using methadone also had a significantly (p<.01) earlier acrophase (13:30±1:27) than those using neither opiates nor methadone (15:22±1:22). There were no differences on the PSQI in any of the groups.
Conclusion: Contrary to our hypothesis, methadone use was associated with shorter sleep duration, more sleep disruption, and earlier acrophase than opiate use in this sample of HIV-infected adults with pain. Pain severity, medication efficacy, and their impact on sleep in this population needs further evaluation.
Support (optional): NIH Grant # R01 MH074358, KA Lee, P.I.

0945

OBJECTIVE SLEEPINESS FOLLOWING SLEEP RESTRICTION IN RHEUMATOID ARTHRITIS AND FIBROMYALGIA

Stout R,[1] Burger A,[1] Villareal A,[2] Gillis M,[2] Lumley M,[1] Roehrs T,[1] Roth T[3]
(1) Wayne State University, Detroit, MI, USA, (2) Henry Ford Hospital Detroit, MI, USA, (3) Detroit, MI, USA

Introduction: Sleep problems and daytime sleepiness are reported by patients with chronic pain. This study of sleep in chronic pain is the first to compare daytime sleepiness assessed by MSLT in people with fibromyalgia (FM) and rheumatoid arthritis (RA), and to test response to sleep restriction.
Methods: Women with FM (N = 17; age M = 48), RA, (N= 12; M = 50), and age-matched Healthy Controls (HC) (N = 10; M = 46) without co-morbid depression, pain or primary sleep disorders spent an 8-hour time in bed (TIB) and a 4-hour TIB sleep restriction night. Sleepiness was assessed after the 8 hour and 4 Hour TIBs using a standard MSLT (1000,1200, 1400, 1600 Hour).
Results: Sleep efficiency was equivalent across groups for the nights of sleep preceding MSLTs. No differences were observed on MSLTs following the 8 hour TIB night (FM: M = 14.4 mins; SD = 4.2; .RA: M = 11.8; SD = 4.3; HC: M =11.3, SD = 4.6; p = .142. As expected, sleep restriction led to greater sleepiness the next day for all groups (p < .05). The FM group was significantly less sleepy than both RA´s and HC´s on the MSLT after the 4-hour TIB (FM: M = 10 mins; SD = 5.3; RA: M = 8.3, SD = 2.9; HC: M = 5.6 mins, SD = 2.8; p < .05). RAs and HCs did not differ from one another on MSLTs following 4-hour TIB.
Conclusion: We conclude that chronic pain conditions affect daytime sleepiness for FM only in that they are less sleepy following sleep restriction. This reduced sleepiness among FMs may be due to a hyperaroused state or reduced sleep drive.

0946

SUBJECTIVE MATERNAL POSTPARTUM SLEEPINESS, MOOD AND PERCEIVED STRESS

Gould C, Clegg M, Montgomery-Downs H
West Virginia University, Morgantown, WV, USA

Introduction: Symptoms of postpartum anxiety and perceived stress have not been as thoroughly studied among postpartum women as depression. Previous studies have found that prenatal anxiety scores are higher than postpartum anxiety scores; however, some studies have found that new cases of postpartum anxiety develop several months postpartum. The current study explored self-reported sleepiness, mood and perceived stress among new mothers.
Methods: Participants began the study at 8 weeks postpartum and participated for 8 continuous weeks as part of a larger study. Using palm-based software Epworth Sleepiness Scale and Stanford Sleepiness Scale ratings were made 2.4 (SD±1.0) times each day. Participants completed the Perceived Stress Scale (PSS) and Profile of Mood States (POMS) at 11 and 15 weeks postpartum.
Results: Analyses were based on the first fifteen participants.. These women were 29.1 years of age (SD±4.1), 93.3% White, and had 16.9 (SD±2.5) years of education. The magnitude of change in the PSS (M=1.0,SD±5.5) points and POMS (M=5.7,SD±21.93) points scores between postpartum weeks 11 and 15 were positively correlated, (r=.679;p=0.005) and the magnitude of change between ESS (M=1.5,SD±0.5) and SSS (M=1.5,SD±0.5) measures were positively correlated (r=.752;p<0.001).
Conclusion: From 11 to 15 weeks postpartum an improvement was found on maternal self-report measures of perceived stress, mood, and sleepiness. These data indicate that perceived stress and mood are related. A goal of the larger study will be to compare these self-report measures with objective sleep data from continuous actigraphy.

0947

POSTPARTUM SLEEP AND PSYCHOMOTOR VIGILANCE PERFORMANCE

Insana S, Montgomery-Downs H
West Virginia University, Morgantown, WV, USA

Introduction: Maternal postpartum sleep disturbance has many deleterious effects and may increase the risk of postpartum depression. The current field-based study addresses the relation between objectively measured postpartum sleep and reaction time performance measured by palm-based Psychomotor Vigilance Test (PVT).
Methods: As part of a larger study, 24-hour sleep measures were continuously monitored during postpartum weeks 8 through 16 using wrist actigraphy. Participants completed a palm-based PVT within 2-hours after final morning awaking. Daily PVT reaction times were compared to sleep during the preceding 24-hours.
Results: Analyses are based on the first seventeen participants from a larger study, each contributing 56 continuous days of recording and daily PVT. Participants were 28.7 (SD±4.7) years and 88% White. Average 24-hour total sleep time was 454.6 (SD±78.6), sleep efficiency was 88.7% (SD±5.3%), and fragmentation during nocturnal sleep was 14.5% (SD±7.1%). Fragmentation significantly decreased p<.001, F=21.4 over 8 weeks. Mean reaction time was 430.1 msec (SD±125.9). 18.1% (SD±18.9) of PVT trials were scored as a lapse (>500 msec).
Conclusion: Although participants appeared to have adequate 24-hour sleep durations, high levels of sleep fragmentation were present. PVT performance was poor and the proportion of lapses high. The PVT performance might be attributable to high rates of fragmentation. Sleep

fragmentation decreased over the 8 weeks. Relation between sleep fragmentation and PVT performance will be examined as part of the larger study.

0948

TREATMENT WITH PREGABALIN IS ASSOCIATED WITH IMPROVED SLEEP OUTCOMES IN PATIENTS WITH FIBROMYALGIA

Arnold L,[1] Martin S,[2] Duan W,[3] Florian H,[3] Young J,[3] Haig G[3]
(1) Women's Health Research Program, University of Cincinnati, Cincinnati, OH, USA, (2) Pfizer Global Research & Development, Ann Arbor, MI, USA, (3) Pfizer Global Research & Development, MI, USA

Introduction: Sleep disturbance is prominent in fibromyalgia. In 2 randomized, controlled trials in fibromyalgia that included sleep evaluations, pregabalin significantly improved these outcomes.
Methods: Patients received placebo or pregabalin 300, 450, or 600 mg/d for 13 (Trial 1, n=751) or 14 (Trial 2, n=745) weeks. Patients completed a daily sleep-quality question (weekly average score, 0-10) and the Medical Outcomes Sleep Scale (MOS-S) at baseline and endpoint. MOS-S includes 7 domains—Disturbance, Snoring, Awaken Short of Breath or with Headache, Somnolence, Quantity, Adequacy, Optimal Sleep—and an overall score, the Sleep Problems Index. All are scored 0-100, except Quantity (0-24) and Optimal Sleep (0,1). ANCOVA used to analyze all scores, except Optimal Sleep (logistic regression).
Results: Patients were randomized to placebo (n=192) or pregabalin 300 (n=185), 450 (n=183), or 600 mg/d (n=191) in Trial 1 and to placebo (n=184) or pregabalin 300 (n=183), 450 (n=190), or 600 mg/d (n=188) in Trial 2. Compared with placebo, pregabalin treatment in Trial 1 significantly improved sleep quality (300 mg/d: -0.86; 450 mg/d: -0.97; 600 mg/d: -1.21), MOS-S Disturbance (300 mg/d: -7.61; 450 mg/d: -10.27; 600 mg/d: -9.85), and MOS-S Sleep Problems Index (300 mg/d: -4.82; 450 mg/d: -6.12; 600 mg/d: -5.2). Similar significant improvements were seen in Trial 2: sleep quality (300 mg/d: -0.74; 450 mg/d:-1.12; 600 mg/d: -1.35), MOS-S Disturbance (300 mg/d: -8.91; 450 mg/d: -10.63; 600 mg/d: -14.93), and MOS-S Sleep Problems Index (300 mg/d: -4.74; 450 mg/d: -6.20; 600 mg/d: -8.44). Significant differences were seen in other domains, with smaller effect sizes. In Trial 1, somnolence score was significantly higher with pregabalin 450 and 600 mg/d than placebo. Improvements in weekly average sleep-quality score were significant for all weeks/pregabalin dosages (P<.001) in Trial 1 and Trial 2 (P<.02) except 300 mg/d, Week 11, Trial 2.
Conclusion: Patients with fibromyalgia experienced improvement on key sleep outcomes with pregabalin.
Support (optional): The trials reported here were funded by Pfizer Inc.

0949

RESPONSE OF GERD SYMPTOMS TO DENTAL APPLIANCE USE FOR THE TREATMENT OF OSAS.

Melby D,[1] Vorona R,[1] Bohnenkamp M,[2] Nottingham J,[2] Cherin J,[2] Ware C[1]
(1) Eastern Virginia Medical School, Norfolk, VA, USA, (2) Eastern Virginia Medical School, VA, USA

Introduction: Controversy exists as to whether obstructive sleep apnea syndrome (OSAS) does or does not cause or exacerbate gastroesophageal reflux disease (GERD). Medical research demonstrates that continuous positive airway pressure (CPAP) improves GERD in the presence or absence of OSAS. This study aims to determine if another OSAS treatment, the dental appliance (DA), might improve GERD symptoms or if such an improvement in GERD is peculiar to CPAP.
Methods: This prospective non-randomized and unblinded study was performed at the EVMS/SNGH Sleep Disorders Center. Investigators utilized polysomnography (PSG) to establish the presence of OSAS in adult (18-79 yr.) patients. OSAS patients electing DA therapy visited 1 of 3 dentists skilled in DA use. Patients completed a validated GERD symptom questionnaire (Shaw, 2001) at initial visit and after satisfactory use of DA. The post-questionnaire also queried subjective DA compliance. A group of bruxism patients visiting these same dentists and requiring bruxism appliances will serve as the comparison group.
Results: To date, N=10: men 6, women 4, mean age 56.2 years (40-72). Mean AHI 16.5 sd 13.9, low SAO2 87.2 sd 3.8. A score greater than 15 (range 0-50) indicated GERD. Pre-GERD Scores 0-18 (mean 4.6), Post-GERD scores 0-33 (mean 4.5). Using a non-parametric Wilcoxon Signed Ranks Test, the p-value was non-significant. There were two patients who manifested GERD symptoms (score > 15.5) prior to the oral appliance and one of these improved to not having GERD post oral appliance. The other patient´s GERD score worsened.
Conclusion: Data do not indicate that use of an oral appliance improved GERD. Presently, this study is limited in power with an N=10, lack of post appliance PSGs, and lack of a bruxism control group. Twenty more participants are enrolled toward a goal of 50. We are recruiting the control group, and planning follow-up PSGs with dental appliance.
Support (optional): Department of Family Medicine
Department of Internal Medicine
Division of Sleep Medicine

0950

CANNABIS IS ASSOCIATED WITH SLEEP DISTURBANCE IN HIV-INFECTED ADULTS

Coggins T,[1] Kelly R,[1] Gay C,[1] Nelson K,[1] Bruce S,[1] Davis H,[2] Lee K[1]
(1) University of California, San Francisco, San Francisco, CA, USA, (2) San Francisco State University, San Francisco, CA, USA

Introduction: Cannabis has been used in HIV treatment primarily for symptoms of nausea and neuropathy. It also has apparent effects on pain, appetite, mood, and sleep. This study examines the use of cannabis for various symptoms and its relationship to sleep.
Methods: As part of an ongoing investigation, HIV-infected men and women were monitored for 72 consecutive weekday hours using wrist actigraphy to determine total sleep time (TST) and wake after sleep onset (WASO). The Memorial Symptom Assessment Scale (MSAS) was used to assess pain and loss of appetite, and the General Sleep Disturbance Scale (GSDS) was used as a subjective measure of sleep quality. Redi-cup urine toxicology was used to exclude those testing positive for illicit stimulants and to determine THC (tetrahydrocannabinol) use.
Results: The sample of 167 adults (101 men, 54 female, 12 transgender) had a mean age of 44.1 ± 8.2 years, and was predominantly African-American (42%) and Caucasian (38%). Compared to the 117 subjects testing negative for THC, the 50 who tested positive had less TST (p=.049) and slightly more WASO (p=.070). Those testing positive also reported more sleep disturbance (p=.004), more frequent (p=.001) and severe pain (p=.007), and more frequent (p=.011) and severe loss of appetite (p=.028). The two groups did not differ in body mass index or CD4 count.
Conclusion: Although these results indicate more sleep disturbance among cannabis users, this correlational study is unable to determine whether cannabis causes poor sleep. It is possible that the symptoms experienced by cannabis users may have been much worse before using cannabis or that the cannabis use is influencing the sleep problems. Randomized clinical trials are needed to better understand the effects of cannabis on sleep among adults with HIV.
Support (optional): NIH Grant #R01 MH074358, KA Lee, P.I.

0951

HOW COULD OBSTRUCTIVE SLEEP APNEA EXACERBATE ASTHMA?

Teodorescu M,[1] Coffey M,[2] Bria W,[2] Consens F,[2] Weatherwax K,[2] Teodorescu M,[1] Palmisano J,[2] Senger C,[3] Chervin R[2]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) University of Michigan, MI, USA, (3) The Johns Hopkins University, MD, USA

Introduction: Among asthmatics, obstructive sleep apnea (OSA) predicts poor asthma control, but potential mechanisms remain uncertain. We tested whether hypoxia or arousals after apneic events may explain spirometric measures of asthma severity.
Methods: Nineteen subjects with persistent asthma (NAEPP steps 2-4 despite optimal therapy) and OSA symptoms underwent nocturnal polysomnography followed by spirometry. Polysomnograhic measures tested for associations with forced expiratory volume in 1 second, expressed as percent of predicted (FEV_1%), included the apnea/hypopnea index (AHI), respiratory arousal (as defined by 1992 ASDA criteria) index, and minimum O_2 saturation.
Results: Thirteen subjects (68%) were women, mean age was 50±10 (s.d.) years, and mean BMI was 35±8 kg/m^2. On polysomnography, the mean AHI was 18±18/hour (range 1-77), minimum O_2 saturation during sleep was 82±6% (range 70-91%), and the respiratory arousal index was 13±9/hour (range 0-32). Thirteen (68%) of the subjects had OSA (AHI>5). On spirometry, FEV_1% was 86.21±19.21 and FEF_{25-75}% was 61.47±26.45. Higher AHIs predicted lower FEV_1% (Spearman rho= -0.53, p=0.02). A diagnosis of OSA predicted a 25.27% lower FEV_1 (R^2=0.39, p=0.004). Higher respiratory arousal indices predicted lower FEV_1% (rho=-0.49, 0=0.03). Lower minimum O_2 saturations predicted a trend toward lower FEV_1% (rho=0.45, p=0.05). After accounting for oxygen saturation, respiratory arousal indices still predicted lower FEV_1%: on average, each 1% increase in the index was associated with a 1% decrease in FEV_1% (s.e.=0.42, p=0.03).
Conclusion: Polysomnographic measures of sleep fragmentation, more than hypoxia, predict lower airways obstruction in patients with OSA and persistent asthma symptoms. Although results could partly reflect measures used, or effects of asthma on OSA, our findings raise the possibility that sleep fragmentation or closely linked processes exacerbate asthma, perhaps through changes in autonomic activation, arousal thresholds, or pro-inflammatory pathways.
Support (optional): NIH M01-RR00042 and 5T32NS07222 (MT).

0952

ASSOCIATION OF CPAP RELATED AEROPHAGIA AND GASTROESOPHAGEAL REFLUX DISEASE

Mystkowski S,[1] Watson N[2]
(1) Department of Medicine, University of Washington, Seattle, WA, USA, (2) University of Washington, Seattle, WA, USA

Introduction: Aerophagia, a complication of CPAP, is characterized by entry of air into the stomach and bowel, rather than the lungs. This can result in symptoms of eructation, abdominal pain, bloating, and flatulence, leading to reduced CPAP compliance. We hypothesized that the development of aerophagia may be related to dysfunctional lower esophageal sphincter (LES) tone, a condition that is also associated with gastroesophageal reflux disease (GERD).
Methods: To test this hypothesis, we retrospectively compared clinical features of obstructive sleep apnea (OSA) patients on CPAP with aerophagia (n=14) to control OSA patients on CPAP without aerophagia (n=14). Controls were matched for age, gender, and body mass index (BMI). Other variables assessed included history, symptoms, or treatment for GERD, caffeine, alcohol, or tobacco use, and polysomnography data [including apnea hypopnea index (AHI), desaturation index (DI), oxygen saturation nadir and mean percentages, arousal index (AI), total sleep time (TST), sleep efficiency (SE), and sleep onset latency(SOL)]. Fisher´s exact test and student's t-test were utilized for statistical analyses.
Results: As expected, clinical characteristics were similar between the aerophagia and control groups (aerophagia group mean age 46.9±9.5, 50% female, mean BMI 31.4±12.2; control group mean age 46.9±9.5, 50% female, mean BMI 30.7±6.9). Seventy-nine percent of the aerophagia group had symptoms of GERD versus 36% of the controls (p=0.05). On evaluating PSG parameters, mean oxygen saturation percentages were lower in the aerophagia group (95.2±2.3%) versus controls (97.0±1.4%; p=0.02). Other studied variables did not reveal significant differences. Interestingly, no one in the aerophagia group (vs 29% of the control group) was a current tobacco user (p=0.10).
Conclusion: These results suggest that aerophagia is significantly associated with GERD symptoms, consistent with the notion that LES competence may be an etiologic factor in the development of aerophagia.

0953

RISK OF HYPOGLYCEMIA IN PATIENTS WITH DIABETES MELLITUS TREATED WITH INSULIN DURING INITIATION TREATMENT WITH CPAP FOR OBSTRUCTIVE SLEEP APNEA SYNDROME

Stefadu Y,[1] Nasr B[2]
(1) Great Lakes Sleep Medicine Institute, Port Huron Hospital Center for Sleep Medicine, Sterling Heights, MI, USA, (2) Port Huron Hospital Center for Sleep Medicine, MI, USA

Introduction: Literature data indicates the relationship between obstructive sleep apnea syndrome, insulin resistance, and diabetes mellitus. We monitored morning glucose level in patients with diabetes mellitus during the initiation treatment with CPAP.
Methods: From the group of 128 consecutive patients with documented obstructive sleep apnea-hypopnea syndrome, 18 had a history of diabetes mellitus. All patients with diabetes had an apnea-hypopnea index greater than 10, and the age of the patients with diabetes ranged from 44 to 76. Diabetes has been diagnosed for at least one year. Patients have been treated with oral hypoglycemic medications, three of the patients used insulin. Patients did not change treatment for at least two weeks prior to initiating CPAP, and they stayed on their usual diet.
Results: After initiating treatment with CPAP, 12 patients did not have any significant changes in the level of glucose in AM. 5 patients significantly improved their level of glucose in the morning and they were able to decrease hypoglycemic medications and one patient stopped treatment. One patient dropped the level of morning sugar to 49 mg/dL after the second and third night of CPAP treatment. This patient was a 56 year old Caucasian man with severe OSA (AHI-52), severe oxygen desaturation to 68%, and a BMI- 37.7. His sugar was always above 120 mg/dL in AM before initiating CPAP. He became euglycemic in the morning only after decreasing the evening dose of insulin to 50%.
Conclusion: Treatment with CPAP improved the level of glucose in some of diabetic patients. Physicians and patients should be aware about possibility of developing hypoglycemia during initiation treatment with CPAP in patients on treatment with insulin. This category of patients should be monitored very closely to prevent the possibility of developing hypoglycemia.

0954

PRELIMINARY FINDINGS FROM ACTIGRAPH DATA AMONG ADOLESCENTS AND ADULTS WITH DIABETES MELLITUS: IMPLICATIONS FOR DIABETIC HEALTH

Perfect M,[1] Elkins G,[2] Lyle-Lahroud T,[3] Curcio J[4]
(1) University of Arizona, Tucson, AZ, USA, (2) Baylor University, TX, USA, (3) Texas Children's Hospital, TX, USA, (4) University of Arizona, AZ, USA

Introduction: There is mounting evidence to support that individuals diagnosed with Diabetes Mellitus (DM) who report insufficient sleep and/or poor sleep quality are more likely to experience medical complications related to DM. Yet, sleep hygiene has been largely overlooked in psychosocial interventions for diabetes management. We present preliminary findings from a small sample of diabetics, ranging from adolescence through middle adulthood.
Methods: Twenty participants, with DM, were enrolled in an ongoing intervention study targeting stress and sleep. Participants wore a wrist actigraph at home for approximately a week. Sleep parameters were calculated using available sleep-wake scoring algorithms. Participants also completed the Pittsburgh Sleep Quality Index (PSQI), Perceived Stress Scale (PSS), and Positive and Negative Affect Scales (PAS/NAS).
Results: Participants (30% Non-White; 3 males) had a mean age of 34.99 ±11.89. Participants slept an average of 6.35±.88 hours each night, ranging from 5.06 to 8.54 hours. Mean sleep parameters were 6.09±4.3 minutes for snoozing, 84.97% ±6.16 for sleep efficiency, 51.14±22.53 minutes for wake after sleep onset, 11.6%±4.55 for percent awake during sleep intervals, and 20.05 for sleep fragmentation. Sleep onset latency was positively skewed (range=0 to 52.31 minutes). The PSQI was significantly correlated with the NAS (r=.45, p=.05) and PSS (r=.65, p < .01); mean scores were 3.20±1.48, 22.85±7.15, and 20.25±6.68, respectively.
Conclusion: Consistent with previous findings, perceived poor sleep quality was related to negative feelings and greater stress. An average sleep duration under 6 ½ hours indicates that participants were getting insufficient sleep. They were awake almost 12% of the night and had less than 90% sleep efficiency, suggesting poor sleep quality. Research is needed using both psychological and physiological markers of sleep in order to advance our understanding of the role of the sleep-wake cycle in the quality of life of diabetics and metabolic control of DM.
Support (optional): Supported by Scott & White Memorial Fund.

0955

PREVALENCE OF OSA IN HISPANIC DIABETIC PATIENTS

Surani S,[1] Subramanian S,[2] Aguillar R,[3] Spears D,[4] Babbar H[2]
(1) Texas A&M University, Corpus Christi, TX, USA, (2) Baylor College of Medicine, Houston, TX, USA, (3) Torr sleep center, Corpus Christi, TX, USA, (4) Christus Spohn Hospital, Corpus Christi, TX, USA

Introduction: Obstructive sleep apnea (OSA) is widely prevalent in patients with diabetes mellitus, with an estimated 40% prevalence. It is believed to play an important role in the pathogenesis of insulin resistance. Minorities have the highest incidence and prevalence of diabetes and related complications compared to other racial groups. No data exist on the incidence of OSA in Hispanic diabetics. The objective of this study was to assess the prevalence of sleep apnea amongst Hispanics seen in a diabetes clinic.
Methods: Consecutive Hispanic patients referred to the diabetes clinic were administered the Berlin questionnaire as well as the Epworth Sleepiness scale. Spanish translations were used when necessary. A positive score on the Berlin questionnaire was defined as two or more out of the three domains being positive.
Results: A total of 70 patients were administered the questionnaire. 39 (57%) of these had a positive score on the Berlin questionnaire. Age (mean - 55.8 +/- 10.8 vs. 58.6 +/- 11.49; p= 0.309), BMI (mean - 36.1 +/- 8.2 vs. 33.0 +/- 9.4; p = 0.156) and gender distribution (41% male vs. 32.2%; p = 0.149) was similar in the groups with and without a positive Berlin score respectively.
Conclusion: There may be a higher prevalence of obstructive sleep apnea in Hispanic population with diabetes mellitus, when screened using a Berlin questionnaire. Surprisingly, neither age, nor gender, nor obesity, seemed to be predictive of presence of sleep disordered breathing. Hispanic patients with diabetes mellitus should be aggressively screened and worked-up for sleep disordered breathing. More studies with polysomnographic confirmation are needed to verify these prevalence data.

0956

SLEEP QUALITY AND DEPRESSION IN HIV INFECTED ADULTS

Minarik P, Portillo C, Lee K, Gay C
University of California, San Francisco, San Francisco, CA, USA

Introduction: The purpose of this study is to describe the relationship between sleep quality and depressive symptoms in HIV-infected adults. Symptoms of HIV/AIDS include disturbed wake/sleep and depressed mood. Whether one symptom precedes another is unclear from prior research. Interaction among these symptoms may impact treatment adherence.
Methods: As part of a descriptive study of sleep in HIV infected persons, data were collected on 236 adults. The Pittsburgh Sleep Quality Index (PSQI) was used to measure self-reported sleep quality. The Memorial Symptom Assessment Scale (MSAS) was used to measure self-reported frequency, severity, and distress of symptoms and 4 additional sleep-related items were added to this tool. The frequency of depressive symptoms was measured using the Center for Epidemiological Studies-Depression (CES-D) scale. Demographic questions assessed gender and age. Severity of illness was assessed with CD-4 cell count. Wrist actigraphy for 72 hours was used to objectively measure mean sleep duration. Multiple linear regression was calculated to determine whether gender, age, CD-4 count, total sleep time, sleep quality, and self reported symptoms predicted level of depressive symptoms.
Results: The sample included in the regression (n=178) had a mean age of 44.48+/-7.8 years, 58.9% were male, 42% were African American, 47% finished high school, 71.2 % had income of less than $1000 per month. Fifty percent had a CD-4 count of 421 or less. A significant regression equation was found (F (10, 167) = 9.396, p<.001), with an R2 of .360. Significant predictors were actigraphy measure of total sleep time, self-reported symptoms of difficulty sleeping, “don´t look like myself”, and PSQI total score and sleep disturbance component score.
Conclusion: Findings suggest that overall perception of one´s sleep quality, rather than objective sleep time, may play a role in depression in HIV-infected adults. Targeted research investigating sleep disturbance and depressive symptoms is warranted.
Support (optional): NIH Grant #R01 MH074358, KA Lee, P.I.

0957

POST-SURGICAL ANALGESIA PREDICTED BY PRE-SURGICAL SELF REPORTED SLEEP

Hyde M,[1] Roehrs T,[2] Greenwald M,[2] Roth T[1]
(1) Henry Ford Hospital Detroit, Detroit, MI, USA, (2) Wayne State University, Detroit, MI, USA

Introduction: Our previous studies have shown that sleep restriction in healthy normals has a hyperalgesic effect. Patients with pain typically report reduced sleep duration and quality. Thus we hypothesized that reduced sleep duration or quality prior to surgery in patients undergoing elective joint-replacement would experience greater post surgical pain and require more analgesia.
Methods: Sixty joint-replacement patients 35-70 yrs (24 M, 46 F), volunteered to complete a questionnaire on self-reported sleep one week prior to surgery. The questionnaire contained questions about sleep, napping, daytime sleepiness (ESS), insomnia, caffeine and alcohol intake, prescription medication use, and co morbid disorders. Each received pain medication post-surgery with a patient-controlled analgesia (PCA) device that limited doses of morphine to 1mg every 10 min. PCA determined number of injections and denials (requests during 10 min lockouts), was recorded for 48 hrs post-surgery.
Results: Multiple regressions were performed between the two PCA outcome measures, number of injections (range 5-119) and number of denials (range 0-218) and the predictor variables of self-reported sleep and daytime sleepiness. The two strongest predictive models included mean hours of sleep on weekdays (M=6.78, SD=1.83), mean hours of sleep on weekends (M=6.93, SD=1.81), mean wake after sleep onset (WASO) in minutes on weekdays (M=17.07, SD=18.10) and on weekends (M=16.81, SD=18.12) as predictors. The models produced a multiple R of 0.62 ($p<0.01$) when correlated with number of injections and a multiple R of 0.55 ($p<0.01$) with number of denials. WASO for weekdays and weekends were the two significant predictor variables ($p<0.01$) in each model, with greater WASO predicting more PCA requests and injections.
Conclusion: Self-reported pre-surgical sleep predicts post-surgical analgesia requests and injections. This suggests that a prophylactic improvement of pre-surgical sleep may result in decreased analgesia use.
Support (optional): The Fund for Henry Ford Hospital, B10914 awarded to Dr Roehrs

0958

THE CORRELATION BETWEEN NEUROCOGNITIVE DEFICITS AND SLEEP DIFFICULTIES IN CIRRHOSIS COMPARED WITH A CHRONIC DISEASE

Auger R,[1] Gurram K,[2] Smith G,[1] Enders F,[2] Nicole S,[2] Stewart C[1]
(1) Mayo Foundation for Medical Education and Research, Rochester, MN, USA, (2) Mayo Foundation for Medical Education and Research, MN, USA

Introduction: Neurocognitive deficits and sleep disturbances are common in patients with cirrhosis. However, there is no reliable method of screening for the presence of sleep disorders in patients with cirrhosis. Aim: To determine whether there is a correlation between the Pittsburgh Sleep Quality Index (PSQI) and neurocognition in patients with cirrhosis compared with patients with inflammatory bowel disease (IBD).
Methods: Prospective study of 2 groups: a group with cirrhosis with minimal hepatic encephalopathy (MHE) and a group with IBD. A traditional, neuropsychological (NP) battery to examine the domains of: attention, information processing speed, learning, memory, visual perception, and motor domains; and the PSQI were administered. A total PSQI value of > 5 indicates difficulties with sleep; and 2 SD below the standardized average mean of the normative population was abnormal for the NP. Using regression analysis, correlations were made between total PSQI score and NP, in both groups. The subscores of the PSQI were assessed if the total PSQI was abnormal.
Results: 34 /57 (11F:23M) patients with cirrhosis and 23/57 (10F:13M) with IBD were compared, there was a significant difference between both groups in total PSQI mean (SD) for cirrhotics vs IBD 9.8(4.9) vs 5.6(4), P.002; age 59(8) vs 54(8), P.03; and educational level 14(2) vs 16(1.8), P.02. Both groups demonstrated significant abnormalities in the PSQI subscores of: disturbance, duration, dysfunction, sleep quality, and sleep latency. Patients with IBD used medications to treat sleep disorders more frequently than cirrhotics. All the cirrhotics demonstrated impairment of the tested neurocognitive domains. After adjusting for age and educational level, deficits in none of the neurocognitive domains predicted sleep difficulties in patients with cirrhosis compared with IBD; but complaints of sleep disturbance predicted learning impairment.
Conclusion: Sleep difficulties of cirrhotics are probably a result of chronic disease. There is an association between sleep disturbance and learning in cirrhosis.
Support (optional): DK 60018

0959

THE EFFECT OF NAPPING ON MOOD IN WOMEN WITH SEVERE PREMENSTRUAL SYMPTOMS

Lamarche L,[1] Driver H,[2] De Koninck J[3]
(1) University of Ottawa, Ottawa, Ontario, Canada, (2) Kingston General Hospital and Departments of Medicine, Ontario, Canada, (3) University of Ottawa, Ontario, Canada

Introduction: Women with Premenstrual Syndrome tend to experience an increase in negative mood and a decrease in positive mood during the late-luteal phase of the menstrual cycle. Among the general population a daytime nap has been found to improve mood. We investigated the effects of a short mid-afternoon nap during the late-luteal phase of the menstrual cycle on mood among women with severe and minimal premenstrual symptoms.
Methods: Ten women with severe emotional/behavioral premenstrual symptoms and nine women with minimal symptoms (mean age 27 years) participated in the study. Participants came to the laboratory in the mid-afternoon for a nap of a maximum duration of 30 minutes. Positive and negative mood was measured before and 30 minutes after the nap, and at two-hourly intervals until nocturnal bedtime. The same procedure was repeated for the `no nap condition´ when participants engaged in a quiet activity rather than a nap. The nap and no nap conditions were counterbalanced.
Results: All women, with the exception of one participant with minimal symptoms, fell asleep; the mean sleep latency for both groups was less than 10 minutes. For both groups, compared to before napping, intensity of negative mood decreased 0.5, 2 and 4 hours after napping, ($p<.05$) and intensity of positive mood increased 0.5 hours after napping ($p<.05$). The improvement in negative mood 0.5 hours after napping was slightly higher in women with severe PMS ($p<.001$). No changes in intensity of negative mood were noted without a nap, while intensity of positive mood significantly decreased after 2 hours and before nocturnal bedtime ($p<.05$).
Conclusion: The results of this study suggest an increased sleep need in young women during the late-luteal phase of the cycle, and an improvement in mood with napping in young women, with potentially more benefit for those with more severe premenstrual symptoms.

0960

SLEEP, SELF REPORTED DAYTIME FUNCTION, AND STIMULANT EFFECTS IN COLLEGE STUDENTS WITH ADHD

Medalie L,[1] Cole W,[2] Sciutto M,[2] August-Fedio A,[3] Shearin E,[3] Huntley E,[4] Lewin D[5]
(1) Muhlenberg College, Argosy University, Children's National Medical Center, Rockville, MD, USA, (2) Muhlenberg College, PA, USA, (3) Argosy University, VA, USA, (4) Children's Hospital, Washington, Washington, DC, USA, (5) Washington, DC, USA

Introduction: There is limited research on sleep and daytime functioning in college students diagnosed with ADHD. Several studies have concluded such relationships in children, including Bouvard and Falissard (2000).
Methods: These findings were derived from data on college students with ADHD on stimulant medications (n = 8, M = 19.3 yrs.) and non-medicated college students with ADHD (N = 11, M = 19.7 yrs.). Participants completed a data log on weekdays for 3 weeks recording medication usage, sleep habits, and academic performance. Regression analysis was used to identify the impact of medication on sleep and medication and sleep on self reported daytime function.
Results: Self reported total sleep time was significantly lower in individuals prescribed stimulant medication (M = 6.1 hrs) compared to individuals not prescribed stimulant medication (M = 7.2 hrs), $p<.001$. Adderall was the sole predictor of decreased sleep in college students with ADHD (340+/-37 min), $p<.04$. Adderal, $p<.02$ and napping, $p<.001$ were associated with self reported improved sleep quality. Only napping was associated with increased alertness, $p < .006$. Self rated class participation was associated with use of Dexedrine, $p<.006$. Adderall was the sole predictor of improved morning academic performance, $p <.05$. Self rated afternoon academic performance was associated with use of Dexedrine, $p <.045$, and napping, $p <.09$, which was of borderline significance
Conclusion: College students with ADHD taking stimulant medication report less sleep than those not taking stimulant medications. Specific stimulant medications and napping appear to have an impact on self reported sleep quality. Besides napping, other sleep variables do not appear to make a significant contribution to perceived performance and alertness. College students with ADHD have many barriers to academic functioning due to problems with attention and concentration (among others), therefore, taking steps to minimize additional barriers to maximal functioning should be strongly considered.

0961

DEPRESSIVE SYMPTOMS AND SLEEP DISTURBANCES AMONG COMMUNITY DWELLING OLDER MEN

Paudel M,[1] Taylor B,[2] Diem S,[1] Stone K,[3] Ancoli-Israel S,[4] Redline S,[5] Ensrud K[1]
(1) University of Minnesota, Minneapolis, MN, USA, (2) Minneapolis-VAMC, MN, USA, (3) California Pacific Medical Center (CPMC), San Francisco, CA, USA, (4) University of California, San Diego, San Diego, CA, USA, (5) Case Western Reserve University, Cleveland, OH, USA

Introduction: Prior studies suggest an association between depression and sleep disturbances in older people, but are limited by sampling methods, small sample sizes and/or reliance on either subjective or objective sleep measures.
Methods: We measured depressive symptoms and subjective and objective parameters of sleep in 3,051 men (mean age 76.4 years) enrolled in the community-based MrOS Sleep study. Depressive symptoms were identified using the 15-item Geriatric Depression Scale and categorized as 0-2 (not depressed, referent group), 3-5 (depressive symptoms) and 6-15 (depressed). Objective sleep measures were ascertained using wrist actigraphy (mean duration 5.2 nights), and subjective sleep measures were assessed using the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS); poor sleep quality was defined by PSQI>5 and excessive daytime sleepiness was defined by ESS>10. Prevalence odds ratios (ORs) were calculated using logistic regression.
Results: After adjustment for multiple potential confounders including medication use, depressive symptoms and depression were strongly associated with subjective sleep disturbances (p-trend<0.001). For example, compared to the referent group, depressed men were 4.5 times more likely to report poor sleep quality and 2.8 times more likely to report excessive daytime sleepiness. There was some evidence of a greater likelihood of > 8 long wake episodes (p-trend=0.068) and sleep efficiency <70% (p-trend=0.038) with depressive symptoms, and a greater likelihood of sleep latency >1 hour (p-trend=0.003) with increasing evidence of depression, however the odds ratios for these objective sleep disturbances (range 1.1 to 1.7) were smaller in magnitude compared to subjective measures. Excluding men taking antidepressants, benzodiazepines or other anxiolytic/hypnotics from the analysis did not alter the results.
Conclusion: In community dwelling older men, depressive symptoms

have a strong, graded association with subjective sleep disturbances, but are not as strongly related to objectively measured sleep disturbances. Future studies should address temporality of depression and sleep disturbances.

0962

PROSPECTIVE ASSOCIATIONS OF INSOMNIA WITH INCIDENT DEPRESSION IN THE WISCONSIN SLEEP COHORT

Szklo-Coxe M, Finn L, Young T
University of Wisconsin-Madison, Madison, WI, USA

Introduction: Chronic insomnia, associated with substantial morbidity and adverse sequelae (e.g., absenteeism, reported by Léger et al (2006)) exacts a heavy societal toll. However, insomnia´s natural history and consequences are poorly understood, given scarce longitudinal research to date, and warrant elucidation (NIH State-of-the-Science insomnia conference statement, 2005). We thus conducted an epidemiologic study of insomnia´s longitudinal relationship to depression. Both are prevalent, costly disorders with significant public health burdens.
Methods: The sample consisted of 595 Wisconsin Sleep Cohort participants who completed baseline(1998-2002) and 4-year(2002-2006) follow-up overnight sleep protocols including eighteen-channel PSG(Grass Heritage), Zung Self-Rating Depression Scale, and health questionnaire containing insomnia (difficulty falling asleep, difficulty maintaining sleep, awakening repeatedly p.m, awakening too early) and antidepressant items. To investigate incident depression, participants depressed at baseline were excluded. Insomnia was defined as having symptoms(s) often(5-15/month) or always(16-30/month) versus sometimes(2-4/month) or less; depression, as Zung>=50(excluding sleep-related items 4 and 10) or antidepressant use. Three multivariable logistic regression models, adjusted for age, sex, chronic illnesses, assessed odds of developing depression with respect to: any insomnia symptom(s)(1, 2, 3 or 4); the individual symptom, difficulty falling asleep; and PSG-measured sleep latency (SL)(time from lights off to stage 2 or REM, categorized as >14 minutes-upper quartile).
Results: One (odds ratio(OR)=0.80) or two (OR=1.4) symptoms did not (P>=0.33) predict depression after adjustments. Three or four symptoms increased depression onset odds ~200% (OR=3.1, 95%CI, 1.4-6.9), even with further adjustments (alcohol, smoking, caffeine, sedatives, apnea-hypopnea index, body mass index) (OR=2.6; 95%CI, 1.1-6.0). Of individual symptoms, difficulty falling asleep predicted depression most, increasing depression odds 2.1-fold (95%CI, 1.0-4.4). Longer SL also predicted depression (Zung>=50 excluding antidepressants) (OR=3.1, 95%CI, 1.2-8.0).
Conclusion: Insomnia strongly predicted depression development in our cohort, supporting prior limited epidemiologic findings by Ford and Kamerow(1989) and Breslau et al(1996). Whether early insomnia identification and treatment can prevent depression merits future research.
Support (optional): This research was supported by NIH grant HL62252.

0963

SLEEP DISTURBANCES AND DEPRESSION IN YOUNG AND OLDER ADULTS

Koffel E, Watson D
University of Iowa, Iowa City, IA, USA

Introduction: The current study explored relations between sleep disturbances and depression and the impact of age on sleep-depression relations. Measures of anxiety were included because there is evidence that sleep problems are also related to a wide-range of anxiety disorders.
Methods: This study used a sample of 251 college students (82 men, 169 women; mean age 19) and 102 older adult community members (30 men, 71 women, 1 unreported; mean age 73). Study recruitment is ongoing. Participants completed measures of depression (e.g., BDI-II, IDAS Dysphoria scale) and anxiety (e.g., BAI, IDAS scales measuring symptoms of post-traumatic stress disorder, social anxiety, panic). Participants also completed retrospective 7-day sleep calendars and standard sleep questionnaires (e.g., PSQI, ESS, IDAS Hypersomnia, Insomnia and Lassitude scales).
Results: For older adults, problems falling asleep and waking up too early were significantly related to depression, whereas for young adults, waking up during the night was related to depression and anxiety. In order to clarify the structure defined by the symptoms of insomnia, hypersomnia and fatigue, the student responses were submitted to principal factor analyses. These analyses indicated two meaningful factors, Insomnia (defined by measures of insomnia) and Lassitude (defined by measures of oversleeping and fatigue). The Insomnia and Lassitude factors correlated significantly with measures of depression, generalized anxiety, post-traumatic stress disorder, social phobia and panic disorder.
Conclusion: Sleep disturbances are associated with depression and anxiety disorders for both young and older adults. Early and late insomnia, however, may be more important symptoms of depression in older adults, whereas middle insomnia is a nonspecific symptom of anxiety and depression in young adults. Factor analyses suggest that sleep disturbances form two related but distinct factors of Insomnia and Lassitude.

0964

EVALUATION OF THE HAMILTON DEPRESSION SCALE FOLLOWING ESZOPICLONE TREATMENT FOR INSOMNIA IN PATIENTS WITH INSOMNIA CO-MORBID WITH MAJOR DEPRESSIVE DISORDER OR GENERALIZED ANXIETY DISORDER

Fava M,[1] Pollack M,[1] Rubens R,[2] Amato D,[3] Krystal A,[4] Hayduk R,[5] McCall W[6]
(1) Massachusetts General Hospital, Boston, MA, USA, (2) Sepracor Inc., Marlborough, MA, USA, (3) Sepracor Inc, MA, USA, (4) Duke University, Durham, NC, USA, (5) Quintiles, San Diego, CA, USA, (6) Wake Forest University, Winston-Salem, NC, USA

Introduction: Major Depressive Disorder (MDD) and generalized anxiety disorder (GAD) can coexist and patients may have insomnia marked by difficulty falling and/or staying asleep and potentially reduced quality of life (QoL). Eszopiclone has been shown to improve sleep in patients with insomnia comorbid with MDD or GAD. This analysis examined the effects of eszopiclone co-therapy on the HAM-D17 in these two patient populations.
Methods: Patients with insomnia comorbid with MDD and baseline HAM-D17>14 (excluding insomnia items; n=545) received morning fluoxetine and were randomized to nightly eszopiclone 3mg or placebo for 8 weeks. Patients with insomnia comorbid with GAD and screening MADRS≤20 (n=593) received daily escitalopram oxalate and were randomized to nightly eszopiclone 3mg or placebo for 8 weeks. Clinician-administered HAM-D17 was evaluated at baseline and Weeks 4 and 8 in both studies.
Results: Baseline HAM-D17 median scores were 22 and 15 in the MDD and GAD populations, respectively. Change from baseline HAM-D17 scores were significantly improved ($p<0.02$) with eszopiclone co-therapy at Weeks 4 (-10.0±7.6) and 8 (-13.6±7.7) relative to fluoxetine monotherapy (-8.4±6.8 and -11.5±7.1) in the MDD population.

Similarly, change from baseline HAM-D17 scores in the GAD population were significantly improved (p<0.002) with eszopiclone co-therapy at Weeks 4 and 8 (-5.8±4.9 and -6.7±5.4) relative to escitalopram monotherapy (-4.3±5.1 and -5.4±5.6). When the insomnia items were removed, there were still significant reductions from baseline in HAM-D17 scores with eszopiclone co-therapy relative to monotherapy at Week 8 in the MDD population (-10.0±6.4 vs -9.0±6.0; p=0.042) and at both Weeks 4 and 8 in the GAD population (-3.3±4.1 vs. -2.6±4.1 and -4.0±4.4 vs -3.4±4.7; p<0.03).
Conclusion: Treatment of insomnia with eszopiclone was associated with significant improvements in HAM-D17 scores relative to fluoxetine or escitalopram monotherapy in patients with insomnia comorbid with MDD or GAD, even after removal of insomnia items from the scale.
Support (optional): Support for this study provided by Sepracor Inc.

0965

EFFECTS OF ESZOPICLONE CO-THERAPY WITH ESCITALOPRAM ON MEASURES OF ANXIETY AND MOOD OUTCOMES IN PATIENTS WITH INSOMNIA AND COMORBID GENERALIZED ANXIETY DISORDER

Pollack M,[1] Rubens R,[2] Amato D,[3] Schaefer K,[2] Pfleeger K,[2] Hayduk R,[4] Roth T[5]
(1) Massachusetts General Hospital, Boston, MA, USA, (2) Sepracor Inc., Marlborough, MA, USA, (3) Sepracor Inc, Marlborough, MA, USA, (4) Quintiles, CA, USA, (5) Henry Ford Health System, Detroit, MI, USA

Introduction: Insomnia may coexist with generalized anxiety disorder (GAD). This study evaluated the efficacy of eszopiclone (ESZ) co-therapy with escitalopram (EO) on sleep, and measures of anxiety and mood relative to escitalopram monotherapy in patients with insomnia and comorbid GAD. Here we report data specific to anxiety and mood.
Methods: Patients meeting DSM-IV-TR criteria for GAD and insomnia received 10 weeks of EO 10mg and were randomized to ESZ 3mg (n=294) or placebo (PBO) (n=301) for 8 weeks, followed by 2-weeks single-blind PBO run-out to evaluate discontinuation. Anxiety and mood symptoms were assessed by the investigators at Weeks 1, 2, 4, 6, 8, and 10 using HAM-A, Clinical Global Impression (CGI-Severity and Improvement) and HAMD-17. Change from baseline analyses were performed for all measures using ANCOVA and time to onset analyses used the Kaplan-Meier method.
Results: Compared to PBO+EO, there were significant improvements from baseline with ESZ+EO in HAM-A total score at each week (p<0.05), and at Weeks 4-10 when the insomnia item was excluded (p<0.05). CGI-I was significantly improved with ESZ+EO at every timepoint (p<0.02), while CGI-S was not significantly different after Week 1. Median time to onset of anxiolytic response was reduced based on HAM-A (29 days for ESZ+EO vs 32 days for PBO+EO; p = 0.023) and CGI-I (18 days vs 28 days, respectively; p=0.052). HAM-A response (63% vs 49%, respectively; p<0.05) and remission (42% vs 36%, respectively; p=0.09) rates at Week 8 were higher in the ESZ+EO group. HAM-D17 total scores were also significantly improved in the ESZ+EO group at all time points (p<0.004). At Week 10, after ESZ discontinuation, significant treatment differences were maintained for HAM-A.
Conclusion: In this study, treatment of insomnia with eszopiclone co-administered with escitalopram oxalate treatment for GAD was associated with significantly greater improvement in measures of anxiety and mood as compared to escitalopram monotherapy.
Support (optional): Support for this study provided by Sepracor Inc.

0966

EFFECTS OF ESZOPICLONE CO-THERAPY WITH ESCITALOPRAM ON SLEEP OUTCOMES IN PATIENTS WITH INSOMNIA AND COMORBID GENERALIZED ANXIETY DISORDER

McCall W,[1] Schaefer K,[2] Rubens R,[2] Huang H,[3] Pfleeger K,[2] Hayduk R,[4] Roth T[5]
(1) Wake Forest University, Winston-Salem, NC, USA, (2) Sepracor Inc., Marlborough, MA, USA, (3) Sepracor Inc, Marlborough, MA, USA, (4) Quintiles, CA, USA, (5) Detroit, MI, USA

Introduction: Insomnia may coexist with generalized anxiety disorder (GAD). This study evaluated the efficacy of eszopiclone (ESZ) co-therapy with escitalopram (EO) on sleep, anxiety and mood outcomes relative to escitalopram monotherapy in patients with insomnia and comorbid GAD. Here we report the data specific to sleep.
Methods: Patients meeting DSM-IV-TR criteria for GAD and insomnia received 10 weeks of EO 10mg and were randomized to ESZ 3mg (n=294) or placebo (PBO;n=301) for 8 weeks. For the following 2 weeks, ESZ was replaced with single-blind PBO to evaluate discontinuation effects. Insomnia symptoms were assessed throughout the study via patient-reported (daily sleep diary) sleep latency (SL), wake time after sleep onset (WASO), total sleep time (TST), sleep quality, and daytime functioning symptoms. The Insomnia Severity Index (ISI) was used to assess patient´s perception of their insomnia at Weeks 1, 4, 8 and 10 and adverse events were collected during the study. Change from baseline analyses were performed using ANCOVA.
Results: Compared with PBO+EO, ESZ+EO significantly improved sleep and next day functioning at each assessment and the average of the double-blind period (p<0.05). At Week 8, significantly more ESZ+EO patients had no clinically meaningful insomnia based on ISI≤7 (47% vs 33% with PBO+EO; p<0.001). After eszopiclone discontinuation, there was no evidence of rebound insomnia as all sleep outcomes were improved from baseline on discontinuation Days 1-14. There were no treatment differences in sleep or daytime function measures during the run-out period. Overall AE rates were 78% for ESZ+EO vs 68% for PBO+EO and 16% in both groups during the single-blind run-out period. The most common AEs with ESZ+EO were unpleasant taste, headache and dry mouth.
Conclusion: Eszopiclone co-therapy with escitalopram significantly improved sleep and daytime functioning measures relative to escitalopram monotherapy and there was no evidence of rebound insomnia upon discontinuation of eszopiclone.
Support (optional): Support for this study provided by Sepracor Inc.

0967

MUSIC AND MUSCLE RELAXATION THERAPIES AS TREATMENT FOR INSOMNIA IN POST TRAUMATIC STRESS DISORDER PATIENTS

Haimov I,[1] Blanaro M,[2] Kremer I,[2] Arnon Z,[1] Ziv N[1]
(1) The Max Stern Academic College of Emek Yizreel, Israel, Emek Yizreel, Israel, (2) Emek Medical Center, Afola, Israel, Afola, AE (Europe), Israel

Introduction: Disturbed sleep is a common complaint among Post Traumatic Stress Disorder (PTSD) patients and has even been referred to as the "hallmark" of PTSD. Since previous studies have demonstrated treatment resistance for sleep-medication treatment for insomnia in these patients, the aim of the present study was to examine the effects of music and muscle relaxation therapies as treatment for insomnia in PTSD patients.
Methods: Thirteen PTSD patients, who had no other major psychiatric,

sleep, or neurological disorders, participated in the study (mean age=45.5, SD=11.8; 7 males and 6 women). The study comprised one 7-day, running-in, no-treatment period, followed by two 7-day experimental periods. The treatments were either Music Therapy or Muscle Relaxation Therapy at desired bedtime. These treatments were randomly assigned. During each of these three experimental periods, subjects' sleep was continuously monitored with a wrist actigraph (Ambulatory Monitoring, Inc.) and subjects were asked to fill out several questionnaires concerned with a wide spectrum of issues, such as depression, anxiety, and life satisfaction.
Results: Analysis revealed a significant increase in sleep efficiency following music therapy. Two-way mixed analysis of variance (ANOVA) with sleep efficiency in three consecutive therapy conditions as within-subject factor and the order of the applied therapy conditions as between-subject factor yielded a significant effect of therapy conditions on sleep efficiency [$F(2,10)=9.21$, $P<0.005$]. No significant effect was found for the order of the applied therapy conditions on sleep efficiency [$F(1,11)<1$], nor to the interaction between the therapy condition and the order of application [$F(2,10)=2.553$, $P>0.127$]. Finally, test of within-subject contrasts revealed a significant increase in sleep efficiency following music therapy, compared with baseline [$F(2,11)=9.955$, $P<0.009$].
Conclusion: Overall, the findings imply the beneficial effect of Music Therapy compared to Muscle Relaxation Therapy as treatment for insomnia in Post Traumatic Stress Disorder patients.

0968

WEB-SURVEY OF PHARMACOLOGICAL AND NONPHARMACOLOGICAL SLEEP INTERVENTIONS FOR CHILDREN WITH EARLY-ONSET BIPOLAR SPECTRUM DISORDERS (EBSD)

Lofthouse N,[1] Splaingard M,[2] Fristad M,[1] Kelleher K,[1] Hayes J,[3] Resko S,[4] Gusfa J[2]
(1) Ohio State University, Columbus, OH, USA, (2) Columbus Children's Hospital, Columbus, OH, USA, (3) Columbus Children's Hospital, OH, USA, (4) Child and Adolescent Bipolar Foundation, IL, USA

Introduction: Although a reduced need for sleep and insomnia/hypersomnia are listed as DSM-IV symptoms of mania or depression, respectively, few publications exist on EBSD-related sleep problems (Lofthouse *et al.*, 2007). Furthermore, despite a variety of commonly utilized pharmacological and nonpharmacological treatments for EBSD-sleep problems, none have been tested with youth (Harvey *et al.*, 2006). Supplementing last year´s APSS presentation on a web-survey of EBSD-sleep problems (Lofthouse *et al.*, 2006), we report additional study findings exploring parent-reported pharmacological and nonpharmacological sleep interventions that improve or worsen sleep.
Methods: 494 parent-members of the Child and Adolescent Bipolar Foundation, who reported their children had been diagnosed with EBSD, completed a web-survey on EBSD-sleep problems and treatment.
Results: The majority of parents reported sleep problems during a "worst mood episode" (98%), other mood episodes (94%) and currently (70%) and consulting a variety of professionals about these problems (psychiatrists: 85%, physicians: 64%, & psychologists: 50%). Medications/supplements identified as helping sleep include: Atypical antipsychotics (54%), Benadryl (21%), mood stabilizers (20%) and anti-hypertensives (20%). Medications/supplements reported as worsening sleep include: Stimulants (34%), SSRI´s (16%), Benadryl (14%), Strattera (13%) and atypical antipsychotics (11%). Non-pharmacological interventions identified as helping sleep include: Sleep routine (52%), nightlight/cuddly-toy/blanket (42%), parents staying with child until asleep (40%), reading tape (32%), massage (30%), changing bedroom environment (26%), bath/shower (24%) and reassurance (23%). Non-pharmacological interventions reported as worsening sleep include: Punishment (35%), parents not staying with child until asleep (29%), earlier/later bedtime (22%) and earlier/later wake-time (21%).
Conclusion: Most parents reported their children had past and current mood-related sleep difficulties and seeking professional help for those problems. Atypical antipsychotics and sleep routines were most frequently identified as helping sleep while stimulants and punishments were most commonly identified as worsening sleep. Limitations of the web-based methodology and clinical and research implications will be discussed at APSS.

0969

SLEEP IN A RAT MODEL OF POST MYOCARDIAL INFARCTION DEPRESSION: A PILOT STUDY

Bah T,[1] Wann B,[1] Chebli M,[2] Le Marec N,[1] Rousseau G,[1] Godbout R[1]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) 1, Montreal, Quebec, Canada

Introduction: Myocardial infarction (MI) is followed within a few months by major depression in 15-30 % of patients. We have replicated this phenomenon in a rat model in which post-MI behavioral signs of depression and limbic apoptosis were blocked by antidepressants (Wann *et al.*, 2006, 2007). We now report preliminary results of a pilot study characterizing sleep patterns of rats following MI.
Methods: Six adult Sprague-Dawley rats were implanted with chronic EEG and EMG electrodes. Five days after surgery, the rats were habituated to the recording equipment for two days and then baseline sleep was recorded for 24h. The following morning MI was induced by occluding the left coronary artery for 40 minutes in three rats; the three other rats were used as sham controls. Sleep was recorded again for 24h two weeks after MI. Comparisons between groups were made using t-tests for independent samples.
Results: Compared to sham rats, MI rats displayed less total sleep time and more minutes in REM sleep. Analysis by fractions of recording time showed that sleep loss was more important during the light-dark transition and that REM sleep was particularly increased during the first part of the light period.
Conclusion: These observations of signs of insomnia and increased REM sleep pressure in rats following MI are compatible with sleep in rat models of depression.
Support (optional): Supported by the Canadian Institutes of Health Research.

0970

SLEEP´S ROLE IN MEMORY CONSOLIDATION: DIFFERENT PROCESSES FOR REMITTED DEPRESSED AND NEVER DEPRESSED INDIVIDUALS

Smith L,[1] Britton W,[2] Bootzin R[3]
(1) University of Arizona, Tucson, AZ, USA, (2) University of Arizona, AZ, USA, (3) University of Arizona, Tuscon, AZ, USA

Introduction: Recent evidence suggests that sleep plays a major role in memory consolidation. Depressed individuals show a negative memory bias, whereas normal controls tend to show a positive bias. These findings suggest that sleep may serve a different memory consolidation function in depressed than in nondepressed individuals.
Methods: Subjects with partially remitted Major Depressive Disorder (n=16) and control subjects with no history of depression (n=13) were shown 30 slides from the International Affective Picture System (with

positive, negative, and neutral valences). Subjects were asked to recall as many pictures as possible after a full night of sleep. Sleep was assessed by overnight polysomnography. Bivariate correlations assessed the relationship between sleep variables and picture recall.
Results: Poorer, lighter sleep, as indicated by increased REM latency, increased stage 1 percent, decreased stage 2 time, and decreased sleep efficiency, was associated with improved recall for neutral pictures in formerly depressed subjects, but not in control subjects ($p<0.05$). Better sleep, as indicated by increased stage 2 time, was associated with improved recall for positive pictures in formerly depressed subjects, but not in controls ($p=0.07$). A different pattern was seen in control subjects in whom better sleep, as indicated by decreased stage 1 time and percent and increased stage 2 time, was associated with improved recall of negative pictures when compared to formerly depressed subjects ($p<0.05$).
Conclusion: Sleep appears to serve different memory consolidation functions for formerly depressed versus control subjects. In formerly depressed subjects, poor sleep facilitates recall of neutral material whereas improved sleep facilitates recall of positive emotional stimuli. In control subjects improved sleep facilitates recall of negative emotionalstimuli. The different memory processes for consolidating emotional memories may reflect differences in the interaction between sleep and memory for formerly depressed and never depressed individuals.

0971

PRESERVED SLOW WAVE SLEEP IN CHILDREN DIAGNOSED WITH BIPOLAR DISORDER

Gusfa J,[1] Lofthouse N,[2] Dzodzomenyo S,[2] Fristad M,[2] Hayes J,[1] Splaingard M[1]
(1) Columbus Children's Hospital, Columbus, OH, USA, (2) Ohio State University, Columbus, OH, USA

Introduction: Youth with Affective Disorders have long been recognized to experience significant dysfunctions in their regulatory processes. Sustained disruptions in sleep, for example, have been a central component in trying to classify children with Bipolar Disorder (BP) from other psychopathologic vulnerabilities. Slow-Wave Sleep (SWS) is thought to mediate in the restorative aspects of sleep and is viewed essential toward early childhood growth and development. This study explores the relationships between BP, age, medication and SWS in youth.
Methods: Participants include 42 children and adolescents with a prior community diagnosis of BP who underwent polysomnography (PSG) as part of evaluation for disrupted sleep in the past 3 years.
Results: There were 32 males (76%), mean age 12.5 years (range 5.5 - 18 years) with 31% of children between 10 -12 years. Ages were otherwise continuously distributed. Linear regression demonstrated a significant linear decline in SWS across the ages (5 to 18) measured (slope=-2.1, R2=.42, $p<.001$). There was an average loss of 2% SWS for every year aged in the sample. A stepwise multiple regression analysis showed that antipsychotic medications ($p=0.16$), antidepressants ($p=0.10$), sleeping agents ($p=0.9$) and stimulants ($p=0.53$) had no association on the % SWS. Anticonvulsants appeared to have a suppressing effect on SWS (mean 5.6% suppression, $p=.03$) increasing the overall R2 to .48 ($p<.001$) when included with age.
Conclusion: This study suggests that children diagnosed with BP spend a greater percentage of their sleep in SWS compared to similarly diagnosed adolescents. The physiologic demands of early development, including greater need for SWS, may override the disruptions in sleep produced by childhood affective dysregulation. An additional finding is that anticonvulsants seem to further suppress SWS. Limitations and future directions for study will be discussed.

0972

PREVALENCE OF MAJOR DEPRESSIVE DISORDER IN PATIENTS WITH SLEEP DISORDERS

Novak W, Budur K
Cleveland Clinic Foundation, Cleveland, OH, USA

Introduction: Clinical experience and a review of literature suggest a high co-morbidity between major depressive disorder (MDD) and sleep disorders. However, the true prevalence and severity of depression among various sleep disorders has not been definitely determined. The aim of the study was to assess the overall prevalence and severity of depression (by means of the Beck Depression Inventory [BDI]) in patients with sleep disorders both with and without history of MDD
Methods: Retrospective chart review of 521 patients seen at the Cleveland Clinic Sleep Disorders Center, who completed the BDI during their initial visit. Demographics and functional variables were extracted from the patients´ charts. Depression and its severity were defined by BDI scores (8-15 mild, 16-25 moderate, >25 severe).
Results: Of 521 patients (263 female, 258 male) ages 16 to 96 years (mean age: 49) evaluated for a sleep disorder(s) the overall mean BDI was 11.98 (95%CI 11.26-12.74), with 69% having a BDI >7. Of those with BDI >7, 41% had prior diagnosis of MDD of which 89% were taking antidepressants. There was no significant difference in prevalence or severity of depression among different age groups. Severity of depression was greater among females than males: mean BDI 13.68 (95%CI 12.61-14.75) and 10.30 (95%CI 9.04-11.56) respectively. The prevalence of depression (BDI >7) among four major primary sleep disorders was: psychophysiological insomnia 83.5% ($p<0.0001$), obstructive sleep apnea syndrome 60% ($p=0.0003$), restless legs syndrome 81.8% ($p=0.30$) and narcolepsy 61.5% ($p=0.66$). Severity of depression was greatest in psychophysiological insomnia; mean BDI 17.37 (95%CI 15.75-18.99).
Conclusion: Optimizing the diagnosis and treatment of both depression and sleep disorders requires a better understanding of their relationship. The findings suggest that depression may be much more common in those with sleep disorders, with its prevalence and severity being greatest in those with psychophysiological insomnia.

0973

SLEEP ARCHITECTURE IN BIPOLAR TYPE II DEPRESSION: A POLYSOMNOGRAPHIC STUDY OF TWENTY PATIENTS

Budur K, Hariadi N
Cleveland Clinic Foundation, Cleveland, OH, USA

Introduction: Bipolar disorder affects over 5.7m Americans every year. Bipolar depression is the most common manifestation of Bipolar disorder, and is a distinct entity from Unipolar depression in its pathogenesis/management. Disrupted sleep is an integral part of Bipolar depression. It is often the first manifestation and also most resistant to treatment. Although the changes in sleep architecture of Unipolar depression are known, there are no polysomnographic studies looking at the changes in sleep architecture of Bipolar depression.
Methods: The polysomnogram´s of 20 patients with a diagnosis of Bipolar Type II, depression phase, were analyzed to study sleep architecture changes and compared to normal controls. These patients were evaluated at the Sleep center.
Results: The mean total sleep time was 371.2 min (95% CI: 319.8-422.6) and the mean sleep efficiency was 79.4% (95%CI: 70.84-88.07). The mean sleep latency was 23.53 min (95%CI: 11.33-35.73) and the mean REM latency was 205 min (95%CI: 128.9-282.0). The mean and

95%CI´s of different sleep stages were: Stage 1 (9.8; 4.0-15.6), Stage 2 (61.5; 53.2-69.8), Stage 3/4 (13.4; 7.3-19.4) and REM (12.8; 7.4-18.3). The arousal index was 15.1(95%CI: 10.8-19.4). The differences in REM latency, sleep stages and the arousal index were statistically significant ($p<0.05$) compared to normal sleep. REM sleep was more disrupted (longer REM latency, decrease in the total REM period) compared to Unipolar depression.
Conclusion: The results of this study show that the sleep architecture in Bipolar depression is distinct and more disrupted when compared to normal sleep and sleep in Unipolar depression. It is possible that the mechanisms underlying sleep disturbances in Bipolar depression are different compared to Unipolar depression. Further research to exclude the first night effect is needed. It needs to be seen if treating sleep problems as a distinct entity in Bipolar depression will lead to an early/sustained remission as seen in Unipolar depression.
Support (optional): None

0974

SLEEP DURATION AND DEPRESSION AMONG AMERICANS WITH VISION PROBLEMS

Zizi F,[1] Jean-Louis G,[1] Singh M,[2] Lazzaro D,[2] Dweck M,[2] Dallara A,[2] Blanco D[2]
(1) State University of New York Health Science Center at Brooklyn, brooklyn, NY, USA, (2) State University of New York Health Science Center at Brooklyn, NY, USA

Introduction: In this study, we examined whether the relationship between visual impairment and depression is mediated by habitual sleep duration.
Methods: In our analysis, we used data from the National Health Interview Survey conducted in 2005. The survey used a cross-sectional, multistage area probability design to acquire data from U.S. households. A total of 29,818 adults representative of the non-institutionalized U.S. population (mean age = 48 ± 18 yrs) participated in the study. Respondents answered questions during face-to-face interviews about chronic conditions. They also provided sociodemographic data, estimated habitual sleep duration, and rated depressed moods experienced in past 30 days (low scores represented greater depression).
Results: Of the sample, 44% were men and 56% were women; Whites and Blacks represented 85% and 15%, respectively. At the time of the interview, 61% had a job. Overall, 35% indicated functional limitation due to chronic conditions: 28% reported hypertension; 8%, heart disease; 8%, cancer; 9%, diabetes; and 23%, arthritis. Ten percent reported visual impairment even with glasses or lens. The average respondent slept 7 hrs habitually. Fisher´s Exact test indicated visually impaired individuals were more likely to report short (≤5 hrs) or long (≥9 hrs) sleep duration [28% vs. 16%; $\chi^2=258$, $p<0.0001$] than their counterparts. ANOVA results indicated that they were more depressed [18 ± 3 vs. 16 ± 4; $F=1239$, $p<0.0001$]. However, effects of visual impairment on depression were dependent on habitual sleep duration [$F=27$, $p<0.0001$]; individuals reporting both visual impairment and short/long sleep tended to be more depressed. The model adjusted for age, sex, and race effects on depression.
Conclusion: Individuals with visual impairment experienced more depression and were characterized by a higher prevalence of short and long sleep. However, depression was worse among respondents who reported both visual impairment and sleeping unusually less or more than the population mode.
Support (optional): This research was supported by funds from NIH (1R24MD001090).

0975

SLEEP DURATION AND EMOTION REGULATION AMONG URBAN MINORITY WOMEN

Compas C,[1] Jean-Louis G,[1] Magai C,[2] Consedine N,[2] Zizi F,[1] Rodriguez O,[3] Brown R[3]
(1) State University of New York Health Science Center at Brooklyn, Brooklyn, NY, USA, (2) Long Island University, NY, USA, (3) State University of New York Health Science Center at Brooklyn, NY, USA

Introduction: This study explored the associations between sleep duration and emotion regulation among urban minority women.
Methods: The study sample comprises 523 Black women (mean age = 59 ± 7 yrs) living in Brooklyn, NY. Recruitment was done using a stratified, cluster sampling technique. Eligible women provided data during face-to-face interviews, conducted with trained women interviewers. Questionnaires were used to acquire demographic, subjective, and physical health data. Additionally, women estimated their habitual sleep duration. A modified version of Weinberger´s conceptual model of repression, the Index of Self-Regulation (ISE) was utilized to measure repressive coping. Consistent with Mendolia´s conceptualization, ISE scores were derived by amalgamating the defensive subscale from the Social Desirability Scale and the anxiety subscale from the State-Trait Anxiety Inventory; high scores represented greater repressive coping ability.
Results: Of the sample, 80% had at least a high school diploma. The median income of those women was $10,000, and the median BMI was 29 kg/m2. Thirty-six percent of the women reported insomnia symptoms; 38% reported heart disease; 66%, arthritis; 23%, respiratory disease; 60% hypertension; and 50%, vision problems. The median habitual sleep time was 7 hrs; 39% slept ≤;6 hrs and 26% slept ≥8 hrs. Overall, 72% of women characterized as highly anxious reported sleep duration either ≤6 hrs or ≥8 hrs; 28% indicated sleep durations within the healthy range (6-8 hrs) [$\chi^2=6.07$, $p<0.01$]. ANCOVA results, adjusting for differences in age, education, and income, indicated that women sleeping within the healthy range had significantly greater scores on the self-regulation scale [$F4,518=22.33$, $p<0.0001$].
Conclusion: Consistent with previous research short and long sleep duration is a strong determinant of the likelihood of experiencing anxiety, but anxiety was more prevalent among women sleeping ≤6 hrs. Women sleeping between 6 and 8 hrs might be more adept at regulating negative emotions in their daily lives.
Support (optional): This research was supported by funds from NIH (1R24MD001090 and SO6GM54650).

0976

EFFECTS OF ESTROGEN THERAPY ON SLEEP IN HEALTHY AND DEPRESSED MENOPAUSAL WOMEN

Nowakowski S, Meliska C, Parry B
University of California, San Diego, La Jolla, CA, USA

Introduction: We hypothesized that estrogen deficiency after menopause contributes to sleep disturbances, and that administering estrogen therapy (ET) would improve sleep quality. To test this hypothesis, we examined sleep polysomnography (PSG) profiles before and after 8-weeks of ET in menopausal women with and without clinical depression.
Methods: In 12 menopausal women, eight normal controls (NC; mean age=54.3+5.5 years) and four depressed patients (DP; mean age=51.8+3.5 years) who met Diagnostic and Statistical Manual (DSM-IV-TR) criteria for a major depressive episode, sleep was recorded by PSG pre- and post-treatment with oral 17-â Estradiol (Estrace) 1-2 mg for eight weeks. A two-factor mixed-model MANOVA was conducted to

examine changes in total sleep time (TST), sleep efficiency (SE), sleep latency (SL), and wake after sleep onset (WASO).
Results: MANOVA revealed main effects of diagnosis (p=.035) and treatment (p=.003). Before treatment, DP had longer SL (51.2 vs. 13.6m; p=.015), more WASO (128.27 vs. 44.59m; p=.030), lower SE (60.8% vs. 85.9%; p=.005), and marginally less TST (280.3 vs. 373.3m; p=.064) when compared with NC. Following ET, WASO decreased (117.1 vs. 55.7m; p=.011) and SE increased (67.8% vs. 78.8%; p=.042). Analysis of a significant treatment x diagnosis interaction (p = .001) showed SL was longer in DP (40.1 vs. 62.2m), and slightly shorter in NC women (15.6 vs. 11.6m) following ET (p=.045).
Conclusion: Menopausal DP vs. NC had impaired sleep quality (lower TST and SE, increased SL and WASO) at baseline. After ET, sleep quality improved in both DP and NC women, and group differences remained significant. Possible mechanisms of ET on sleep quality could be a direct effect, or ET could indirectly affect sleep by other mechanisms such as improved mood, reduced hot flashes, or synchronizing circadian rhythms. The small sample size limits the interpretations of the findings.

0977

SLEEP DISTURBANCE AS A UNIQUE RISK FACTOR FOR COMPLETED SUICIDE

Bernert R,[1] Turvey C,[2] Conwell Y,[3] Joiner T[4]
(1) Florida State University, Tallahassee, FL, USA, (2) University of Iowa, Iowa City, IA, USA, (3) University of Rochester, Center for the Study and Prevention of Suicide, NY, USA, (4) Florida State University, FL, USA

Introduction: Research suggests that sleep disturbances may constitute an important and modifiable risk factor for elevated suicidality. Sleep complaints are closely coupled with the single best predictor of suicide, depression. Even so, a paucity of research has investigated how poor sleep may uniquely predict increased risk for suicide. Suicidal behavior ranges in severity from ideation to suicide attempts to completed suicide; however, a study has yet to examine whether poor self-reported sleep quality, controlling for depression, prospectively predicts completed suicide.
Methods: Data were collected among 14,456 community elders over a 10-year period in a longitudinal, multi-site cohort study (EPESE: Established Populations for Epidemiological Studies of the Elderly). A 5-item Sleep Quality Scale was used to evaluate the presence and frequency of self-reported sleep complaints (difficulty falling asleep/staying asleep, early-morning awakenings, daytime sleepiness, and feelings of restfulness during the day); the CES-D symptom inventory was used to assess the presence of depression; and vital statistics were obtained for all participants. Over a 10-year-period, 21 individuals died by suicide. Using a case-control design, each suicide was matched to 20 randomly-selected controls. Poor baseline sleep was hypothesized to significantly predict completed suicide after controlling for depression.
Results: A hierarchical logistic multiple regression revealed that poor self-reported sleep disturbances at baseline, controlling for depressive symptoms, significantly predicted completed suicide (X2=10.97, df=1, p<.001). Follow-up logistic regressions were conducted to explore whether individual sleep items predicted completed suicide, again controlling for depression. One sleep item, feeling rested during the day, individually predicted suicide at follow-up (X2=3.65, df=1, p=.056).
Conclusion: Poor self-reported sleep at baseline predicted eventual death by suicide even after controlling for the influence of depression. These findings suggest that sleep disturbances confer considerable risk, independent of depression, for the most severe suicidal behaviors. A more rigorous evaluation of sleep may therefore inform clinical decision-making and guide suicide risk assessment.

0978

GENDER DIFFERENCES ON THE MMPI-2 HYPOCHONDRIASIS SCALE IN SLEEP APNEA PATIENTS

Shaffer J,[1] Norman Z,[2] Bourey R[2]
(1) Regional Center for Sleep Medicine, Toledo, OH, USA, (2) Regional Center for Sleep Medicine, OH, USA

Introduction: Elevations of Scale 1 (Hypochondriasis) on the MMPI-2 reflect concerns about health. This study investigated gender differences on Scale 1 for Obstructive Sleep Apnea (OSA) patients.
Methods: The MMPI-2 was administered to 551 patients (210 females, 341 males) who underwent polysomnographic evaluation for OSA. Hypochondriasis data were analyzed by age, gender, and Apnea/Hypopnea indices (AHI).
Results: Females had higher hypochondriasis scores than males (mean T=67.3 versus T=63.4). Females were dichotomized at the median age, 48.5. Younger females (mean=37.8 years) had essentially the same T scores as older females (mean=57.3 years), T=67.0 versus T=67.5. Males were dichotomized at the median age, 50.0. Younger males (mean=39.8 years) had average T scores of 62.6 versus 64.1 for older males (mean=58.4 years). Gender differences were analyzed as a function of AHI. For an AHI <5, the female mean T score was 69.0 (n=48) versus 58.7 for males (n=29). For an AHI 5-14, the female mean T score was 64.8 (n=86) versus 62.7 for males (n=111). For an AHI 15-30, the female mean T score was 69.2 (n=51) versus 62.7 for males (n=101). For an AHI >30, the female mean T score was 68.6 (n=25) versus 66.2 for males (n=100). The mean AHI for all females was 17.0 and for males, 27.8. Hypochondriasis scores were elevated (T>=65) in 59.5% of females and 42.5% of males. Females with an elevated Scale 1 score had approximately the same AHI (mean=16.7) as females with a non-elevated score (mean=17.4). Males with an elevated score had a significantly higher AHI (mean=32.9) than males whose score was non-elevated (mean=24.0).
Conclusion: Females who present with symptoms of OSA have elevated hypochondriasis scores independent of their AHIs. In contrast, males with high hypochondriasis scores are more likely to have clinically significant OSA. Males with normal AHIs have normal hypochondriasis scores.
Support (optional): none

0979

SLEEP ARCHITECTURE ALTERATIONS IN ADOLESCENTS UNDERGOING MARIJUANA WITHDRAWAL

Cohen-Zion M,[1] Padula C,[1] Arlene S,[2] Ryan W,[2] Tapert S,[1] Drummond S[1]
(1) University of California, San Diego, Department of Psychiatry, San Diego, CA, USA, (2) VA San Diego Healthcare System, Research Service, San Diego, CA, USA

Introduction: Marijuana (MJ) is the most commonly used drug among teens. The adult literature has suggested sleep alterations in MJ users during use and acute withdrawal. To date, there are no published reports in adolescence.
Methods: Fifteen chronic heavy MJ-users (4F, 17.6±1.1yrs) and 19 healthy control (C) (8F, 18.1±1.1yrs) adolescents participated in a 28-day protocol, including 4 in-lab PSGs (nights 1, 2, 27, 28). All teens underwent bi-weekly urine toxicology screening to ensure continued abstinence; all MJ-users screened positive at day 1, suggesting recent use. All C completed 4 PSG nights; all MJ-users completed the first 2 nights, however only 9 remained abstinent to complete the last 2 nights.

We examined sleep differences between the groups in acute (night 2) and extended (night 28) abstinence.
Results: No differences were found for any sleep measure on night 2. On night 28, relative to C, MJ-using teens exhibited higher %REM (21.9% vs. 19.6%; p<.08) and %Stage1 (5.7 vs. 3.6; p<.06) with less %Stage2 sleep (50.7% vs. 55.1%; p=ns) and lower SE (88.3% vs. 92.6%; p<.03). Similarly, no differences were found in PLMs or PLM arousal index (PLMAI) on night 2, but MJ users had a higher PLMAI relative to C (3.4/hr vs. 0.7/hr; p<.05) on night 28.
Conclusion: No architecture differences were seen during the first few abstinence days, however with increasing abstinence, a "REM rebound" phenomenon was observed. One explanation for the lack of initial differences may be that it takes several days for MJ to be fully metabolized, thereby delaying sleep-related withdrawal effects. Additionally, MJ-users showed increased PLM arousals during sustained withdrawal, possibly reflecting CNS dopaminergic dysfunction and possibly creating the lower SE seen in this group. Additional data in MJ-users are currently being collected to further examine these issues, particularly longitudinal changes and the hypothesis that PLMs may accompany sleep difficulties during withdrawal.
Support (optional): NIDA R01 DA021182, NIMH T32 MH18399, UCSD GCRC M01 RR00827

0980

THERAPEUTIC EFFECTS OF A SEDATING ANTIDEPRESSANT ON DAYTIME SLEEPINESS AND FATIGUE IN PATIENTS WITH DEPRESSION

Shen J,[1] Shapiro C[2]
(1) University of Toronto, Toronto, Ontario, Canada, (2) University of Toronto, Ontario, Canada

Introduction: The objectives of this study were to compare the severity of daytime sleepiness and fatigue between depression patients and normal individuals and to systematically investigate therapeutic effects of a sedating antidepressant on these symptoms.
Methods: Subjective measures of sleepiness and fatigue were compared between depression patients (n = 42) and normal controls (n = 32). Thereafter, 16 depression patients took part in a study evaluating the effects of a sedating antidepressant. The Multiple Sleep Latency Test (MSLT), the Epworth Sleepiness Scale (ESS), the Stanford Sleepiness Scale (SSS), the Fatigue Impact Scale (FIS), the FACES Checklist-Fatigue subscale (FAF) and the Fatigue Assessment Instrument (FAI) were performed at baseline and on days 2, 9, 16, 30 and 58. Student t-test and repeated measures analysis of variance (rMANOVA) were used for data analyses.
Results: At baseline, there was no difference on age between patient group (43.9 ± 12.5) and control group (39.7 ± 13.4), but there were significant group differences on the ESS (8.4 ± 4.7 vs. 4.8 ± 3.4; P = 0.001), the SSS (4.1 ± 1.4 vs. 2.0 ± 0.8; P < 0.001), the FSS (5.1 ± 1.4 vs. 2.5 ± 1.2; P < 0.001) and the FIS (82.2 ± 40.8 vs. 13.9 ± 13.1; P < 0.001). There was a linear effect on the MSLT (F = 3.215, P = 0.011), the ESS (F = 3.675, P = 0.021), the SSS (F = 4.454, P = 0.001), the FIS (F = 5.796, P = 0.002) and the FAF (F = 4.731, P = 0.004) during the treatment.
Conclusion: Sleepiness and fatigue are severe in depressed patients. Mirtazapine, a sedating antidepressant, decreased the severity of sleepiness and fatigue in this group of depressive patients.

0981

OPPOSITE CORRELATIONS BETWEEN REM DENSITY AND LEFT VENTRAL ANTERIOR CINGULATE PERFUSION IN MAJOR DEPRESSION PATIENTS AND HEALTHY CONTROLS

Clark C,[1] Brown G,[2] Braun D,[3] Thomas L,[2] Sutherland A,[2] Golshan S,[4] Gillin J[2]
(1) La Jolla, CA, USA, (2) UCSD, CA, USA, (3) CA, USA, (4) University of California, San Diego, La Jolla, CA, USA

Introduction: In our functional MRI study of 1 night's late-night (awake beginning at 3 am) partial sleep deprivation (PSD) in unmedicated major depression patients we reported 1) greater baseline left ventral anterior cingulate (AC) perfusion in responders than nonresponders; 2) decrease in left ventral AC (LVAC) perfusion from baseline to PSD specifically in the responder group; 3) greater baseline bilateral amygdalar perfusion in responders than nonresponders; and 4) right amygdalar perfusion increased with PSD in nonresponders and decreased in responders.
Methods: We analyzed correlations between baseline polysomnographic (PSG) variables and baseline perfusion for whole brain and each region of interest (ROI), calculating correlation coefficients (Pearson´s) separately for depressed (n=17) and control (n=8) groups. PSG was obtained using standard montage and visually scored according to Rechtschaffen & Kales criteria. A priori medial frontal regions of interest (ROIs) were derived from the Talairach Daemon based on PET studies of antidepressants and SD and on Mayberg´s three-compartment model of depression. Amygdalar ROIs were manually delineated on segmented structural MR images.
Results: Baseline LVAC perfusion correlated negatively with baseline REM density in patients (r = -0.360) and positively with REM density (r = 0.641) in controls. Increased baseline REM density has been linked with poor response to SD or interpersonal psychotherapy in depression and may be a marker for poor prognosis in other psychiatric disorders, e.g., relapse in alcoholism. This is the first report linking functional imaging and PSG findings associated with SD response.
Conclusion: Opposite directions of correlations in depressed and control groups are consistent with altered REM regulation in depression, which may reflect altered cholinergic/ aminergic balance. These results are also consistent with the overarousal hypothesis of SD.
Support (optional): Supported by the Sleep Research Society Foundation J. Christian Gillin, M.D. Research Award, 5 K08 MH01642, M01RR00827, the VISN 22 Mental Illness, Research, Education and Clinical Center, and a Veterans´ Administration Merit Review Award.

0982

SLEEP DISORDERS IN FIRST NATIONS´ PEOPLE: A COMMUNITY-BASED STUDY IN NORTHERN BRITISH COLUMBIA (BC)

Froese C,[1] Fleming J,[2] Speirs M,[3] Gosnell C,[4] Butt A,[4] Cheema R,[5] Fleetham J,[2] Mulgrew A,[6] Ayas N[7]
(1) University of British Columbia, Vancouver, British Columbia, Canada, (2) University of British Columbia, British Columbia, Canada, (3) Sleep Disorders Program UBC, British Columbia, Canada, (4) Sleep Disorders Program, UBC, British Columbia, Canada, (5) Sleep Disorders Program, University British Columbia, British Columbia, Canada, (6) University British Columbia, British Columbia, Canada, (7) Vancouver General Hospital, Vancouver, British Columbia, Canada

Introduction: Sleep disorders contribute to daytime sleepiness, depression, chronic health problems, and motor vehicle crashes (MVC). The purpose of this study was to assess the prevalence of common sleep problems in a population at high risk of these outcomes (i.e., First

Nations´, North American Indian) who have little access to sleep-related health services.
Methods: In an ongoing door-to-door survey of adult First Nations people living in the northwestern part of BC, we administered a comprehensive questionnaire including: Epworth Sleepiness Scale (ESS), International Diagnostic Criteria for Restless Legs Syndrome (RLS), and validated depression score (PHQ9). Subjects also had their height, weight, and neck circumference measured.
Results: Thus far, a total of 195 subjects have completed the study; mean (SD) age
was 41.7 yrs (13.5), BMI was 30.7 kg/m2 (10.3), and ESS was 4.40 (3.8). 43% were male, and 30% were obese (i.e. BMI>30). 19% complained of insomnia every night or almost every night; insomnia was significantly associated with depression score ($p<0.01$), and ESS ($p=0.01$). 6 % had RLS (mean symptom duration 27 years); RLS was significantly associated with BMI ($p<0.01$), depression score ($p<0.01$), but not with age or ESS. 36 % of patients snored frequently (>3 nights/week), and 7% were told they stopped breathing during sleep frequently. Frequent snoring was significantly associated with a MVC over the preceding year ($p=0.05$), with a trend to an association with neck circumference ($p=0.07$). ESS was significantly associated with depression score ($p<0.01$), frequent snoring ($p=0.03$), and near-miss MVC ($p=0.01$); with trends to associations with age ($p=0.07$) and BMI ($p=0.07$).
Conclusion: In this ongoing study, sleep complaints were common in this population; access to sleep-related services should be improved in them. Future studies are required to assess the health and safety impacts of these disorders in this vulnerable population.
Support (optional): Michael Smith Foundation Infrastructure Grant (Sleep Disordered Breathing), BCLA, CIHR, Departmental Scholar Award UBC

0983

SUBJECTIVE SLEEP MEASURES IN ABSTINENT ADOLESCENT MARIJUANA USERS

Padula C, Cohen-Zion M, McQueeny T, Winward J, Tapert S, Drummond S
University of California, San Diego, San Diego, CA, USA

Introduction: Marijuana is the most widely used illegal drug among adolescents. Marijuana impacts objective and subjective sleep during acute use, and withdrawal in adults. However, no studies have examined sleep in adolescents during longer-term abstinence. Here, we examined subjective sleep in heavy marijuana using (MJ) adolescents undergoing withdrawal and control (C) adolescents. We hypothesized sleep alterations in MJ during the first week of abstinence only.
Methods: As part of a larger study, 12 MJ and 23 C (age 17.7±1.3) abstained from all drugs and alcohol for 28 days, verified by toxicology screening every 3-4 days, and subjective sleep was measured by daily completion of sleep diaries. Total sleep time, sleep latency, wake after sleep onset, nighttime awakenings, morning alertness, sleep quality, and caffeine consumption were averaged for each 7-day period across 4 weeks. Repeated-measures mixed design 2 (group) x 4 (time) ANOVAs were performed and significant findings were followed up with t-tests.
Results: No subjective measures of sleep quantity or quality showed significant interactions or main effects of groups. A marginally significant main effect of group for caffeine consumption emerged ($F[1,33]=3.09$, $p=0.09$), with follow-up tests suggesting this result was driven by the second (MJ=1.1±1.0, C=0.6±0.6; $p=0.05$) and third (MJ=1.1±1.2, C=0.6±0.5; $p=0.09$) weeks.
Conclusion: Caffeine consumption differences between the groups may reflect a baseline difference or an overall increase in caffeine consumption related to withdrawal effects. Lack of differences in subjective sleep measures between the groups was unexpected and may suggest: 1) MJ users do not perceive any sleep abnormalities during abstinence; 2) Effects are sufficiently acute as to last less than the first week of abstinence; and/or 3) subjective measures may not be good indicators of adolescent sleep since their schedules and sleep patterns are highly erratic. Finally, power may be an issue. Additional data are currently being collected to further examine these hypotheses.
Support (optional): UCSD GCRC M01 RR00827, R01 DA021182, and T32 MH18399.

0984

ASSESSING INSOMNIA SEVERITY IN DEPRESSED PREGNANT WOMEN

Gress J,[1] Manber R[2]
(1) Stanford University, Palo Alto, CA, USA, (2) Stanford University, Stanford, CA, USA

Introduction: Previous research found agreement between the sleep items of the Hamilton Ratings Scales for Depression (HRSD) and their corresponding sleep diary measures in chronically depressed patients (Manber *et al.* 2005 J Psych Resch 39:481-488). The present study examined the agreement between HRSD and diary measures in a sample of pregnant women with Major Depressive Disorder (MDD).
Methods: Participants were 97 pregnant women (20.1±5.7 week gestation; age 32.8±4.6) with MDD and HRSD17 score ≥ 14. Participants were in good health, normal thyroid function, and no comorbid psychiatric disorders. Measures included the early (EARLY) and middle (MIDDLE) insomnia HRSD items (score range: 0 to 2) and one week sleep diary. The weekly average of sleep onset latency (LAT), total sleep time (TST), quality (QUAL), number of awakenings (WASON), and minutes awake after sleep onset (WASO) were extracted from the diary.
Results: Correlation analysis revealed a statistically significant correlation between the EARLY and LAT ($r=.53$, $p<.0001$), but low and non-significant correlation between MIDDLE and WASO and WASON ($p>.36$). The total HRSD sleep score (mean of EARLY, MIDDLE, and the late insomnia sleep item) was significantly correlated with TST (-.32, $p<.01$) but not with the other four diary measures. Analysis of variance revealed that a score of 2 on EARLY corresponds to 42.2±26.0 minutes of LAT, which was significantly greater than a score of 1 (22.7±9.0) and 0 (19.1±20.1). In contrast, a score of 2 on MIDDLE, which corresponds to 51.7±36.7 minutes WASO, was not significantly different from a score of 1 (46.1±28.9) or 0 (41.0±26.8).
Conclusion: In the current sample, the early insomnia, but not the middle insomnia item, was in agreement with its corresponding diary item. The discrepancy on the middle insomnia item might be related to a high prevalence of sleep continuity disturbances during pregnancy, which may have altered subjective distress about poor sleep.
Support (optional): This research was supported by the Agency for Health Research and Quality (AHRQ) and the National Center for Complementary and Alternative Medicine (NCAM), grant number HS09988.

0985

SELF-REPORTED SLEEP COMPLAINTS IN LATE PREGNANCY PREDICT POST-PARTUM DEPRESSION REOCCURRENCE

Okun M, Hanusa B, Hall M, Wisner K
University of Pittsburgh, Pittsburgh, PA, USA

Introduction: Postpartum major depression (PPMD) is a serious and widespread medical condition affecting 12-14% of all women post delivery. Without effective treatment, PPMD can persist after delivery and affect a woman´s well-being and her functioning as a mother. Data stemming from over 40 years of research have provided evidence that poor sleep precedes an index or recurrent depressive episode, including PPMD. Indeed, writing from the 1800s note "miserable sleeplessness" was a chief prodromal sign of postpartum emotional disturbances. Nonetheless, few studies have evaluated self-reported sleep during pregnancy and its relation to recurrence of PPMD. We evaluated the relationship between sleep complaints and recurrence of PPMD within 1 year of delivery.
Methods: Participants were 69 pregnant women (31 ± 4.0 years of age) with a history of PPMD, but no current depression, who were enrolled in a study designed to prevent recurrences of PPMD. Participants were randomized immediately after delivery to either an SSRI or placebo. Sleep complaints as measured by the PSQI were collected at 36 weeks gestation. Sleep complaints were coded as clinically significant if the overall PSQI ≥ 5.
Results: Using survival analysis we found that, when considered independent of drug status, participants with clinically significant sleep complaints at 36 weeks were more likely to develop recurrent PPMD sooner than were participants without clinically significant sleep complaints (log rank $\chi^2 = 3.95$, $p < .05$).
Conclusion: Our data complement several epidemiological studies showing a correlation between poor sleep and development of a depressive episode (Breslau *et al.*, 1996; Dryman and Eaton, 1991; Ford and Kamerow, 1989). The rate of recurrence of PPMD in women with at least one prior episode is 25% (Wisner *et al.*, 2006). Taken together, our data suggest that clinical documentation of sleep during pregnancy by a clinician may be important if the woman has a history of PPMD.

0986

SLEEP QUALITY, DEPRESSION, AND MEDICATION ADHERENCE

Kelly R, Gay C, Coggins T, Portillo C, Lee K
University of California, San Francisco, San Francisco, CA, USA

Introduction: HIV patients frequently have difficulty adhering to medication schedules, where approximately only 20% successfully adhere over a 12-month period. Depression is a common barrier to adherence, and sleep disturbances are frequently linked with depression. Specifically, nearly 36% of HIV patients meet criteria for depression and 75% experience sleep problems. Whether one symptom precedes another is unclear from prior research, and how both complaints influence adherence is relatively unknown. The purpose of this study was to highlight the relationship that depression and sleep may share with medication adherence.
Methods: As part of a descriptive study of sleep in HIV+ adults, data were collected on 145 patients. The 16-item self-report Pittsburgh Sleep Quality Index measured sleep quality. The 20-item Center for Epidemiological Studies Depression Scale subjectively measured depression and the 9-item Adult Aids Clinical Trials Group Adherence Instrument measured medication adherence. CD4 was obtained from lab reports and demographic questions assessed age, ethnicity, gender, time since diagnosis, income, and education. Actigraphy objectively measured total sleep time (TST) and wake after sleep onset (WASO).
Results: Preliminary results are available for 95 men and 50 women. They are primarily Caucasian (42%) and African American (39%); mean age = 45 (± 7.9 SD) and CD4 cell count ranged from 4 to 1740 (463 ± 277.9 SD). The regression model explained 22.3% of the variance in medication adherence. Depressive symptoms ($p = 0.002$) and subjective sleep disturbance ($p = .021$) were significant predictors, but CD4, demographic variables, TST, and WASO were not.
Conclusion: Regardless of CD4 and demographic variables, depressive symptoms and subjective sleep reports were linked to adherence. The high comorbidity of depressive symptoms and sleep problems may cause fatigue and cognitive impairment, which in turn, may lower adherence. Clinicians should be aware that depression and sleep problems may be indicators of poor adherence.
Support (optional): NIH Grant # R01 MH074358, KA Lee, P.I.

0987

RAPID EYE MOVEMENT (REM) DENSITY AND EYE MOVEMENT DISTRIBUTION IN PATIENTS TAKING SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRI)

Ahmad M,[1] Caffrey P,[2] Freeman J,[2] Lund S[3]
(1) Clinilabs, The Sleep Disorders Institute, New York, NY, New York, NY, USA, (2) Clinilabs, The Sleep Disorders Institute, New York, NY, NY, USA, (3) Sleep Disorders Institute, New York, NY, USA

Introduction: Increased REM density and a shift in eye movement distribution between REM and non-REM sleep on PSGs of patients taking SSRIs, informally termed "Prozac eyes," has been observed. Although REM density is known to increase for patients taking SSRIs, it is not clear if the increased REM density is related to fewer REM periods or to a change in eye movement distribution across all sleep stages.
Methods: A retrospective chart and NPSG review of patients on SSRIs and those of age- and gender-matched contrast patients was conducted. The NPSG was reviewed to examine REM density as well as the distribution of eye movements across the night through all sleep stages. Three categories of eye movements were utilized, each category requiring an electrooculogram deflection of at least 25 microvolts amplitude: slow-rolling eye movements (greater than 1.5 seconds duration from trough to peak), rapid eye movements (less than 0.5 seconds from trough to peak), and what we termed "intermediate eye movements" (greater than 0.5 seconds, but less than 1.5 seconds from trough to peak). Repeated-Measures ANOVA was used to statistically compare frequency distributions of the eye movement categories by group, across sleep stages.
Results: The NPSGs of 3 SSRI patients and 3 contrast patients were reviewed. Data was analyzed for sleep stages 1, 2 and REM. Subjects were equivalent in terms of percentage of stages of sleep, AHI, and SaO2 measures. Results indicate that the distribution of eye movements between groups is significantly different with the SSRI group demonstrating more eye movements in REM sleep and the contrast group showing more eye movements in stages 1 and 2 sleep ($F=10.47$, $df=1$, $p<.03$).
Conclusion: Although these findings are somewhat counter-intuitive, given the limited number of subjects, more charts and NPSGs will be reviewed before any conclusions can be drawn.

0988

SLEEP AND DREAMING IN CHILDREN AND ADOLESCENTS WITH ANXIETY DISORDERS: A QUESTIONNAIRE STUDY

Chevrette T,[1] Bouvier H,[2] Godbout R[3]
(1) Hopital Rivières des prairies - CANADA, Montreal, Quebec, Canada, (2) Department of Psychiatry, Université de Montréal, (Québec) Canada, Montreal, Quebec, Canada, (3) Universite de Montreal, Montreal, Quebec, Canada

Introduction: Children and adolescents with pathological anxiety readily report sleep related problems. The purpose of the present study was to evaluate three dimensions of sleep in young patients with anxiety disorders using questionnaires on sleep habits, dreaming habits and chronotype.
Methods: 101 children and adolescents (32 girls, 69 boys, 13.0 ± 2.5 years old, range 7-17) were evaluated for Anxiety Disorders in a specialized clinic of a large pedopsychiatric hospital. None of the patients were consulting specifically for difficulties with sleep and all of them eventually received a primary diagnosis of Anxiety Disorders using DSM-IV criteria. Each patient completed three questionnaires before their first visit to the clinic: Sleep Habits, Dream Habits, and Morningness-Eveningness (Horne and Ostberg, 1976). During the first (evaluation) visit, patients were also interviewed on their sleep patterns and whether they used sleep aids.
Results: Sleep Habits: 48% of the patients reported taking more than 30 minutes to fall asleep at night, 3 or more times per week. 69% reported 1 to 3 awakenings per night and 6% reported 4 or more awakenings per night. 37% were dissatisfied with sleep and 40% felt not refreshed in the morning. A significant proportion of the patients reported taking naps during weekdays (14%) and weekends (13%). 53% of the patients were taking medication at the time of evaluation, but none were specifically prescribed for sleep difficulties. Dream Habits: 20% of the patients reported never dreaming. In the remaining, 75% reported having bad dreams (i.e., not associated with an awakening), 89% reported nightmares (i.e., associated with an awakening), and 54% reported recurrent dreaming. Chronotype: Up to 20% described themselves as morning types while 17% describe themselves as evening types. 44% reported feeling at their best in the morning and 56% reported feeling at their best in the afternoon. 60% said that their best performance would be between 8 hr and 13 hr.
Conclusion: Children and adolescents with pathological anxiety describe their sleep as delayed, unsatisfactory and non-restful. Whether these problems are behaviorally-based or physiologically-based still need to be determined, including interaction with medication. Results will be extended to include an age-matched group of healthy children and adolescents using the same questionnaires.

0989

AN EVALUATION OF SUBJECTIVE SLEEP QUALITY IN PSYCHIATRIC INPATIENTS: RESULTS OF A BEHAVIORAL SLEEP MEDICINE PILOT INTERVENTION

Haynes P,[1] Kersh B,[2] Bootzin R[3]
(1) University of Arizona, Tucson, AZ, USA, (2) New Mexico VA Healthcare System, Albuquerque, NM, USA, (3) University of Arizona, Tuscon, AZ, USA

Introduction: The goals of this study were twofold. The first goal was to describe subjective sleep quality in 94 consecutive inpatients hospitalized for a wide-range of psychiatric disorders. Next, we sought to determine whether participation in one session of an insomnia behavioral therapy group was associated with sleep quality improvement in those inpatients still hospitalized one week later (n = 21). To our knowledge, no studies have examined subjective sleep quality or sleep treatments in a naturalistic psychiatric inpatient population.
Methods: Participants consisted of 94 veterans admitted to the New Mexico VA Healthcare System inpatient ward from September 2002-February 2003. Data collected included: age, date of admission, length of admission, date of attendance at an insomnia group, and numerical score on the Insomnia Severity Index (ISI). The treatment was an open-enrollment, manualized one-hour psychotherapy group held once per week. The ISI was administered prior to group and approximately one week after group participation.
Results: The majority of patients (n = 57) had clinical insomnia in the moderate to severe range (37% moderate, 23% severe), and only 14% of the sample reported no clinically significant insomnia (n = 13). There were no associations between ISI score, days of admission, and age. A repeated measures ANOVA demonstrated a significant reduction in overall ISI scores one-week after the group therapy (M Δ = 4.43), $F(1,20) = 5.47$, $p < .05$. No significant Length of Stay x Session interactions emerged indicating that length of time in the hospital did not appear to be a factor associated with improvement in insomnia.
Conclusion: These results suggest that insomnia complaints are of sufficient clinical severity among psychiatric inpatients that they warrant separate assessment for potential adjunct treatment. Furthermore, behavioral therapy may be a particularly useful treatment option given polypharmacy and addiction issues often arising in this population.

0990

SLEEP PATHOLOGY IS A PARTIAL MEDIATOR BETWEEN STRESS AND PSYCHOPATHOLOGY IN COMBAT VETERANS

Picchioni D, Cabrera O, McGurk D, Thomas J, Castro C, Balkin T, Bliese P, Hoge C
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Introduction: In order to address issues of cause in the context of the relationship between sleep pathology and psychopathology, one needs to apply research techniques that can separate the variance shared between the relevant variables in a directional manner. We assessed whether nightmares/insomnia would mediate all or part of the relationship between stress and PTSD/depression in U.S. Army veterans.
Methods: A group of 805 Iraq veterans were given a self-administered questionnaire that assessed combat stressors and a variety of current symptoms. Stress was measured with the sum of a 33-item scale assessing combat experiences during the soldiers' most recent deployment. Nightmares were measured with a single item that assessed post-traumatic nightmares. PTSD symptoms were measured with the sum of the 17-item PTSD Checklist with the sleep items removed. Insomnia symptoms were measured with the sum of a three-item scale (initiation, maintenance, early morning). Depression symptoms were measured with the sum of the nine-item depression subscale of the Patient Health Questionnaire with the sleep items removed.
Results: Both sleep variables were partial mediators. The semi-partial correlation between stress and PTSD when nightmares was included in the model was +0.11, which represented a 71% decrease from the zero-order correlation. The semi-partial correlation between stress and depression when insomnia was included in the model was +0.08, which represented a 59% decrease from the zero-order correlation.
Conclusion: This is the first study that empirically addressed whether these sleep pathologies are an inherent feature and/or a cause of the associated psychopathologies. Nightmares may act as a mediator for PTSD by reinforcing the negative memory associations that result from the trauma. Insomnia may act as a mediator for depression by exacerbating feelings of helplessness. Both may act as a mediator by interfering with the putative mechanisms occurring during sleep that

serve to maintain waking emotional stability.
Support (optional): DP is supported by the National Academy of Sciences-National Research Council Postdoctoral Research Associateship Program.

0991

THE RELATIONSHIP BETWEEN MATERNAL BONDING AND SLEEP IN ADULTS WITH AND WITHOUT DEPRESSION

Bosshart T,[1] Williamson M,[1] McQuaid J,[2] Ancoli-Israel S,[2] Haynes P[1]
(1) University of Arizona, Tucson, AZ, USA, (2) VA San Diego Healthcare System, University of California, San Diego, San Diego, CA, USA

Introduction: Previous research has shown a relationship between parental bonding and depression, indicating that depression is correlated with low perceived parental care. Additionally, research has shown that depressed individuals experience worse sleep than never-depressed individuals. No research to our knowledge has examined the relationship between sleep and maternal bonding in adults with depression. The purpose of this study is to examine whether a history of poor maternal bonding is associated with worse sleep in depressed individuals as compared to never depressed controls.
Methods: Thirty-five depressed and 36 never- depressed individuals completed the Parental Bonding Instrument (PBI) for mothers, a 25-item self-report scale that yields two subscales, (1) the amount of care and (2) and the amount of overprotection received from one's mother during childhood (ages 0-16). Sleep was assessed via actigraphy over an average of 5 days (SD= 1.51). Linear regression was used to analyze the impact of Depression, each Bonding Subscale, and the Depression x Bonding Subscale interaction on sleep.
Results: Across both depressed and normal controls, higher levels of caring from the mother were associated with greater sleep times (β= 2.693, SE=.045, p< .05), greater total time spent in bed (β= 2.601, SE= 1.124, p< .05), and later wake times in the morning (β= .061, SE= .025, p< .05). This relationship did not vary as a function of depression. No significant main effects emerged for the overprotection subscale.
Conclusion: Adults who perceive their mother as more caring during childhood spend more time in bed, sleep longer, and awaken later than adults who perceive their mother as less caring. These findings suggest that the quality of maternal relationships may play an important role sleep quantity as an adult. Longitudinal studies are necessary to test the directionality of these findings.
Support (optional): NIMH NRSA 1F31MH064255, NIA AG08415, NCI CA85264 and the research service of the VASDHS.

0992

PREVALENCE OF ADULT ATTENTION DEFICIT DISORDER IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

Subramanian S,[1] Shetty R,[2] Surani S,[3] Rebbapragada V,[1] Aguiliar R,[4] Wiggins T,[5] Early T[1]
(1) Baylor College of Medicine, Houston, TX, USA, (2) Baylor College of Medicine, TX, USA, (3) Baylor College of Medicine, Corpus Christi, TX, USA, (4) Torr Sleep Center, Corpus Christi, TX, USA, (5) St.Lukes Episcopal Hospital, Houston, TX, USA

Introduction: Attention Deficit (Hyperactivity) Disorder (ADD) is believed to be uncommon in adults – prevalence estimates 1 - 6%. Unlike the pediatric literature, adult studies linking ADD and obstructive sleep apnea (OSA) are not common. The purpose of this study was to assess the prevalence of ADD in adult patients with OSA.
Methods: Consecutive patients presenting for polysomnography (PSG) were administered the Adult ADHD Self-Report Scale. This scale has two parts and a score of at least 4 on part A was considered diagnostic of ADD. Patients also completed a
standard sleep questionnaire including an Epworth Sleepiness Scale (ESS). Inclusion criteria: Age above 18 years. Diagnosis of OSA - Apnea Hypopnea Index (AHI) > 5. Exclusion criteria: Patients with concomitant psychiatric illness or
on treatment with psychotropic medications.
Results: A total of 105 patients with OSA were included in the study. Of these patents 20% met criteria for a diagnosis of ADD. Comparison was made between the patients who had a negative diagnosis of ADD with those who scored positive. Age (55.9 +/- 13.6 vs 51.1 +/- 10.4; p = 0.641), Gender (59% male vs. 57.1%; p = 0.19), and BMI (35.9 +/- 9.25 vs. 34.9 +/- 7.0; p = 0.59) were evenly matched. Although severity of OSA as measured by AHI was higher in the group without ADD (32.5 +/- 28.3 vs.19.9 +/- 17.7; p = 0.014), this group had less sleepiness than the group with ADD as measured by an abnormal ESS (>10) (39.24% vs. 76.2%; p = 0.002)
Conclusion: There is a high prevalence of ADD in patients with OSA. Patients with excess daytime sleepiness seem to be at higher risk, suggesting that this may be related to sleep disruption.
Support (optional): None

0993

SLEEP AND SLOW-WAVE ACTIVITY IMPAIRMENT IN PATIENTS RECOVERING FROM ALCOHOL DEPENDENCE

Arnedt J,[1] Hoffmann R,[2] Brower K,[1] Armitage R[1]
(1) University of Michigan, Ann Arbor, MI, USA, (2) Ann Arbor, MI, USA

Introduction: Sleep disturbances during recovery from alcohol dependence are common, persistent, and contribute to relapse. Many of the sleep disturbances associated with alcohol dependence have also been identified in major depressive disorders (MDD). However, only a few studies have directly compared sleep EEG in alcohol recovery and depression. We evaluated baseline sleep macroarchitecture and slow-wave activity (SWA) in recovering alcoholic patients, in those with MDD patients and in healthy controls.
Methods: Nine abstinent alcoholic outpatients (mean age 36.0 ± 7.4 years, 6 women) were recruited to participate in a placebo-controlled non-medication insomnia treatment trial. Participants were otherwise free of medical, psychiatric, and sleep disorders. Before participation, subjects underwent a screening night of polysomnography on their preferred sleep schedule. Sleep macroarchitecture and SWA were compared to age- and sex-matched MDD subjects and Controls from our archival database. Visual stage scoring was conducted according to standard criteria. SWA was quantified by power spectral analysis in successive NREM episodes (stages 2, 3, and 4 excluding Stage 1). Relative SWA power was derived by expressing power in each NREM period to average SWA power.
Results: Alcoholic men and women had greater REM% (F (5,21)=4.6, p=.005) and REM density (F(5,21)=6.7, p=.001) than either MDD or Controls. No group main effects or group by sex interactions emerged for relative SWA power in the first NREM period or across NREM periods. Exponential regressions of relative SWA power, however, showed that in Alcoholics, the intercept and rate of decay of SWA (b=116.4, c=-0.00052) fell outside the 95% CI for both the MDD (b=125.1, c=-0.00081) and Control (b=124.3, c=-0.00101) groups.
Conclusion: Abstinent alcoholic men and women had more extensive baseline REM abnormalities and a more abnormal SWA time course than depressed patients. We are continuing to explore gender differences in SWA in recovering alcoholic patients using challenge paradigms.
Support (optional): Research supported by AA014408, MH61515 and

by the University of Michigan Department of Psychiatry Rachel Upjohn Clinical Scholars Award.

0994

EFFECTS OF ANTIPSYCHOTIC TREATMENT ON POLYSSOMNOGRAPHIC MEASURES IN MANIA. A DOUBLE-BLIND COMPARISON OF HALOPERIDOL AND OLANZAPINE.

Hanna M,[1] Moreno R,[2] Tavares S[3]
(1) Federal University of Goás, Goiânia, Goiás, Brazil, (2) University of São Paulo, Brazil, São Paulo, Brazil, (3) University of São Paulo, Brazil., São Paulo, Brazil

Introduction: Antipsychotics are efficacious in treating mania. Polysomnography may provide useful information about pathophysiology of mania and how it is affected by treatment with typical and atypical antipsychotics agents. However, controlled data on the effects of antipsychotics on EEG sleep in patients with mania is absent. The present study evaluated and compared olanzapine and haloperidol effects on polysomnographic aspects in bipolar patients along manic episode.
Methods: In this study, 12 patients meeting DSM-IV criteria for mania were randomly assigned to receive either olanzapine or haloperidol in a 6-week double-blind randomized controlled design. One-night polysomnographic evaluations were made immediately before and approximately 6 weeks after olanzapine or haloperidol treatment was initiated. Psychopathology and severity were rated with the Young Mania Rating Scale (YMRS) and the Clinical Global Impressions (CGI). Statistical analysis was performed using two tailed Wilcoxon signed rank test and two tailed paired t-test to compare sleep measures at drug free baseline and after treatment with olanzapine or haloperidol.
Results: The major findings were a remarkable improvement on sleep continuity measures (increased sleep efficiency; reduced total wake time and wake time after sleep onset) and increased of slow wave sleep (SWS) in the first third of the night after olanzapine treatment. In the group treated with haloperidol, there were no significant alterations on polysomnographic variables. In both groups, there were highly significant improvement on the YMRS and CGI at the end of the trial compared to baseline.
Conclusion: This study suggests that olanzapine is of comparable efficacy to haloperidol in the treatment of mania. However, olanzapine appears to be more effective than haloperidol in sleep promoting effects.
Support (optional): Supported by FAPESP 99/07290-5.

0995

SLEEP DISRUPTION IN COMBAT VETERANS WITH CHRONIC PTSD ON AND OFF PRAZOSIN

Gross C,[1] Vitiello M,[1] Peskind E,[1] Conybeare D,[2] Raskind M[1]
(1) University of Washington, Seattle, WA, USA, (2) Department of Veterans Affairs, Seattle, WA, USA

Introduction: Prazosin, a CNS active alpha-1 adrenoreceptor antagonist, improves nightmares and insomnia in controlled studies of combat-related PTSD. However, the relationship between prazosin-induced symptom reduction and changes in objective sleep measures in PTSD is unknown. This ongoing study evaluates PTSD symptoms and subjective and objective sleep in veterans with PTSD on and off prazosin.
Methods: Seven veterans with PTSD and a history of self-reported improved sleep on prazosin completed 3 days of in-home objective sleep measurement with the REMView device while on prazosin. Prazosin was then discontinued, and after a ≥ 2 day washout period, participants completed another 3 days of sleep recordings. Subjective sleep was assessed with the Clinician Administered PTSD Scale (CAPS) "recurrent distressing dreams" and "disturbed sleep" items, Pittsburgh Sleep Quality Index Addendum for PTSD (PSQI-A), and Insomnia Severity Index (ISI).
Results: CAPS "disturbed sleep" was significantly elevated ($p < 0.02$) in subjects off relative to on prazosin. There were no significant differences in CAPS "recurrent distressing dreams", PSQI-A, and ISI. In the 4 subjects for whom complete REMView data was available, prazosin discontinuation was associated with a decreased total sleep time of 21 minutes ($p=0.056$), and with non-significant decreases in sleep efficiency, sleep latency, length of REM episodes and REM%; and, non-significant increases in number of mid-sleep awakenings and the number of REM episodes.
Conclusion: In veterans with chronic PTSD, prazosin discontinuation was associated with a pattern of results indicating increased sleep disturbance. Significant subjective worsening was associated with trends towards objective disruption. The decreased sleep duration seen while off prazosin was not accompanied by an increase in sleep latency and suggests that alpha-1 blockade may primarily influence sleep maintenance and not onset. The small current sample size of this study limits the power of objective measurement in this relationship but should be clarified as additional subjects are studied.

0996

OBSTRUCTIVE SLEEP APNEA ASSOCIATED QEEG ABNORMALITIES IN PEDIATRIC PATIENTS WITH QEEG BASED DIAGNOSIS OF AD/HD

Pagel J,[1] Snyder S[2]
(1) University of Colorado Health Sciences Center, Pueblo, CO, USA, (2) Asst Professor Adjunct, UNT Health Science Center, Boulder, CO, USA

Introduction: Quantitative EEG analysis (QEEG) analysis has shown high correlation with pediatric AD/HD diagnosis. Abnormalities in theta/beta ratios on QEEG are currently being used to diagnosis or support the diagnosis in pediatric patients suspected to have AD/HD based on psychological testing and/or psychiatric evaluation.
Methods: Retrospective study of Pediatric Psychiatry Clinic patients with the diagnosis of AD/HD based on DSM-IV, positive psychological tests, and abnormal theta/beta ratios on waking QEEG analysis (N=24, Age: mean 10.7, range 6-16). All patients evaluated with full night PSG and daytime QEEG analysis. Relative and absolute power calculated for the physiological EEG rhythms (beta, alpha, theta, and delta) from the hypothetical central C-Z site, and at EEG sites routinely used in PSG analysis (C-3 and C-4). Indiviuduals divided into groups for analysis based on OAHI: < 2.5 (N=5), >2.5<5.0 (N=6), and > 5.0 (N=13).
Results: 1) Significant effects on delta absolute power between the oahi < 2.5 group and the oahi > 5.0 group with eyes closed at CZ (F=4.026;P=0.033);and C4 (F=3.462;P=0.050); and eyes open at C3 (F=4.295;P=0.027): 2) Significant effects on theta absolute power between the oahi < 2.5 group and the oahi > 5.0 group with eyes closed at CZ (F=5.307;P=0.014), C3 (F=5.854;P=0.010), and C4 (F=4.668;P=0.021): 3) Significant effects on alpha absolute power between the oahi < 2.5 group and the oahi > 5.0 group with eyes open at CZ (F=8.057;P=0.003), and C3 (F=4.606;P=0.022):4) Significant effects on beta absolute power between the oahi < 2.5 group and the oahi > 5.0 group with eyes open at CZ (F=5.862;P=0.003), C3 (F=7.085;P=0.004), and C4 (F=6.926;P=0.005).
Conclusion: For individuals meeting QEEG criteria for diagnosis of AD/HD, higher OAHI values are assocaited with a significant reduction in EEG power the physiologic frequency ranges analyzed. In this pediatric population, OSA is assocaited with consistant alterations in QEEG. Such EEG abnormalities could potentially be associated with the symptomatic presentation of these patients.

0997

A NOVEL MEASURE OF THE SEVERITY OF SLEEP DISORDERED BREATHING USING FINGER PHOTOPLETHYSMOGRAPHY-BASED AUTONOMIC VARIABILITY

Harrell D,[1] Lai Y,[1] Riggins M,[1] Kapur V,[2] Wright-Kinghorn R[2]
(1) Pro-Tech Services, Inc, Mukilteo, WA, USA, (2) University of Washington, Seattle, WA, USA

Introduction: The study of the autonomic nervous system (ANS) has sparked increasing interest in recent years. Studies of the ANS during sleep have demonstrated that perturbation of the ANS may be a marker for sleep-disordered breathing (SDB). The shortcomings of pulse transit time (PTT) and peripheral arterial tonometry (PAT) required a new approach to ANS monitoring for sleep. A new technique called pulse transitional slope (PTS) utilizes standard finger photoplethysmography (FPG) recording to assess ANS activity during sleep. We present data that compared PTS to standard polysomnography (PSG) measures of SDB.
Methods: A total of 35 subjects were recruited from a sleep laboratory. Simultaneous FPG recording was acquired during whole-night PSG, and 21 subjects (M=13, F=8) had at least 4 hours of available data. These FPG data were digitally band-pass filtered and then subjected to a signature extraction algorithm. In order to quantitatively describe the variation of the ANS activity (ANV), we used the standard deviation of the first derivative of PTS (a ratio of the pulse wave´s slope and amplitude). Inter-subject Pearson correlation coefficients between ANV and standard PSG measures of SDB were calculated using SPSS 14.0.
Results: The 21 subjects had a mean BMI of 34.0 (±11) and a mean age of 50 years (±12). The ANV data varied between subjects and had good correlation with respiratory arousal index (r=0.67, p=0.001) and apnea-hypopnea index (r=0.63, p=0.002).
Conclusion: This pilot study demonstrated that using PTS-based ANV may be a useful tool for assessment of SDB severity. Also, this study demonstrated that the PTS technique is technologically feasible and a promising approach to conveniently determine SDB severity. To demonstrate the advantages of PTS, further analyses comparing PTS with PTT, PAT, and PSG are planned. Larger studies are necessary for further validation and clinical application of this technique.
Support (optional): Washington Technology Center RTD Grant, NIH/NIMH SBIR Grant (1R43MH075109-01)

0998

AUTOMATIC 24H ESTIMATION OF WAKEFULNESS AND SLEEP USING ELECTRO-OCULOGRAPHY

Virkkala J,[1] Hasan J,[2] VäRri A,[3] Himanen S,[2] MüLler K[1]
(1) Brain Work Research Center, Finnish Institute of Occupational Health, Helsinki, Finland, (2) Medical Imaging Centre, Pirkanmaa Hospital District, Tampere, Finland, (3) Institute of Signal Processing, Tampere University of Technology, Tampere, Finland

Introduction: We have recently demonstrated the possibility of automatic slow-wave sleep (SWS) detection using a standard two-channel sleep electro-oculography (EOG). The method could be self-applicable with self-adhesive electrodes. We have also extended the published results of automatic slow-wave sleep detection for detecting unintentional sleep onset during daytime Maintenance of Wakefulness (MWT) recordings. In this study we examined how the daytime algorithm could be used for automatic 24h estimation of wakefulness and sleep.
Methods: An automatic two-channel electro-oculography was based on the standard EOG L-M1, EOG R-M1 and calculated EOG L-R. The data was analyzed in two-second segments by calculating slow eye movements, cross-correlations, synchronous peak-to-peak amplitude differences, alpha power and beta power. No spindle or sigma activity was used. Automatic detection was compared to standard visual analysis by calculating epoch by epoch agreement and Cohen's Kappa. The total number of subjects was 276. Half of the data was used for training the algorithm and the other half for the validation. Only binary (wakefulness, sleep) classification was studied.
Results: Daytime data contained 3 % sleep epochs and night-time data contained 84 % sleep epochs. Epoch by epoch agreement (and Cohen's Kappa) for separation of wakefulness and sleep from day- and night-time recordings were 98 % (0.67) and 88 % (0.57). The optimal algorithms were different for daytime and night-time data. The used synchronous peak-to-peak amplitude difference and slow eye movement detection proved to be unimportant for night-time data. For the night-time algorithm alpha power threshold was two times the threshold of daytime threshold.
Conclusion: The automatic 24h estimation of wakefulness and sleep in ambulatory settings could be carried out by a standard two-channel sleep electro-oculography. The daytime unintentional and nigh-time

intentional sleep estimation require different algorithms. The difference is most likely due to the larger amount of SREM and eye closures during night-time.
Support (optional): The Finnish Work Environment Fund project `Computerized testing of railway traffic safety workers, assessment of vigilance and cognitive performance´ and National Technology Agency of Finland project `Analysis method of studying the microstructure of sleep´.

0999

ACTIGRAPHY MEASUREMENT IN DEPRESSED INSOMNIACS

McCall W,[1] Galla J,[2] Dunn A,[3] Boggs N,[3] Kimball J,[3] Rosenquist P[3]
(1) Wake Forest University Health Sciences, Winston-Salem, NC, USA, (2) WFUHS, MT, USA, (3) WFUHS, NC, USA

Introduction: Polysomnography (PSG) is currently considered to be the "gold standard" in measuring sleep, but it is usually not a feasible method for continuous or long-term monitoring. Actigraphy eliminates many of the problems with PSG, but its agreement with PSG is debated. Sleep diaries are yet another method for evaluating sleep. To our knowledge, these 3 methods have never been simultaneously compared in a sample of depressed insomniacs
Methods: A total of 22 subjects were studied (8 males, 14 females, (mean + SD) age 38.4 + 12.3). All subjects were determined to be suffering from both a current depressive episode and insomnia and were free of psychoactive medications for the preceding 2 weeks. Each subject completed one night of 8-hour PSG while wearing an actigraph (Respironics/Mini Mitter), and completed a sleep diary the following morning. Contrasts between actigraphy, diary and PSG were completed with Pearson´s r and matched-pairs analysis. The calculated sleep variables for each form of measurement included sleep latency, wakefulness after sleep onset (WASO), and total sleep time (TST). For PSG, sleep latency was calculated as both the latency to the first epoch of sleep, and the latency to persistent sleep (LPS; 10 minutes of uninterrupted sleep)
Results: Analysis of the data using Pearson correlation coefficients showed significant correlations for LPS between PSG and diary ($r=0.43$, $p<0.05$); for WASO between PSG and diary ($r=0.45$, $p<0.05$) and between PSG and actigraphy ($r=0.65$, $p<0.001$); and for TST between PSG and actigraphy ($r=0.52$, $p<0.05$) . Matched-pairs analysis of the data showed that there were significant differences between PSG and diary for both measures of sleep latency, but there were no significant differences between actigraphy and PSG for any measure.
Conclusion: These results indicate actigraphy performs particularly well against PSG in the measurement of WASO and TST in depressed insomniacs.
Support (optional): this project was supported by NIH MH70821 and M01-RR07122, and by Sepracor and Respironics/Mini Mitter.

1000

MAINTENANCE OF WAKEFULNESS TEST: RELIABILITY AND PREDICTORS IN NORMAL, HEALTHY SUBJECTS

Arroyo S, Banks S, Dinges D
University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: The Maintenance of Wakefulness Test (MWT) examines an individual´s ability to stay awake in an environment of decreased sensory stimulation. In an effort to get novel data on its psychometric properties in a healthy non-sleepy population, we evaluated the relationship of MWT sleep latency to other variables, and assessed its test-retest reliability.
Methods: N=9 healthy adults (23-37y; 6 females), underwent 11 consecutive laboratory nights of 10h TIB (10:00pm to 08:00am), and completed the Composite Scale of Morningness and Eveningness (CSME), Eysenck Personality Inventory (EPI), Beck Depression Inventory (BDI), the Karolinska Sleepiness Scale (KSS) and Psychomotor Vigilance Test (PVT). Modified single trials (30min) of MWT were conducted between 14:30h-16:00h on days 2 and 7; sleep latency was defined as time to first appearance of sleep (10sec). Nocturnal PSGs were recorded before daytime MWTs. Change scores were calculated between day 2 and 7 for MWT sleep latency, PVT, KSS and total sleep time (TST).
Results: The test-retest reliability of the MWT was $r=0.65$ ($p=0.05$). MWT scores increased from day 2 (M=15.4min) to day 7 (M=22.2min) by an average of 6.8 minutes ($p=0.047$), despite TST decreasing across nights (M=34min, $p=0.053$). Forward stepwise multiple regression on the MWT difference score between day 2 and day 7, with age, gender, CSME, BDI, EPI, KSS, PVT and TST as predictors revealed that only CSME predicted MWT change across days (adj R square=0.61, $p=0.008$). Evening types had larger improvement in MWT latency from day 2 to 7.
Conclusion: MWT latency increased and was relatively reproducible among healthy adult subjects receiving 10h TIB. Evening types appeared to benefit more by 10h TIB.
Support (optional): Supported by NIH NR 004281 and RR00040

1001

AUTOMATIC ANALYSIS OF MUSCLE ACTIVITY FOR THE INVESTIGATION OF REM SLEEP BEHAVIOR DISORDER

Canisius S,[1] Kesper K,[1] Thomas P,[1] Koehler U,[1] Mayer G[2]
(1) Philipps-University Marburg, Marburg, Hessen, Germany, (2) Hephata Klinik Schwalmstadt-Treysa, Schwalmstadt-Treysa, Hessen, Germany

Introduction: Rapid Eye Movement Sleep Behaviour Disorder (RBD) is associated with an increased muscle activity during REM sleep. A quantification of electromyographic (EMG) activation in REM sleep was discussed as a promising approach for the investigation of the still unknown aetiology of RBD. The frequency of short-lasting EMG activity in REM sleep was suggested as a probable metric for the identification of neurodegenerative conditions. Therefore this study intends to validate an automatic EMG analysis algorithm, developed to facilitate the scoring of short-lasting activity in REM sleep (i.e. phasic muscle twitching) as well as long lasting EMG activation, normally accompanied with complex limb movements.
Methods: The 1st step of the analysis calculates the amplitude curve of the digitally recorded electromyogram by differentiation of the upper and lower envelopes on the EMG curve. An EMG event is classified, when the amplitude curve surpasses a dynamical threshold value, which is generated in a 2nd step by (a) averaging the amplitude curve over 200 seconds as an approximation of the mean tonic muscle activity, (b) multiplication with a factor 2.0 and (c) adding an offset of 10 microvolts. In a 3rd step, clustered events are summarized, when the interval between them is less than 1 sec. Long-lasting EMG activation was classified for events with 0.5 to 5 sec of duration in accordance to the ASDA classification standards for periodic limb movements. Short-lasting activation was scored for events shorter than 0.5 sec.
Results: Preliminary results proved good agreement with events scored visually by a scoring expert. Detailed validation results will be presented during the conference.
Conclusion: The quantitative analysis of muscle activity during REM sleep might be a helpful diagnostic tool for RBD, but also for other disorders like narcolepsy or Parkinson's disease, which are often accompanied with increased muscle activity.

1002

DIRECT PLACEMENT OF BODY POSITION SENSOR ON THE CHEST, PROVIDES MORE RELIABLE INFORMATION DURING A SLEEP STUDY.

Pe'Er A,[1] Pillar G,[2] Herscovici S,[3] Preiszler M,[3] Lusky R,[3] Sheffy K[3]
(1) Itamar Medical Ltd. Cesarea, Israel & Sleep Laboratory, Rambam Hospital, Haifa, Israel, Caesarea, Israel, (2) Technion- Israel Institute of Technology, Haifa, Israel, (3) Itamar Medical Ltd. Cesarea, Israel., Caesarea, Israel

Introduction: Body position (BP) appears to have an important influence on the incidence and severity of obstructive sleep apnea (OSA) in addition to determining optimal treatment. The gold standard for BP assessment is visual scoring of video monitoring during standard PSG, however both attended and portable monitoring studies are commonly recording the BP using a sensor attached to a thoracic belt. We hypothesized that direct attachment of the BP sensor to the chest provides more accurate information.
Methods: We prospectively studied 17 patients, 14 males, 3 females, aged 41.1 ± 21.6 and BMI of 30.1 ± 6.2, undergoing in-lab full night evaluation for suspected OSA. All patients had a standard PSG with a simultaneous Watch_PAT100 (WP100) recording, a wrist worn device for the ambulatory diagnosis of sleep apnea which includes BP sensor attached to the skin above the sternum with adhesive tape. The BP recording of the PSG was utilizing the same sensor but attached to a thoracic belt in the conventional manner. Video recording of the patient throughout the study was performed simultaneously as well. The WP100 and PSG BP recordings were compared to independent blind scoring of the videotapes. Agreements were calculated within epochs of one second.
Results: The agreement of the BP determined by the video recording with the WP100 (80%±0.18) was significantly higher that with the PSG-BP (49%±0.33, p; < 0.05).
Conclusion: Direct placement of the posture sensor on the chest wall provides significantly more accurate recording than one attached to an elastic belt in the conventional manner. The sensor attached to the belt is more likely to be mis-positioned and shift during the night especially in OSA patients having excessive movements. Taken that this study was conducted in the well observed environment of the sleep lab, the difference between the two methods in the unattended setting is likely to be higher.
Support (optional): The study was sponsored by Itamar-Medical Ltd.

1003

PSYCHOMETRIC STUDY OF THE PITTSBURGH INSOMNIA RATING SCALE (PIRS) IN AN INITIAL CALIBRATION SAMPLE

Moul D, Mai E, Miewald J, Shablesky M, Pilkonis P, Buysse D
University of Pittsburgh, Pittsburgh, PA, USA

Introduction: There is need for a better-validated, theory-indifferent patient-reported outcome measure (PROM) covering both day- and nighttime symptoms of insomnia. To meet this need, the PIRS contains 65 items all with 4-category responses, covering the past week. We report here its psychometrics from an initial calibration sample of insomnia subjects and controls.
Methods: Data from the PIRS and other self-report questionnaires and sleep logs were obtained. The PIRS was examined for its classic test theory characteristics, including internal consistency, test-retest reliability, factor structure, and construct validity.
Results: 287 subjects (179 Primary Insomnia, 71 without insomnia, 35 other insomnia; 116 men,171 women; age 49±19) comprised the sample. Cronbach´s alpha for the PIRS was 0.97. Bland-Altman plotting supported test-retest reliability. A total score change of fifteen points was identified as a minimal clinical difference. Factor analysis with maximum likelihood methods identified Fatigue, Daytime Coping Distress, Sleep Parameters, Sleep Quality, and Sleep Latency as orthogonal factors, explaining 52% of the variance. Concurrent validity was supported with the Medical Outcome Survey (Pearson´s r = -0.79), Multidimensional Fatigue Inventory (r=0.87), Spielman Insomnia Symptom Questionnaire (r=0.94), Brief Symptom Inventory subscales for Anxiety (r=0.82) and Depression (r=0.83), and Pittsburgh Sleep Quality Index (PSQI) (r=0.82) was present. The first eigenvalue of the inter-item correlation matrix was 24, and the second 4, with this difference suggesting overall unidimensionality. Sleep parameter items correlated well with past-week sleep log data. Using a PSQI score reduction of 3 points as a concurrent measure of treatment response, the PIRS total score (t=2.5, df=55, p<0.016) and all factors demonstrated treatment response.
Conclusion: The PIRS improves upon the psychometrics of other PROMs in symptom domain coverage, reduced theory-dependency, simplicity of scoring, and correlation with sleep log data. Item response theory analysis is now needed to help refine and shorten the PIRS further.
Support (optional): Supported by MH 24652-29, 1 U01 AR052155-01, and 5 P01 AG20677-02.

1004

CHANGES OF ACOUSTIC PHARYNGOMETRIC INDICES AFTER ADENOTONSILLECTOMY IN CHILDREN

Cho W,[1] Lee S,[1] Choi J,[2] Lee S,[2] Lee H,[2] Kwon S,[2] Shin C[3]
(1) Otorhinolaryngology, Korea University, Ansan-City, Gyeonggi-do, South Korea, (2) Otorhinolaryngology, Korea University, Seoul, South Korea, (3) Internal Medicine, Korea University, Seoul, South Korea

Introduction: Acoustic pharyngometry is a noninvasive technique that is able to quantitatively evaluate the upper airway obstruction. The aim of this study was to evaluate the usefulness of the acoustic pharyngometry by comparing the acoustic pharyngometric data before and after surgical treatments in children with adenotonsllar hypertrophy.
Methods: Acoustic pharyngometry was carried out in 29 children with adenotonsillar hypertrophy before and at least 4 weeks after an adenotonsillectomy. We compared pre-operative with post-operative acoustic pharyngometric data, such as oropharyngeal junction area (OPJ, cm2), pharyngeal volume (Vp, cm3), glottic area (GL, cm2), maximal pharyngeal cross-sectional area (Apmax, cm2), minimal pharyngeal cross-sectional area (Apmin, cm2), and mean pharyngeal cross-sectional area (Apmean, cm2).
Results: Statistically significant difference was noted in the Apmean (cm2) measurements which increased from 1.75 ± 0.81 before the surgery to 2.24 ± 0.89 after the surgery (p = 0.000). In addition, there were statistically significant changes in the OPJ (cm2) from 1.03 ± 0.62 before to 1.53 ± 0.77 (p = 0.000), the Apmin (cm2) from 0.99 ± 0.51 before to 1.38 ± 0.69 (p = 0.003) and Vp (cm3) from 14.45 ± 7.05 to 18.89 ± 7.72 (p = 0.000) after the surgical treatment.
Conclusion: In children with adenotonsillar hypertrophy, acoustic pharyngometry is noninvasive, reproducible method that reflects the upper airway changes after surgery. Therefore, we suggest that acoustic pharyngometry can be very useful method to evaluate the upper airway of the children with adenotonsillar hypertrophy.
Support (optional): This study was supported by a Korea University Grant

1005

A COMPARISON OF NIGHTLY AND WEEKLY PATIENT REPORTS OF SLEEP BY INSOMNIACS USING INTEGRATED VOICE RESPONSE SYSTEM (IVRS)

Amato D,[1] McCall W,[2] Roth T,[3] Schaefer K,[4] Rubens R,[4] Wilson P,[5] Walsh J[6]

(1) Sepracor Inc, Marlborough, MA, USA, (2) Wake Forest University, Winston-Salem, NC, USA, (3) Detroit, MI, USA, (4) Sepracor Inc., Marlborough, MA, USA, (5) Sepracor Inc., MA, USA, (6) St. Luke´s Hospital, Chesterfield, MS, USA

Introduction: Studies of eszopiclone treatment for insomnia have utilized nightly and weekly patient-reports of sleep via Integrated Voice Response System (IVRS). Weekly assessments are reflective and may incorporate patient recall, while nightly assessments are more immediate. We compared correlations between 2 consecutive weeks of weekly IVRS data with correlations between nightly and weekly IVRS data in primary insomnia to determine whether the two methods are consistent.
Methods: In this six-month, double-blind, placebo-controlled study of eszopiclone 3mg in 830 primary insomniacs, sleep latency (SL), wake time after sleep onset (WASO), and total sleep time (TST) were collected with weekly IVRS during the double-blind period except for the last week of Month 6, when it was collected nightly. Correlations were computed to determine the relationship between the last two weekly assessments (Weeks 2 and 3 of Month 6) and between the average of the daily assessments and the last weekly assessment. Descriptive data are presented for the last 2 weekly assessments and the last week of nightly assessments.
Results: For each sleep endpoint, the last weekly assessment (Month 6, Week 3) was highly correlated ($r=0.59-0.79$; all $p<0.0001$) with the previous weekly assessment (Month 6, Week 2). There were strong correlations ($r=0.64-0.84$; all $p<0.0001$) between average nightly and prior weekly sleep endpoints. Median sleep values were similar when collected nightly and weekly (placebo: SL 44min nightly vs 34min weekly, WASO 16min vs 20min, TST 351min vs 360min; eszopiclone: SL 23min vs 20min, WASO 5min and 10min, TST: 398min and 407min). Measures of daytime functioning were similar when collected nightly vs weekly.
Conclusion: Correlations between nightly and weekly assessments were high and similar to correlations between the two weekly assessments in both treatment groups, suggesting that weekly and nightly patient-reports provide similar information.
Support (optional): Support for this study provided by Sepracor Inc.

1006

A LONG-TERM MONITORING OF FETAL MOVEMENT: EVOKED MATERNAL MICRO-AROUSALS DURING SLEEP

Nishihara K,[1] Horiuchi S,[2] Eto H,[2] Honda M[1]

(1) Tokyo Institute of Psychiatry, Tokyo, Japan, (2) St. Luke´s College of Nursing, Tokyo, Japan

Introduction: Pregnant women´s sleep disturbance due to fetal movement is well known. Fetal movement is thought to be an index of fetal well-being. However, as there has never been a way to easily and reliably record fetal movement, psychophysiological studies of pregnant women´s sleep disturbance and fetal well-being have not been done. To solve these methodological issues, we developed a new sensor with electrostatic capacity. We verified the reliability of our fetal movement recording system using the sensor in Experiment I, and used it as a long-term monitoring at home in Experiment II.
Methods: I: Thirty-one pregnant women, ranging from 19 to 39 weeks of gestation, were asked to lie down on a bed for one and a half hours in the daytime and to press a button as a subjective marker when they felt fetal movement. We simultaneously recorded maternal EEG, EMG, EOG, respiration and ECG, and fetal movement using a Medilog recorder. II: We recorded seven pregnant women´s polysomnograms and fetal movement simultaneously during all-night sleep at home using a Medilog recorder during weeks 33 and 36 of gestation.
Results: I: We detected fetal movement signals for the maternal subjective markers with a high correlation value of 84.4 ± 11.07 %. There were significant differences in fetal movement signals recorded by our system and count values of maternal subjective markers trough the gestation weeks. II: We were able for the first time to record maternal micro-arousal evoked by fetal movement for all the subjects, though not every fetal movement evoked a micro-arousal.
Conclusion: This recording method using the new sensor is entirely non-invasive and can be used repeatedly for home monitoring of fetal well-being. The existence of micro-arousal evoked by fetal movement opens the door to maternal-fetal relationship study.
Support (optional): A Grant-in-Aid for Scientific Research provided by the Ministry of Education, Science and Culture of Japan.

1007

AN ECG-BASED ALGORITHM FOR THE AUTOMATIC IDENTIFICATION OF AUTONOMIC ACTIVATIONS ASSOCIATED WITH CORTICAL AROUSAL

Basner M,[1] Griefahn B,[2] MüLler U,[1] Plath G,[1] Samel A[1]

(1) German Aerospace Center (DLR), Cologne, Germany, (2) Institute for Working Environment and Human Factors at the University of Dortmund, Germany

Introduction: EEG arousals are associated with autonomic activations including increases in heart rate. Visual EEG arousal scoring is time consuming and suffers from low inter-observer agreement. We hypothesized that information on changes in heart rate alone suffice to predict the occurrence of cortical arousal.
Methods: AASM EEG arousal scorings of 56 healthy subjects (mean age 37.0 +/- 12.8 years, 26 male) were obtained by a human scorer and by an automatic scoring system (The Siesta GroupTM). For each of five heartbeats following the onset of 2697 consensus EEG arousal and of an equal number of control conditions, differences to a moving median were calculated and used to estimate likelihood ratios (LRs) for 10 categories of heartbeat differences. Comparable to five consecutive diagnostic tests, these LRs were used to calculate the probability of heart rate responses being associated with cortical arousal.
Results: EEG and ECG arousal indexes agreed well across a wide range of decision thresholds, resulting in a receiver operating characteristic (ROC) with an area under the curve (AUC) of 0.95. For the decision threshold chosen for the final analyses, a sensitivity of 80% and a specificity of 94.5% were obtained. ECG and EEG arousal indexes were significantly correlated ($r=0.41$, $p<0.001$). The Bland-Altman plot showed an unbiased estimation of EEG arousal indexes by ECG arousal indexes with a reasonably small variance. In about 2/3 of all cases, an ECG arousal scoring was matched by at least one (26.4%) or by both (39.1%) of the human or automatic scoring.
Conclusion: We conclude that, in a non-clinical population, it is possible to reliably predict autonomic activations associated with cortical arousal by changes in heart rate alone, and that it may be valuable to supplement visual EEG arousal scoring by this automatic, objective, reproducible, cheap and time-saving method.
Support (optional): This work was partially financed by the HGF-Virtual Institute “Transportation Noise Effects on Sleep and Performance” (grant #VH-VI-111). The data used for the analysis were

financed within the DLR/HGF-project "Quiet Air Traffic".

1008

MISPERCEPTION OF SLEEP DURATION IN THE GENERAL ELDERLY POPULATION. THE ROTTERDAM STUDY.

Van Den Berg J,[1] Knuistingh Neven A,[2] Miedema H,[3] Tiemeier H[4]
(1) Erasmus MC, Rotterdam, The Netherlands, Rotterdam, Netherlands, (2) Leiden University Medical Center, Leiden, The Netherlands, Netherlands, (3) Netherlands Organisation for Applied Scientific Research (TNO), Netherlands, (4) Erasmus MC, Rotterdam, The Netherlands, Netherlands

Introduction: Epidemiological studies have consistently shown that short as well as very long sleep duration is associated with increased mortality and morbidity. However, in population-based studies, data on sleep duration are often obtained by means of questionnaires only. Our study aims to investigate disagreement between objectively measured and subjectively estimated total sleep duration, and to examine determinants of over- or underestimation of sleep duration, in community-dwelling elderly.
Methods: Our study was carried out within the Rotterdam Study, an ongoing population-based cohort study in people 55 years and over. We included 1,008 participants, who wore an actigraph, in order to obtain objective sleep data, and kept a sleep diary, for 7 consecutive nights. We assessed psychosocial and health variables in a home interview, and we administered the Pittsburgh Sleep Quality Index to investigate subjective sleep quality.
Results: Substantial overestimation of total sleep duration, of, on average, 1 hour or more per night, is common (27.9%) in a normal population. Moreover, 11.3% of our study population substantially underestimated total sleep duration. Individuals who overestimated their total sleep time were more often male, younger, had worse cognitive function and better subjective sleep quality, than under- and accurate estimators. On the other hand, substantial underestimation of sleep duration was mainly associated with poor subjective sleep quality (multivariate adjusted OR = 1.34, 95% CI 1.25-1.43), and not independently with age, gender, cognitive function, depressive symptoms or somatic illness.
Conclusion: Self-reported estimates of total sleep time are not always accurate. This has important implications for research with questionnaire data, as the systematic misclassification may introduce bias. Subjective sleep quality is the most important determinant of under- or overestimation of total sleep time. Actigraphy may not be the gold standard for distinguishing sleep from waking, however, polysomnography is not feasible in large studies with repeated home assessments.
Support (optional): n/a

1009

WIRELESS SLEEP STUDY SENSORS

Havey G,[1] Mahowald M,[2] Riggins M,[3] Kramer K,[1] Gibson P,[1] Seifert G,[1] Hedin D,[1] Patrick L[1]
(1) Advanced Medical Electronics Corp., Maple Grove, MN, USA, (2) University of Minnesota, Minneapolis, MN, USA, (3) Pro-Tech Services, Inc, Mukilteo, WA, USA

Introduction: Wireless polysomnograph sensors have been developed using a digital wireless networking standard called Bluetooth. The sensors are individual wireless sleep study sensors (e.g. finger pulse oximeter, periodic limb movement sensors, chest-worn 17-channel electroencephalograph, effort belts, etc.). Each patient becomes a wireless network with up to seven separate wireless devices operating independently. The sensors maintain time synchronization via a specialized timing protocol. Up to dozens of patients can be wirelessly accessed in this way in the sleep lab, home environment, or in temporary remote clinics setup for example in hotels. The wireless sleep sensors are placed on the patient in a much simpler fashion than customary wired sensors. The developed system has been demonstrated to operate reliably at indoor ranges in excess of 30 meters with several walls between the sleeping patient and monitoring computer. A software development kit (SDK) allows the wireless sensors to be integrated with any commercially available sleep study scoring and analysis review software package.
Methods: Patients were prepared with duplicate sensors from the developed Bluetooth wireless sensors and a gold standard polysomnograph. Pairs of skin electrodes were placed as near as practical to each other to obtain equivalent signals. There was no interference between the skin electrodes of the two systems because the wireless system is battery powered. The patients had two sets of effort bands and two pulse oximeters. Wireless data transfer statistics were maintained and data files resulting from both the Bluetooth sensor system and gold standard polysomnograph system were captured.
Results: The wireless system reliably maintained connection and transferred data to both a standard windows PC computer and a windows smartphone.
Conclusion: Bluetooth networking represents a reliable, inexpensive method for providing a body-worn time-synchronized network of polysomnograph sensors.
Support (optional): This work was supported by NIH grant 2R44MH62251

1010

MORNINGNESS-EVENINGNESS AND INTELLIGENCE

Lipizzi E,[1] Richards J,[1] Balkin T,[1] Grugle N,[2] Killgore W[1]
(1) Walter Reed Army Institute of Research, Silver Spring, MD, USA, (2) Walter Reed Army Institute of Research, MD, USA

Introduction: Morningness-Eveningness (M-E) has been widely studied and is related to a variety of physical, demographic, and psychological variables, including age, gender, and personality traits. Only two studies have assessed the relationship between M-E and cognitive abilities such as intelligence (IQ). One study suggested that the trait of Eveningness is related to higher intelligence, while the second study failed to find a relationship. Neither study, however, used a clinically accepted, standardized, and psychometrically validated measure of intelligence.
Methods: Fifty-four healthy volunteers (29 men; Mage = 23.5 years, SD = 4.0) completed the Morningness-Eveningness Questionnaire and were assessed for intelligence with the Wechsler Abbreviated Scale of Intelligence (WASI). We correlated scores on the Morningness-Eveningness Questionnaire with the WASI (Pearson´s r, one tailed tests predicting a negative correlation).
Results: For the entire sample, M-E was not correlated with either Full Scale IQ (FSIQ; r=-.19, p=.09) or Performance IQ (PIQ; r=-.10, p=.25), but did show a significant negative correlation with Verbal IQ (VIQ; r=-.23, p=.05). We also analyzed the correlations separately for each gender. None of the relationships between M-E and IQ reached significance for men (FSIQ r=-.12, p=.27; PIQ r=-.14, p=.24; VIQ r=-.09, p=.32). For the women, the relationship between M-E did not reach significance for FSIQ (r=-.30, p=.07) or PIQ (r=-.07, p=.36), but did show a significant negative correlation between M-E and VIQ (r=-.44, p=.01), suggesting that for women, higher Eveningness scores were associated with higher verbal intelligence.
Conclusion: We found a significant relationship between greater Eveningness-orientation and higher verbal intelligence. This

relationship, however, appears to be moderated by gender and is only statistically significant in women. The reasons for this relationship remain unknown, but likely candidates may include sex-related developmental differences in brain structure and function or sex-differences in neuroendocrine function that jointly influence the sleep-wake cycle and intellectual development.

1011

EVALUATION OF AN AUTOMATED SYSTEM FOR IN-HOME BEHAVIORAL TREATMENT OF CHRONIC INSOMNIA: PART III

Kaplan R,[1] Wang Y,[1] Loparo K,[1] Bootzin R[2]
(1) Consolidated Research of Richmond, Inc., Euclid, OH, USA, (2) University of Arizona, Tuscon, AZ, USA

Introduction: A multi-year effort has been dedicated to the development of a single-channel EEG-based system to facilitate in-home use of Stimulus Control Therapy for insomnia. System functions include: alerts to get out of bed in accordance with stimulus control instructions, automatic sleep variable entries, and daily sleep feedback to enable users to review their progress. A pilot study was directed toward evaluating the usability of this system in individuals with chronic sleep onset insomnia.
Methods: 5 paid volunteers with chronic sleep onset insomnia participated in this IRB approved study. 2F/3M, 30-42 years (median 33) used the EEG-based system in-home for 11-21 nights (median 18 nights) to test feasibility and changes in sleep. Each subject received 30 minutes of instruction on system use, including electrode placement and stimulus control instructions. The self-reported Pittsburgh Sleep Quality Index (PSQI) was administered pre- and post-study.
Results: The pre-study to post-study means (standard deviations) and Cohen d effect sizes were:

PSQI Composite score: 12.0(1.9) to 6.4(4.3); d=1.685
PSQI SE: 75.8(13.6) to 88.4(8.9) %; d=1.096
PSQI SOL: 55.0(38.4) to 24.3(20.4) minutes; d=.998
PSQI TST: 5.6(0.8) to 6.2(0.4) hours; d=.949
PSQI SPT: 7.5(0.8) to 7(0.5) hours; d=.750
PSQI Rating of Overall Sleep Quality: “Fairly bad” to “Fairly good”

Improvement and increased sleep satisfaction were reported by 4 of 5 subjects, with 1 subject reporting no improvement. Post-study scores for the 4 subjects who improved were all <30 minutes on SOL, >85% on SE, and either 4 or 5 on the PSQI composite score.
Conclusion: This first report of treatment outcomes of the automated home system produced substantial improvement in individuals with sleep-onset insomnia. All effect sizes would be considered “large” in magnitude. We anticipate that increasing the number of days using the system and adding clinician involvement would only serve to improve efficacy in future studies.

1012

DEVELOPMENT OF A SHORTEN VERSION OF THE FOSQ

Chasens E,[1] Ratcliffe S,[2] Weaver T[2]
(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) University of Pennsylvania, Philadelphia, PA, USA

Introduction: The Functional Outcomes of Sleep Questionnaire (FOSQ) is widely used in research and clinical practice to measure activities sensitive to sleep disruption. The purpose of this study was to develop a shorter version for clinical application that maintains the validity of the original instrument.
Methods: Data from a multisite study of OSA patients (n =155, age 46.3 ± 9.2 years; BMI= 37.7 ± 8.5 kg/m^2; AHI= 63 ± 31) was utilized in the development of the short version. Of the 30 original items, 10 questions representing each subscale (General Productivity, Social Outcome, Activity Level, Vigilance, Intimate Relationships/ Sexual Activity) were selected that had normal distribution of responses and the largest pre- to post-treatment effect size within each subscale. The instrument was then prospectively tested on a second, independent sample of OSA patients (n =51, age 48.1 ± 9.3 years; BMI= 34.0 ± 5.8 kg/m^2, AHI= 51 ± 28).
Results: Psychometric evaluation of the FOSQ-10 was performed using Sample 2. Internal consistency of the FOSQ-10 was Cronbach´s alpha = 0.866. Pre-treatment correlations of the FOSQ-10 with the original FOSQ were r= 0.83 - 0.96 for subscales and r= 0.96 for total scale; after 3-months treatment: subscale range r= 0.90 - 0.95 and total scale r = .97, all p-values < 0.0001. Paired t-tests comparing the total scores of the FOSQ-10 with the original FOSQ showed a statistical difference at baseline (mean =0.63, p < .0001) but not after 3-months treatment. Changes in the total score following treatment were found for both instruments: the change was slightly larger for the short version (FOSQ-10 effect size = 1.43 vs. original FOSQ effect size = 1.36, p-values < .0001).
Conclusion: The FOSQ-10 is a psychometrically strong instrument that is rapidly completed and easily scored. It shows promise as a robust instrument for the clinical evaluation of CPAP efficacy.
Support (optional): HL 60287 and R01 HL076101

1013

COMPARISON OF TOTAL SLEEP TIME FROM ACTIGRAPHY AND POLYSOMNOGRAPHY IN OLDER MEN: THE MROS SLEEP STUDY.

Blackwell T,[1] Redline S,[2] Ancoli-Israel S,[3] Stone K[1]
(1) California Pacific Medical Center (CPMC), San Francisco, CA, USA, (2) Case Western Reserve University, OH, USA, (3) University of California, San Diego, San Diego, CA, USA

Introduction: Polysomnography (PSG) is considered the gold standard in assessing sleep but it can be costly and difficult to gather in large epidemiologic studies. Actigraphy is less cumbersome and less expensive than PSG. We examined whether total sleep time (TST) assessed by actigraphy gathered in 3 different modes was comparable to TST measured by PSG in community dwelling older men. Each of the 3 modes was compared to PSG to determine which was more accurate. Associations of the difference in TST (PSG – actigraphy) with sleep characteristics were examined.
Methods: Concurrent measurement of both actigraphic data (SleepWatch-O ®, Ambulatory Monitoring, Inc) and PSG data (Safiro, Compumedics) were performed on 909 men (mean age 76.3) in the MrOS Sleep Study, a prospective cohort study of older men. Actigraphy data were gathered in 3 modes: zero crossings (ZCM), proportional integration (PIM) and time above threshold (TAT). Actigraphy data were truncated to match the recording times from PSG. Differences in TST between PSG and actigraphy data were examined with correlations and paired t-tests. Associations of this difference (PSG-actigraphy) with sleep characteristics were examined with linear regression.
Results: The differences between all 3 modes of actigraphy and PSG were statistically significant (p<0.0001). The correlations of TST from PSG to the 3 modes of ZCM(0.39), TAT(0.54) and PIM(0.61) were moderate. The PIM mode corresponded better to PSG in this population, with an average overestimation of TST by 12.5 minutes. There were significant differences between TST from the PIM mode and PSG for many sleep outcomes (p<0.05). For example, those with respiratory

distress index>=15 had an underestimation of TST by the PIM mode of 17.13 minutes on average.
Conclusion: The PIM mode of actigraphy correlated best to PSG in this population. Actigraphy may provide variable estimation of TST among populations with different movement and sleep patterns.
Support (optional): The National Heart, Lung, and Blood Institute (NHLBI) provides funding for the MrOS Sleep ancillary study "Outcomes of Sleep Disorders in Older Men" under the following grant numbers: R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, R01 HL070837, R01 HL070838, and R01 HL070839.

1014

FITTING A POWER FUNCTION TO TIME INTERVALS BETWEEN RAPID EYE MOVEMENTS MAY PREDICT THE RATE OF HUMAN PGO WAVES

Douglass A,[1] Ward M,[2] Godbout M,[2] Biard K[1]
(1) University of Ottawa, Ottawa, Ontario, Canada, (2) Royal Ottawa Hospital, Ottawa, Ontario, Canada

Introduction: The development of digital sleep recordings and software for rapid-eye-movement (rem) detection allows use of the rich information present in the timing of individual rems. Previous work has utilized REM density (RD) derived from visual detection and counting of rems divided by REM time. However, RD has been defined differently, leading to the inability to compare studies. It is also not clear whether RD predicts the underlying rate of PGO waves, known from animal studies to underlie each rem, since RD averages together rems in "burst" and "isolated" subgroups.
Methods: The Stellate Harmonie 6.0 software system was used to detect rems in 9 healthy normal adults (mean age 22.7, SD 2.5) and to measure the number of milliseconds between each (Inter-rem-Interval, IRI). The system detected IRIs of 250 ms or greater, which were then histogrammed in bins of 200 ms up to 5 s (fine-scale) and bins of 5 s up to 60 s (coarse-scale). A negative exponential function consistent with random IRIs was fitted to coarse-scale data from 20 to 60 s ("isolated" rems), R^2=0.9241. This function was then extended to the left and subtracted from the observed fine-scale data (deconvolution) to reveal a function characterizing "burst" rems. Using calculus, the 99%-ile of the area under this function was found.
Results: The deconvoluted fine-scale data fit a power function (Y = 0.0923 X^ -1.5491) with very low error (R^2= 0.9998). There was some deviation from this function (i.e., fewer rems) in bins 250--750 ms, suggesting mechanical inertia of the eyeball, so the function was fitted excluding those data. This resulted in a smooth curve from 0.25 to 5.0 s. The 99%-ile of this function fell at IRI = 3.38 s.
Conclusion: We conclude that "burst" rems are characterized by a power function, and that IRI = 3.38 s represents the most reliable threshold to separate "burst" from "isolated" rems. We speculate that this power function also predicts the probability of occurrence of the (unobservable) PGO waves that underlie each rem.
Support (optional): Royal Ottawa Foundation University of Ottawa Medical Research Fund

1015

ACTIGRAPHY VS. POLYSOMNOGRAPHY IN HEALTHY ADOLESCENTS AND MARIJUANA USERS: A VALIDATION STUDY

Kanady J,[1] Cohen-Zion M,[2] Wong R,[3] Schlosser A,[3] Padula C,[2] Tapert S,[2] Drummond S[2]
(1) VA San Diego Health Care System, Research Service, San Diego, CA, USA, (2) University of California, San Diego, Dept. of Psychiatry, CA, USA, (3) VA San Diego Health Care System, Research Service, CA, USA

Introduction: Few studies have compared the concordance between actigraphy and PSG in adolescents, and none in adolescent marijuana users. The objective of this study was to determine whether actigraphy is a suitable substitute for PSG for both teenage marijuana users (MJ) and healthy controls (C).
Methods: A total of 37 adolescents (MJ=19, C=18; 14F; mean age 17.9±1.1) underwent in-lab PSG while simultaneously wearing actigraphs (Octagonal Motionlogger-L; AMI, Ardsley NY). Descriptive statistics suggested non-normal distribution of data and thus Spearman correlations were performed to compare PSG and actigraphic (UCSD algorithm) sleep variables. For all significant correlations, Bland-Altman graphs examined the agreement between these two measures.
Results: For healthy controls, all sleep parameters showed significant correlations between actigraphy and PSG, with TST having the highest correlation (r=0.78, p<.01), followed by SL (r=0.67, p<.01), WASO (r=0.55, p<.02), and SE (r=0.53, p<.03). For MJ users, only TST was significant (r=0.90, p<.01), while SL (r=.04), WASO (r=0.39) and SE (r =0.23) were not. Bland-Altman plots showed that actigraphic-recorded TST (+6.5min) and SE (+3.1%) were overestimated in healthy controls compared to PSG, whereas SL (-12.3min) and WASO (-4.2min) were underestimated. In the MJ group, TST was also overestimated (+6.3min).
Conclusion: While actigraphy and PSG were correlated for all variables in healthy adolescents, only TST was correlated among MJ users. The Bland-Altman technique demonstrates the tendency of actigraphy to overestimate sleep and underestimate wake in healthy adolescents, suggesting it has high sensitivity but low specificity. Actigraphy seemed to be less accurate for adolescent marijuana users. Given these correlations are notably lower than those published for other populations, the UCSD algorithm (similar to Cole-Kripke) may not be optimal for use with adolescents, even with older adolescents such as those in this study. Further analyses will examine the Sadeh algorithm to determine whether this improves the correlations.
Support (optional): UCSD GCRC M01 RR00827, R01 DA021182, T32 MH18399

1016

A PILOT STUDY ON A BRIEF, DAYTIME POSITIVE AIRWAY PRESSURE (PAP) THERAPY PROCEDURE TO ENHANCE PAP ADHERENCE

Ulibarri V,[1] Krakow B,[2] Melendrez D,[3] Shara K,[1] Laura T[1]
(1) Maimonides Sleep Arts and Sciences, LTD, Albuquerque, NM, USA, (2) Sleep and Human Health Institute, Albuquerque, NM, USA, (3) Quality Sleep Solutions, Albuquerque, NM, USA

Introduction: Adherence to PAP therapy increases with more hands-on education and follow-up for patients. However, this clinical time is often not reimbursable under E & M codes. To increase contact time with SDB patients and enhance PAP therapy adherence, we devised a daytime, reimbursable PAP therapy procedure—the PAP-NAP.
Methods: Forty SDB patients (52% male; mean AHI 34.43 + 26.21; mean RDI of 57.54 + 25.66) with multiple psychological barriers to PAP therapy were scheduled for daytime PAP-NAPs. Patients were treated through a Sleep Dynamic Therapy framework, which approaches SDB as a mind-body disorder, requiring mask and pressure desensitization, emotion focused therapy to overcome embarrassment and anxiety, and mental imagery to relieve patient discomfort. CPAP or bilevel therapy is used during desensitization and napping. Lead placement meets requirements of CPT code 95807 (pulse, SaO2, snore,

chest/abdomen excursion, airflow via pressure transducer, and video monitoring). Patients nap for 60 to 120 minutes, during which pressure is adjusted for obvious SDB events, but the procedure is not a titration. Post-test, patients report and discuss their experiences and are encouraged to complete a full-night titration.
Results: Average PAP-NAP procedure lasted 3.5 hours in these 40 patients, including an average of 96 minutes of recorded naptime. Subsequently, 90% of patients completed overnight titrations, and 85% filled PAP therapy prescriptions and used at home. Sixty-seven percent maintained regular use of the device for an average of 11 months (range 2 to 24 months). Objective data downloads revealed patient use per month as: 24.3 nights (81% of month); 5.9 hrs interface time on actual nights used; 4.7 hrs/night overall use. All studies were reimbursed by insurance carriers using CPT 95807-52 (52 = short study code).
Conclusion: The PAP-NAP is a useful, introductory, brief, reimbursable procedure to facilitate adherence in patients with barriers to PAP therapy use.

1017

PILOT STUDY ON THE VALIDITY OF THE VISUAL ANALOGUE SLEEPINESS SCALE TO OBJECTIVELY MEASURE SLEEPINESS

Halliwell K
SUNY at Buffalo Department of Neurology, East Amherst, NY, USA

Introduction: Obstructive sleep apnea often results in excessive daytime sleepiness. However, it is difficult to objectively measure sleepiness in these patients. It would be desirable to have a clinical tool to measure sleepiness that is reliable, valid, and practical.
Methods: The proposed Visual Analogue Sleepiness Scale (VASS) is a visual analogue linear scale scored from 0 to 10. Patients at sleep laboratories were given this scale and asked to circle a single number in response to the question "How sleepy do you normally feel on an average day using a scale from 0-10; with 0 being wide awake and 10 being about to fall asleep? This refers to your usual way of life in recent times." 58 subjects completed this scale before undergoing nocturnal polysomnograms. VASS scores were analyzed and correlated with RDI, sleep latency, REM latency, sleep efficiency, sleep arousal index, PLM index, oxygen saturation nadir, and proportions of stage I, II, delta, and REM sleep.
Results: There was no significant correlation between the VASS and RDI, or other stated measures except for REM sleep percentage in women. There was a significant direct correlation between female subjects´ VASS scores and the amount of measured REM sleep ($p < 0.05$).
Conclusion: The VASS does not correlate with most polysomnographic variables, making its validity as an objective measure of sleepiness questionable. The significance of the positive correlation between VASS and amount of REM sleep in women is unclear. One possibility is a REM rebound in the laboratory after some degree of previous sleep restriction. Another explanation might be an underlying depression in these patients. We continue enrollment to elucidate this finding, and verify lack of correlation with other polysomnographic parameters.

1018

COMPARISON OF THE DETECTION OF OBSTRUCTIVE SLEEP APNEA USING CARDIO-RESPIRATORY MONITORING AND MODIFIED SONOGRAPHIC TECHNOLOGY EMBEDDED IN A MATTRESS OVERLAY

Norman M, Edwards N, Sullivan C
University of Sydney, Sydney, New South Wales, Australia

Introduction: While the utility of in laboratory polysomnography (PSG) for the diagnosis of obstructive sleep apnea (OSA) is undeniable, waiting lists for PSG continue to increase, thereby delaying diagnosis. The impact of OSA on health, cognitive function and safety makes the ability to diagnose this disorder quickly and accurately extremely important. Our hypothesis in this ongoing study is that a modified sonographic system, which removes the need for the attachment of any sensors to the subject, will provide an accurate method of diagnosing OSA.
Methods: Simultaneous overnight recordings using cardio-respiratory monitoring (CRM) and a modified sonographic technique were performed at home on eighteen subjects (age 32 ± 19). The sonographic system comprises four sensors, which detect sound and movement, embedded in a mattress overlay. The detection and classification of respiratory events was performed using nasal flow and thoracoabdominal excursion in the case of CRM, and respiratory sounds and breathing movements using the sonographic system. All recordings were scored blindly for the presence of apnoeas and hypopneas.
Results: Three studies from CRM were unreliable because of poor or absent nasal flow. All sonographic recordings were technically successful. The number of respiratory events detected per hour of recording was similar (13 ± 15 for CRM and 14 ± 15 for sonography, $p = 0.82$). There was a significant correlation ($R2 = 0.96$) between the number of respiratory events recorded using the two different devices. Using Chicago criteria for severity ranges, the two methods were identical in the resultant categorisation of apnea severity for all subjects.
Conclusion: The Sonomat can accurately detect the presence and severity of OSA across a wide range of age groups and a wide range of disease severity. This system clearly provides an accurate method for the diagnosis of OSA even in the absence of a nasal flow signal.

1019

EFFECT OF A PORTABLE SLEEP MONITORING PROGRAM ON CONTINUOUS POSITIVE AIRWAY PRESSURE ADHERENCE.

Swartz S,[1] Rosas J,[2] Anderson W,[3] Andrews A,[4] Foulis P[5]
(1) University of South Florida - Department of Epidemiology and Biostatistic, Tampa, FL, USA, (2) James A. Haley VA Hospital - Nursing Service, Tampa, FL, USA, (3) University of South Florida - Division of Pulmonary, Critical Care & Sleep Medicine, Tampa, FL, USA, (4) University of South Florida - Divison of Pulmonary, Critical Care and Sleep Medicine, Tampa, FL, USA, (5) University of South Florida, Tampa, FL, USA

Introduction: In many VA hospitals, the practice of laboratory-based polysomnography (PSG) is hampered by demand that far outweighs availability. To address increasing referrals, the JA Haley Veterans Hospital initiated new diagnostic and treatment protocols. Prior to November, 2004, all patients were diagnosed by full laboratory PSG. Beginning in November, 2004, patients with clinically determined obstructive sleep apnea (OSA) were referred for portable home monitoring (PHM). If staff believed the patient would have trouble using PHM or PHM was used but did not indicate OSA, the patient was scheduled for laboratory-based PSG, split-study protocol with CPAP. If

PHM confirmed OSA, the patient was treated with auto-titrating CPAP. It is unknown whether the new protocols impacted CPAP therapy adherence.
Methods: Patients were screened clinically and referred for confirmatory OSA testing. Adherence was measured by a CPAP microprocessor monitor and was defined as percent of total nights CPAP used ^{3} 4 hours. Patients first diagnosed with OSA 18 months after (Group A) and 18 months before (Group B) the new protocols were initiated, were compared using a t-test, Wilcoxon and ANOVA adjusting for follow-up time.
Results: CPAP adherence information was available for 734/1162 (63%) Group A patients and 477/768 (62%) Group B patients. The average follow-up was 134 days for Group A and 326 days for Group B, who were diagnosed earlier. Average hours of use per day was similar between groups (3.99 and 3.97 for groups A and B respectively (NS)); as was patient adherence (50.3 vs. 49.5 respectively (NS)). After adjusting for length of follow-up, Group A had significantly higher adherence than Group B ($p<0.01$). Furthermore, among patients in Group A, CPAP-adherence was similar for those diagnosed with PHM and those triaged to the lab.
Conclusion: The procedural switch-over from full laboratory PSG to PHM did not adversley affect patient adherence to CPAP.

1020

EVALUATING THE RADIO FREQUENCY ENVIRONMENT IS NEEDED BEFORE SELECTING A WIRELESS PSG SYSTEM

Weimer S, Halley D, Grogan A, Kayyali H, Frederick C
Cleveland Medical Devices Inc., Cleveland, OH, USA

Introduction: Wireless technologies are being adopted in hospitals at an unprecedented rate and is expected to double by 2011. Wireless PSG is expected to play a major role in this growth as it permits real time sleep disorders assessment on the hospital floor. The evaluation of inpatients during their hospital stay can speed diagnosis, improve patient outcome, and prevent postoperative complications caused by undiagnosed sleep disordered breathing. Users of wireless PSG technologies, however, must be aware of radio frequency (RF) interference issues intrinsic to their environment.
Methods: The RF activity was collected in hospitals using a computer based real time spectrum sweep. The RF was monitored in both the 900 MHz and 2.4 GHz band. Wireless PSG systems are currently available that transmit data in both of these bands.
Results: An analysis of the RF environment in a major hospital in northeast Ohio showed a very crowded 2.4 GHz frequency band (41% utilization), and a quieter 900 MHz band (9% utilization). The high occupancy level of the 2.4 GHz can be attributed to microwave ovens and several wireless LAN access points. At a hospital in southwest Ohio the band utilization was 8% for 2.4 GHz and 6% for 900 MHz. Guidelines suggest that band utilization of less than 25% is optimal, between 25 and 50% is a warning and over 50% is not recommended. With increased band utilization the incidence of data loss increases.
Conclusion: Other hospital environments will likely exhibit different frequency distributions, but these results suggest that different wireless bands may be needed in various environments. Another alternative is the wireless medical telemetry bands (WMTS) (600 MHz, and 1.4 GHz) a frequency coordinator at each facility assigns a unique operating frequency to eliminate interference. This study confirms the need for an RF analysis before a wireless PSG device can be selected.

1021

CLEMSON AUDIO TASK: EVALUATING THE SENSITIVITY OF A DUAL-PERFORMANCE AUDIO TASK TO SUSTAINED OPERATIONS AND SLEEP DEPRIVATION CONDITIONS

Pottorff G,[1] Pilcher J,[1] Allen J,[1] Lindquist T,[1] Wright C,[1] McCubbin J[2]
(1) Clemson University, Clemson, SC, USA, (2) Clemson University, SC, USA

Introduction: Past research has indicated that performance is negatively affected under sustained operations and sleep deprivation conditions; however, few studies have examined performance on a task that combines a complex audio task and an audio vigilance task. The purpose of this study was to evaluate the sensitivity of the Clemson Audio Task (CAT) to sustained operations and sleep deprivation conditions.
Methods: Thirty-eight, non-native English speaking students (age: 24.3 ± 2.5) were paid to complete a variety of tasks. Two training and four testing periods were completed during a 30-hour experimental period. The testing sessions took place overnight from 6:30 – 10:30PM, 11:00PM – 3:00AM, 3:30 – 7:30AM, and 8:00 – 12:00PM. All tasks were completed once in each testing session and were counter-balanced across the participants. The CAT was designed to test participants´ ability to recognize specific keywords and identify main points simultaneously while listening to 25 minute segments of non-fiction audio books. Participants were told which keyword to listen for and that they would identify the 3 main points from the passage at the conclusion.
Results: Repeated-measures ANOVAs were conducted to determine if performance changed across the testing sessions. Performance on the keyword portion of the CAT decreased across the testing sessions: ability to correctly identify the keywords ($p=.003$) and reaction time in responding to hearing the keyword ($p=.003$). Performance on ability to identify the 3 main points of the passage also decreased across the testing sessions ($p=.000$).
Conclusion: These findings indicate that the CAT is sensitive to the effects of sustained operations and sleep deprivation. This result is relevant in that almost all work settings require audio language performance yet few audio tasks exist for use in a laboratory setting. The CAT provides a much needed tool for examining the effects of sustained operations and sleep deprivation.
Support (optional): This research was funded by the Department of Defense and the Center for Advance Study of Language at the University of Maryland.

1022

EVALUATION OF AUTOMATED AND SEMI-AUTOMATED SCORING OF POLYSOMNOGRAPHIC RECORDINGS FROM A CLINICAL TRIAL USING ZOLPIDEM IN THE TREATMENT OF INSOMNIA

Svetnik V,[1] Ma J,[1] Soper K,[1] Doran S,[2] Renger J,[3] Deacon S,[4] Koblan K[5]
(1) Merck Research Laboratories, Rahway, NJ, USA, (2) Merck & Co. Inc., West Point, PA, USA, (3) Merck Research Laboratories, Sleep & Schizophrenia, Philadelphia, PA, USA, (4) Lundbeck Ltd., Milton Keynes, United Kingdom, (5) Merck Research Laboratories, Neuroscience, Philadelphia, PA, USA

Introduction: The performance of two automated systems, Morpheus™ and Somnolyzer24X7™, with various levels of human review and editing, in the scoring of polysomnographic (PSG) recordings was evaluated from a clinical trial using zolpidem in a model of transient insomnia.
Methods: 164 all-night PSG recordings from 82 subjects collected

during 2 nights of sleep, one under placebo and one under zolpidem (10 mg) treatment for each subject were used in a 4h phase advance model of transient insomnia. For each recording, 6 different (manual, automated and semi-automated) methods were used to provide sleep stage scores based on Rechtschaffen & Kales criteria: 1) full manual scoring, 2) automated scoring by Morpheus™ 3) automated scoring by Somnolyzer24X7™ and the following semi-automated methods using a degree of manual review/editing - 4) automated scoring by Morpheus™ with full manual review 5) automated scoring by Morpheus™ with partial manual review, 6) automated scoring by Somnolyzer24X7™ with partial manual review. Ten traditional clinical endpoints representing traditional efficacy measures of sleep initiation, maintenance and architecture were calculated using these different methods.
Results: Pair-wise epoch by epoch agreements between fully automated and manual scores were in the range of inter-site manual scoring agreements reported in the literature (70-72%). Pair-wise epoch by epoch agreements between automated scores manually reviewed were higher (73-76%). The direction and statistical significance of treatment effect size estimates using the traditional efficacy endpoints were essentially the same whether scores were automated, semi-automated, or fully manual. As the degree of manual review increased, the magnitude of the effect size approached those estimated with fully manual scoring.
Conclusion: Automated or semi-automated sleep PSG scoring offers valuable alternatives to costly, time consuming, and inter-site variable R&K based manual scoring especially in large multi-centre clinical trials. Protocols for partial review and editing of automated scores however should be further improved.
Support (optional): Merck Research Laboratories and H.Lundbeck A/S

1023

THE PUPILLARY UNREST INDEX (PUI) AS AN OBJECTIVE MEASURE OF SLEEPINESS IN HEALTHY MEN AND WOMEN

Kutty R, Prasad B, Olopade C, Carley D
University of Illinois at Chicago, Chicago, IL, USA

Introduction: Multiple Sleep Latency Testing (MSLT) is the 'gold standard' for sleepiness evaluation. However, it is expensive and time-consuming. PUI assessment, conversely, is fast and relatively simple. We tested the PUI as an objective measure of sleepiness and predictor of psychomotor vigilance testing (PVT) in healthy adults.
Methods: In 23 healthy subjects (14M, 9F), overnight polysomnograms were followed by: sleep latency (SL) tests at 10AM, 12PM, 2PM and 4PM; PUI assessments at 9 AM, 11AM, 1PM and 3 PM; and PVT assessments at 11:30AM and 3:30PM. For analysis, PUI measures were compared with the succeeding SL; PVT measures were compared with the mean of the preceding and succeeding PUI or SL values.
Results: Male and female subjects did not differ with respect to any tested variable ($p > 0.11$ for each; ANOVA). A statistically significant but gender specific correlation was observed between PUI and SL ($r = -0.29$, $p=0.05$ overall; $r = -0.60$, $p=0.01$ in women; $r = 0.04$, $p=0.84$ in men) although SL ranged from < 3 to 20 min. in male and female subjects. Overall, SL and PUI correlated with various PVT measures (e.g. SD of reaction times: $r = -0.39$, $p=0.008$ for SL; $r = 0.31$, $p=0.04$ for PUI), but again, in gender-specific patterns. For example, SL predicted PVT errors only in males ($r = -0.46$, $p=0.01$), whereas PUI predicted PVT errors only in females ($r = -0.52$, $p=0.03$).
Conclusion: PUI increases with decreasing sleep latency in healthy adults, but this relationship is particularly strong in women. Both SL and PUI correlate with psychomotor performance, but in strongly gender-specific ways. These findings suggest that pupillometry merits further study both as a complement to MSLT and as an independent sleepiness assessment tool.
Support (optional): NIH NR004959

1024

ALGORITHMS FOR SLEEP-WAKE IDENTIFICATION USING ACTIGRAPHY: A COMPARATIVE STUDY AND NEW RESULTS

Tilmanne J,[1] Urbaine J,[2] Vande Wouver A,[3] Kothare M,[4] Sanjeev K[5]
(1) Faculte Polytechnique de Mons, Belgium, Brussels, Belgium, (2) Faculte Polytechnique de Mons, Belgium, Brussels, Belgium, (3) Automatic Control Laboratory, Faculty Polytechnique de Mons, Mons, Belgium, (4) Department of Chemical Engineering, Lehigh University, Bethlehem, PA, USA, (5) Drexel University, Philadelphia, PA, USA

Introduction: Actigraphy has been widely recognized as a low cost alternative for screening of sleep disorders, with special emphasis on sleep wake cycles. The objective of this study was to develop algorithms for automatic sleep/wake scoring using actigraphy with validation of the scoring with available PSG data using established and new algorithms.
Methods: The database was composed of 354 nights of PSG recordings, with simultaneous actigraphy of infants aged less than one year, performed from 1994 to 1998 in the context of the Collaborative Infant Home Monitoring Evaluation (CHIME) study. Two new algorithms that employ tools from neural networks and decision trees to model the optimal classification for sleep and wake states using actigraphy compared to PSG was performed and compared to previously developed actigraphy algorithms reported by other groups.
Results: The selection of the most discriminant actigraphy features was carried out using Fisher´s discriminant analysis. Approximately 80% of all the epochs were used to train the neural network and decision tree models. The models were then validated on the remaining 20% of the epochs. The neural network model gave an accuracy of 80.5%, a sensitivity of 92.5% and a specificity of 52%. With the decision tree model, these numbers were respectively 82.1%, 92.2% and 58.1%. The quality of the models was considerably improved by including more "wake" epochs in the training phase.
Conclusion: The use of neural networks and decision trees was able to capture potentially nonlinear classification characteristics, as compared to the previously reported linear combination methods. The large size of the database (approximately 338,000 epochs for 354 patients) provided a solid basis for determining the efficacy of actigraphy in sleep scoring. Our models, when trained for a specific actimeter, can provide an automatic low cost method for scoring sleep in a larger population than is currently possible.

1025

VALIDATING THE MATTRESS-BASED KINETOCARDIOGRAM

Woodward S,[1] Arsenault N,[2] Karin V,[1] Nguyen T,[3] Lynch J,[1] Leskin L,[1] Leskin G,[4] Sheikh J[5]
(1) Stanford University, Menlo Park, CA, USA, (2) Department of Veterans Affairs, Menlo Park, CA, USA, (3) Stanford Univerity, Menlo Park, CA, USA, (4) Palo Alto VA Health Care System, Menlo Park, CA, USA, (5) Stanford University, Stanford, CA, USA

Introduction: We have previously described a zero-burden mattress actigraphy system employing accelerometers embedded in a thin topper. This system was shown to transduce thoracic respiratory movements in close correspondence to inductive plethysmography. In this presentation, we will examine the ability of the same system to capture indices of cardiac function via comparison to simultaneously-recorded ECG.
Methods: Data were derived from 25 subjects who provided both mattress-derived kinetocardiogram (KCG) and ECG during laboratory

studies. Subjects were men and women aged 24-55. Apnea rates were low. KCG beat detection utilized a signal processing technique that is robust to the high variability of the KCG complex. ECG beat detection was based upon conventional identification of R-waves. KCG and ECG-based estimates of all-night heart rate (HR) and respiratory sinus arrhythmia (RSA) magnitude were calculated and compared.
Results: The KCG is highly sensitive to movement artifact. As a result, KCG-based estimates of HR and RSA were available for only 28% of the sleep period, on average (~139 minutes). Nevertheless, all-night estimates of HR and RSA from KCG were highly correlated with those derived from ECG (r = 0.97, rho = 0.91). A bias toward lower HR and higher RSA estimates from KCG was attributable to two sources. Movement-free epochs were generally characterized by lower arousal, and were more likely to derive from the latter half of the sleep period.
Conclusion: Mattress actigraphy can provide nightly heart rate and RSA estimates for indefinite periods of time without burdening sleepers in any way. Such intensive longitudinal estimates of sleep cardiac function represent a new class of data available to sleep researchers and cardiologists that may address important gaps in our knowledge of sleep cardiac function. For example, such a system could provide nightly RSA estimates covering the weeks and days prior to myocardial infarction or sudden cardiac death.
Support (optional): Supported by NIH/NIMH Grant MH64724 to Javaid Sheikh and by the Department of Veterans Affairs.

1026

A VIDEO BASED METHOD TO STUDY SLEEP IN DROSOPHILA MELANOGASTER

Zimmerman J, Raizen D, Maycock M, Pack A
University of Pennsylvania, Philadelphia, PA, USA

Introduction: The standard assay for Drosophila sleep uses infrared beam technology. While powerful for studying gross activity patterns, this technology has limitations for studying sleep. The aim of this study is to develop a video-based method that offers advantages over prior sleep-monitoring methods in flies.
Methods: Infrared Beam Break System (IBBS): Beam breaks were recorded every 30 seconds using the Drosophila Activity Monitoring System. Video System (VS): Images where acquired at 5 second intervals using a digital camera and Image Pro software. Absence of movement was identified by subtracting pairs of video images. Behavioral Analysis: Sleep was defined as 5 minutes or more of quiescence. Sleep architecture was determined for both the IBBS and video using software developed in our laboratory. Statistics: Unpaired t test with Welch correction between IBBS and video estimations of total sleep, sleep bout number and mean sleep bout duration.
Results: 69% of 30-second periods where the IBBS system identified the fly as not crossing the beam, the fly had moved. These movements can be more than the body length of the fly and significantly affect estimates of sleep bout duration. The mean bout duration as determined by IBBS was 52.7 ± 21.4 minutes (mean ± SD) and as determined by VS was 18.3 ± 5.8 minutes (mean ± SD) ($p<0.001$). The estimation of total sleep by VS (42.3 ± 9.8 %, mean ± SD) was also less than by IBBS (59.0 ± 8.1 %, mean ± SD) ($p<0.001$). There was increased precision in the determination of sleep bout duration, as reflected by a smaller coefficient of variance for VS (27.7%) versus IBBS (40.6%).
Conclusion: We have demonstrated that video system offers improved accuracy and precision in the measurement of sleep bout duration. Video analysis identifies even small movements independent of where the movement occurs.
Support (optional): K08 NS48914, AG17628

1027

PSYCHOMOTOR PERFORMANCE AND PUPILLARY UNREST INDEX (PUI) IN EXCESSIVELY SLEEPY INDIVIDUALS DEPEND ON DIAGNOSIS

Prasad B, Kutty R, Olopade C, Carley D
University of Illinois at Chicago, Chicago, IL, USA

Introduction: The relationship between sleepiness and cognitive performance is poorly understood. Multiple Sleep Latency Testing (MSLT) is the standard for objective sleepiness assessment, but alternative measures, including the PUI, have also been suggested. We tested the relationship between PUI and performance on psychomotor vigilance testing (PVT) in adults with obstructive sleep apnea (OSA), narcolepsy (N) and without any sleep disorder (C).
Methods: We tested 23 healthy subjects, 5 untreated OSA patients and 5 untreated narcolepsy patients by polysomnography (PSG) followed the next day by: MSLT (4 naps), PUI (4 tests) and PVT (2 tests). Although primary sleep disorder was excluded, 8 of the control subjects were found to have a mean sleep latency (SL) of < 10 minutes and were included here as the sleepy "control" group.
Results: Mean SL demonstrated excessive and equivalent sleepiness in all groups (C = 5.0±0.8 min, N = 4.5±1.2 min, OSA = 5.0±1.0 min; p=0.93). Despite equivalent sleepiness, PUI differed among the groups (C = 9.4±0.6, N = 12.5±1.2, OSA = 10.1±0.8; p=0.04). Moreover, N patients showed more significant impairment on multiple PVT measures with respect to both C and OSA groups, especially in the standard deviation of reactions times (N = 253.7±80.2 ms, OSA = 69.4±15.8 ms, C = 63.6±5.4 ms; p=0.008). Pooling all subjects, significant correlations were observed between PUI and mean reaction time (r = 0.42, p=0.04) and SD of reaction times (r = 0.47, p=0.02).
Conclusion: Short sleep latency correlates with decreased cognitive performance even in healthy sleepers, but when mean sleep latency is matched, patients with narcolepsy exhibit greater PVT performance deficits than do OSA patients or sleepy controls. Moreover, PUI can predict the degree of this performance decrement. These findings suggest that pupillometry merits further study as a complement to MSLT or as an independent sleepiness assessment tool.
Support (optional): NIH NR004959

1028

A COMPARISON OF SUBJECTIVE SLEEPINESS SCALES IN THE IDENTIFICATION OF OSA

Rosenthal L,[1] Dolan D,[2] Becker P,[1] Jamieson A,[1] Taylor D,[2] Schmidt-Nowara W[1]
(1) Sleep Medicine Associates of Texas, Dallas, TX, USA, (2) University of North Texas, Denton, TX, USA

Introduction: To determine the sensitivity of the Epworth Sleepiness Scale (ESS) and the Time of Day Sleepiness Scale (ToDSS) in identifying Obstructive Sleep Apnea (OSA).
Methods: Retrospective chart reviews of two patient cohorts were conducted. Both cohorts completed diagnostic polysomnography and OSA was defined as an apnea/hypopnea index (AHI) >10/hour. The first cohort consisted of 272 (190 male/82 female) patients who were evaluated at a Sleep Medicine Clinic between August 2000 and October 2002. The cohort was found to have a BMI of 35.6±9.1, and an AHI of 36.2±33.6. The second cohort consisted of 156 consecutive patients diagnosed with OSA (104 male/52 female) between January 2005 and September 2006 (BMI= 35.2±8.4; AHI= 48.8±30.8). All patients completed the ESS and the Time of Day Sleepiness Scale (ToDSS). A cutoff of >=10 and 12 on the ESS was defined as sleepiness. The ToDSS provides 3 scores of sleepiness: am, pm and evening. It has previously

been shown to provide differential self-reported sleepiness levels across the day. The ToDSS cutoff scores are >=3 for am, >=7 for pm, and >=10 for evening. Sleepiness is defined as the presence of one or more elevations at any time of day.
Results: The sensitivity of the ESS was 69% and 58% using ≥ 10 and ≥ 12 criteria in the first cohort. The ToDSS yielded a sensitivity of 87%. For the second cohort, the ESS was shown to result in a sensitivity of 61% and 52% respectively. The ToDSS yielded a sensitivity of 82%.
Conclusion: Use of the ToDSS as a screening measure of Excessive Daytime Sleepiness results in greater sensitivity in identifying patients with OSA when compared to the currently recommended ESS criteria.

1029

MOUTH LEAK EVENTS & SLEEP DISRUPTION IN PATIENTS TREATED WITH NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE

Baltzan M,[1] Kassissia I,[2] Garcia-Asensi A,[3] Sully J,[1] Tanzimat G,[2] Wolkove N[1]
(1) Mount Sinai Montreal, Montreal, Quebec, Canada, (2) OSR Medical, Montreal, Quebec, Canada, (3) OSR Medical, Quebec, Canada

Introduction: Compliance with continuous positive airway pressure (nCPAP) is often difficult, leading to inadequate treatment of obstructive sleep apnea (OSA). Mouth breathing has been described in OSA and during nCPAP treatment. It has been associated with reduced nCPAP compliance. We sought to characterize mouth breathing with attention to signal quality, event definition and associated sleep disruption.
Methods: Eight patients with OSA and nCPAP (range 7 to 15 cm H2O) were studied with custom polysomnography 4 weeks after initiating therapy for the first time. Tidal volume was measured with a pneumotachometer in line with the nasal mask. Oral breath signal was generated with a peri-oral pressure transducer as well as a polyvinylidene fluoride (PVDF) film airflow sensor. Scoring criteria were developed. Signal loss was assessed based on the percent of epochs with interpretable waveforms. Two scorers rated the signals.
Results: Mouth breathing during calibration and in sleep shows both a fast frequency `puffing´ waveform and a slow waveform in phase with tidal breathing. The fast `puffing´ appeared during stable REM and NREM sleep and with cortical arousals from sleep. Slow events occurred more frequently and were associated with stable sleep, as well as persistent hypopneas in sleep despite nCPAP. Some mouth leak events immediately preceded cortical arousals suggesting a causal relationship. The PVDF sensor demonstrated better signal sensitivity and reliability.
Conclusion: Mouth leak events are observed during stable sleep, as well as before and during arousals from sleep. These may be a source of sleep disruption in patients treated with nCPAP.
Support (optional): Mount Sinai Hospital Research Foundation and OSR Medical

1030

WAKE DETECTION CAPACITY OF ACTIGRAPHY DURING SLEEP

Carrier J,[1] Paquet J,[2] Kawinska A,[3] Maheu M[3]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) Hôpital du Sacré-Coeur de Montréal, Quebec, Canada, (3) Universite de Montreal, Quebec, Canada

Introduction: Actigraphy measures of sleep usually showed good epoch-by-epoch accuracy and good sleep parameters correlations with PSG. However, the ability of actigraphy to detect wakefulness has been questioned recently. The main objective of the study was to evaluate the ability of actigraphy compared to polysomnography (PSG) to detect wakefulness in subjects submitted to three sleep conditions with different amounts of wakefulness. A second objective was to compare the ability of four different scoring algorithms (two threshold algorithms and two regression analysis algorithms) to detect wake in the three sleep conditions.
Methods: Fifteen healthy subjects were monitored with actigraphy and PSG recorded at the same time in three sleep conditions: a nocturnal sleep episode, a daytime recovery sleep episode after the administration of a placebo and a daytime recovery sleep episode after the administration of 200 mg of caffeine. Four scoring algorithms for estimating sleep parameters derived from actigraphy counts were compared; two thresholds based algorithms (low; 20 and medium; 40) and two algorithms based on regression analysis.
Results: An epoch-by-epoch comparison between actigraphy and PSG showed a significant decrease in actigraphy accuracy with increased wakefulness in sleep conditions due to the low sleep specificity of actigraphy (generally < 50%). Actigraphy more strongly overestimated total sleep time and sleep efficiency in conditions with more wakefulness. Compared to the two regression algorithms, the two threshold algorithms were less able to detect wake in higher wakefulness conditions during the sleep episode, and they overestimated the number of awakenings.
Conclusion: The very low ability of actigraphy to detect wakefulness casts doubt on its validity to measure sleep quality in clinical populations with fragmented sleep or in situations where the sleep-wake cycle is challenged, such as jet lag and shift work.
Support (optional): The Fonds de recherche en Santé du Quebec, Natural Sciences and Engineering Research Council of Canada

1031

EFFICIENT COMPUTATIONAL PROCEDURE FOR INDIVIDUALIZATION OF SLEEP/WAKE MODEL PARAMETERS

Smith A, McCauley P, Belenky G, Van Dongen H
Washington State University, Spokane, WA, USA

Introduction: Novel approaches in biomathematical modeling allow sleep and performance prediction for individuals through Bayesian individualization of model parameters. Current computer implementations of these approaches involve comprehensive searches through the parameter space ("grid searching"). This guarantees correct results but is an inefficient process of order N^D (D is the number of parameters; N is the number of grid points). Such inefficiency is computationally prohibitive for models with more than a few parameters. Using the wake function for the homeostatic process of the two-process model as a modeling platform, we set out to improve the computational efficiency of estimating individualized model parameters and their confidence intervals.
Methods: A Bayesian forecasting equation was applied to simulated data to individualize three parameters: basal homeostatic level, homeostatic buildup rate, and initial homeostatic state. We demonstrated that the equation has a single maximum, determining the individualized parameter estimates. To locate the maximum, partial derivatives to the parameters were taken, and set to equal zero. This system of nonlinear equations was reduced to one nonlinear equation, which was solved numerically. Once the maximum was found, each parameter was considered separately, fixing the others at the maximum. The 95% confidence intervals for the basal level and initial state parameters were derived in closed form. For the buildup rate parameter, a single nonlinear equation was integrated numerically.
Results: The computations required finding the root of a nonlinear

equation, which is a process of order log(*N*); and integrating another nonlinear equation, which is a process of order *N*.
Conclusion: The computational burden of individualized model parameter estimation with confidence intervals was reduced to order *N* regardless of the number of parameters. For the full two-process model with six individualized parameters, grid searching would be of order N^6. Thus, computational efficiency was improved by five orders of magnitude, making individualized predictions feasible in real-time.
Support (optional): AFOSR grant FA9550-05-1-0086; DURIP grant FA9550-06-1-0281; congressionally directed funding W81XWH-01-0099.

1032

COMPARISON OF SUBJECTIVE AND OBJECTIVE ASSESSMENT OF SLEEP ONSET (SO) ON THE MULITPLE SLEEP LATENCY TEST (MSLT) USING STANDARD AND MICROSLEEP CRITERIA.

Verma N, Konstantinova N, Freeman J, Lund S
Sleep Disorders Institute, New York, NY, USA

Introduction: The MSLT is an objective test of daytime somnolence which measures SO under soporific conditions. Patients subjectively assess SO using a post-sleep questionnaire. Discord in the SO between the patient questionnaire and the MSLT has been observed. Shorter periods of sleep (lasting between 5 and 15 seconds), known as microsleeps, may be more sensitive to determine SO. We explored if there is a significant difference between subjective report of SO and MSLT SO using standard (MSLT-s) and microsleep criteria (MSLT-m).
Methods: A retrospective chart review of patients ≥18 yr, with both MSLT and post-MSLT questionnaires from 7/1/06 until 12/1/2006 were eligible. Patients with idiopathic hypersomnia or narcolepsy were excluded. Two independent reviewers determined MSLT-m SO. The responses from the post-MSLT questionnaire were compared to MSLT-s and MSLT-m.
Results: Seventeen patients, (9M, 8F) aged 43.1 (±17.0) years with BMI 29.9 (±8.3) and AHI 26.2 (±21.0) were identified. The mean subjective SO was 12.4 (±6.2) for Nap1, 12.1 (±6.9) for Nap2, 13.8 (±5.2) for Nap3, and 12.7 (±5.9) for Nap4. The mean MSLT-s SO was 10.4 (±7.3) for Nap1, 10.2 (±5.9) for Nap2, 10.7 (±6.9) for Nap3, and 11.4 (±6.9) for Nap4. The mean MSLT-m SO was 8.3 (±6.6) for Nap1, 8.7 (±6.4) for Nap2, 10.3 (±7.4) for Nap3, and 10.9 (±7.0) for Nap4. No significant difference was observed between subjective SO and MSLT-s SO except in Nap3. No significant difference was observed between subjective SO and MSLT-m SO except in Nap1 and Nap3. The accuracy of the subjective assessment of SO compared with MSLT-s SO was between 88 – 94 %; with MSLT-m SO it was between 82-94 %.
Conclusion: In patients studied thus far, there was no significant difference between subjective and objective measurement of SO using standard criteria or microsleep criteria.
Support (optional): None.

1033

AUTOMATED NEURAL NETWORK DETECTION AND PREDICTION OF SLEEP APNEA

Waxman J, Graupe D, Radulovacki M, Carley D
University of Illinois at Chicago, Chicago, IL, USA

Introduction: The detection and prediction of obstructive sleep apnea (OSA) is increasingly important considering the morbidity and prevalence of this disorder. Currently, diagnosis of OSA relies on analysis of overnight polysomnogram (PSG) data. Accurate automated detection of apnea from PSG data is thus a necessity. Additionally, reliable prediction of apnea would be extremely useful for dynamic control of CPAP treatment. While many methods of OSA screening exist, there are few methods to forecast apnea. In addition, none of these methods utilizes an artificial neural network (ANN) to process PSG data. ANNs are particularly well suited for these tasks as they are capable of learning about and representing highly complex nonlinear processes. We attempted to detect and predict apneas using a LAMSTAR neural network.
Methods: LAMSTAR neural networks are designed to efficiently handle large scale multivariate storage-retrieval tasks. LAMSTAR networks also provide unique data analysis capabilities that can reveal correlations among the inputs. For the detection and prediction of apnea, the inputs to the network were derived from wavelet transforms of EEG, ECG, nasal pressure, and oronasal temperature data obtained from overnight PSG recordings in 11 untreated OSA patients.
Results: For detection, the network had a sensitivity of 80.4+-4.2%, a specificity of 59.0+-6.0%, a positive predictive value of 66.3+-3.4%, and a negative predictive value of 75.1+-4.4% For prediction, the network had a sensitivity of 64.7+-4.8%, a specificity of 56.0+-5.7%, a PPV of 59.6+-3.0%, and an NPV of 61.4+-3.4%. In addition, the network revealed that the most robust input to the network was temperature.
Conclusion: The LAMSTAR network is capable of both detecting and predicting apnea, but with a high false positive rates. This suggests that further optimization of network inputs, particularly those derived from oronasal temperature, may yield an improved approach to automated CPAP control.

1034

SLEEP STAGE DYNAMICS DISTINGUISH FIBROMYALGIA PATIENTS FROM CONTROLS

Burns J,[1] Crofford L,[2] Chervin R[3]
(1) Michigan Technological University, Ann Arbor, MI, USA, (2) University of Kentucky, Lexington, KY, USA, (3) University of Michigan, Ann Arbor, MI, USA

Introduction: Sleep stage dynamics, as reflected by the variation in sleep stage duration, follow characteristic statistical distributions (Lo C *et al.*, Europhys. Lett.; 57 (5) :625-631. Penzel T *et al.*, Neuropsychopharmacology; 28: S48-S53). Whether variations in distribution parameters may have diagnostic value in clinical settings remains largely unknown. We compared continguous durations of specific sleep stages in women with fibromyalgia syndrome (FMS) and healthy controls.
Methods: Female rheumatology clinic FMS patients (n=15, screened to exclude other sleep disorders) and healthy female age-matched volunteers (n=15) were studied with nocturnal polysomnography, 2-week pain diaries, and a measure of current pain intensity. Sleep stages were scored manually by a single board-certified technologist masked to subject group (FMS vs. control) using standard criteria (Rechtshaffen and Kales, 1968). Mean sleep stage durations were computed for each subject and compared to clinical diagnosis and pain measures.
Results: The mean duration of total sleep, stage 1 sleep, stage 3/4 sleep, and REM sleep did not separate FMS and control subjects (Wilcoxon rank sum tests, each p>.10). In contrast, mean stage 2 sleep duration distinguished the groups well (p=.006). Specifically, mean stage 2 duration was shorter in FMS subjects (5.3 ± 1.9 min) than in controls (7.3 ± 2.3 min). Shorter stage 2 durations were associated with higher pain diary scores (Spearman rho=-.56, p=.0014) and current pain intensity (rho=-.71, p<0.0001).
Conclusion: Sleep stage dynamics, at least as described by mean stage 2 durations, can distinguish FMS and control women subjects and

correlate with the pain they experience. Characterization of specific sleep stage durations, in addition to the usual sleep stage amounts and percentages commonly listed in polysomnogram reports, may provide novel clinical utility.
Support (optional): This work was supported by grants from the Arthritis Foundation, Michigan Chapter; Pfizer, Inc.; and the University of Michigan General Clinical Research Center (M01-RR00042).

1035

PERFORMANCE IN REPEATED DRIVING SIMULATOR TESTS USING A RURAL DRIVE SCENARIO IN HEALTHY PARTICIPANTS DOES NOT CHANGE OVER A TWO WEEK PERIOD

Ennis W,[1] Ware J,[1] Zhao Y,[2] Johnson D[2]
(1) Eastern Virginia Medical School, Norfolk, VA, USA, (2) Eastern Virginia Medical School, VA, USA

Introduction: Performance during driving simulator (DS) testing appears sensitive to the effects of sleep disturbance in patients (Risser et al, 2000) and healthy participants (Ware et al, this meeting). This study examined performance reliability on a rural drive scenario in healthy participants both within and between DS trials.
Methods: Ten naïve participants (6 females; ages 27-52 years; mean ± SD; 32.9 ± 9.6) underwent DS testing between 1200 and 1700 hours after their normal lunchtime and again two weeks later. The scenario consisted of a one-hour rural drive. A 10-minute city practice drive preceded each test. Dependent variables included lane position variability (LPV), speed variability, and steering adjustments. Performance was analyzed over six ten-minute periods for each drive.
Results: The primary variable, LPV, did not change from the first to second drives; M =1.2 ft, sd = 0.25 and M =1.2 ft, sd = 0.35, p = ns. Speed was 56.5 mph, sd = 4.2 and 58.0 mph, sd = 4.2 for the first and second drives respectively, p = ns. Neither age nor sex affected the results. Also, performance did not change over time within each drive. The Epworth Sleepiness Scale score did not differ between the drives (8.3 + 3.3 and 6.5 + 3.1, p = ns).
Conclusion: To use a DS to evaluate treatment effects, knowledge of change over time is necessary. In this study, there was no significant change in performance for healthy participants in any dependent measure. The lack of improvement during the hour long drives and between the first the second ten minutes of each drive indicate that practice effects are minimal. Combined with studies demonstrating sensitivity to sleep disturbance, these results support the use of this DS paradigm to measure treatment effects in sleep disordered patients, for example, after treatment with CPAP or with medications.
Support (optional): Division of Sleep Medicine
Eastern Virginia Medical School

1036

ASSESSING INTERDAILY STABILITY AND INTRADAILY VARIABILITY OF REST-ACTIVITY RHYTHMS IN DEPRESSED AND NEVER-DEPRESSED PARTICIPANTS

Kelly M,[1] Martin J,[2] Ancoli-Israel S,[3] McQuaid J,[3] Haynes P[1]
(1) University of Arizona, Tucson, AZ, USA, (2) University of California, Los Angeles, North Hills, CA, USA, (3) VA San Diego Healthcare System, University of California, San Diego, San Diego, CA, USA

Introduction: Researchers have found that interdaily stability (IS) and intradaily variability (IV) indices are superior to cosinor variables in modeling the rest-activity rhythms in Alzheimer´s disease patients. However, no research to our knowledge has examined IS and IV in depression. The purpose of this methodological project is to assess whether IS and IV are sensitive indices of rest-activity disturbance in depressed compared to never-depressed participants.
Methods: Twenty-three depressed outpatients and 21 never-depressed controls wore actigraphs over a period of 3 to 7 days and completed the Social Rhythm Metric (SRM) over 2 weeks. The following variables were computed: IS (variability between days), IV (rest-activity transitions within days), cosinor variables (mesor, amplitude, and goodness of fit to the cosine curve), and the SRM variable (regularity of habitual behaviors). We used ANOVA, bivariate correlations and logistic regression analysis techniques.
Results: No significant differences were found between depressed and never-depressed participants on IS or IV indices. Irregular social rhythms increased the likelihood of depression when controlling for IS (Odds Ratio=.11, p<.01). Higher levels of interdaily stability were associated with higher values of the mesor (r=.31, p< .01), amplitude (r=.44, p<.05), goodness of fit (r=.81, p<.01) and SRM variable (r=.32, p<.01). Individuals with less intradaily variability had more interdaily stability (r=-.47, p<.01) and a higher goodness of fit statistic (r=-.69, p<.01).
Conclusion: Contrary to our hypothesis, IS and IV were not better predictors of depression than cosinor variables. However, both IS and IV correlated with the goodness of fit statistic, indicating that IS and IV yield comparable values to cosinor models in depressed and never-depressed adults. Results also indicated that the regularity of habitual behaviors might mediate the relationship between IS and depression. Future research utilizing IS and IV in other clinical populations might further our understanding of the role of daily rhythm variability in sleep/wake disturbances.
Support (optional): NIMH NRSA 1F31MH064255, NIA AG08415, NCI CA85264 and the research service of the VASDHS.

1037

ELECTROCARDIOGRAM BASED SLEEP RELATED BREATHING DISORDER DIAGNOSIS

Shinar Z,[1] Akselrod S,[2] Kahan C,[3] Baharav A[4]
(1) HypnoCore, Netanya, Isarel, Israel, (2) Tel Aviv University, Israel, (3) Sharey Zedek Medical Center, Israel, (4) Sharey Zedek Medical Center, Savyon, Israel

Introduction: The recognition of OSAS as an important contributor to increased cardiovascular morbidity and mortality triggered the need to develop alternative diagnostic methods. The electrocardiogram (ECG) is an easy to acquire signal influenced by changes in the thoracic volume and posture. The quantification of changes in the geometry of the ECG waveforms allows estimating respiration. We developed an algorithm that calculates ECG derived respiration (EDR) and our goal was to evaluate its clinical applicability.
Methods: Data from 14 adults referred to polysomnography (PSG) was evaluated. Inclusion criteria were: good quality PSG and ECG (sampled at 200Hz). All studies were manually scored by two experts. ECG quality evaluation was based on signal-to-noise ratio, percentage of good quality signal and no movement artifacts, as well as the dynamic range of the signal. The respiration signal obtained was based on the continuous calculation of R wave amplitude and duration. Changes in these measures were counted during sleep only and when followed by an autonomic arousal. Events were detected separately: (1) manually based on ASDA criteria; (2) automatically by our algorithm.
Results: EDR parameters change as a result of the displacements of the thorax and abdomen during respiration that causes measurable fluctuations in the relative angle between the electrical axes of the heart the ECG electrodes axis. These parameters resembled signals acquired

with piezoelectric sensors, as they reflect changes in body wall position, not effort. The obtained signal decreased during both central and obstructive events, however the decrease was significantly higher for central ones ($p<0.01$) A linear regression between the number of events resulting from the manual score and the number of events from the EDR automated score showed a very good correlation between the two with r2=0.93, a=1.16, b=-30.
Conclusion: Provided a good quality ECG recording respiratory events during sleep can be detected and quantified reliably. This novel method allows for multiple nights respiratory evaluation with obvious advantages in terms of comfort for the patient in the home environment and reduced cost per study.

1038

CONTINUOUS EEG/EMG RECORDING IN SUCKLING RAT PUPS

Morrissey M,[1] Yamada K,[2] Gru A,[2] Deerausquin G,[2] Duntley S[3]
(1) Washington University, Saint Louis Missouri, Saint Louis, MO, USA, (2) Washington University, MO, USA, (3) Washington University in St. Louis, Saint Louis, MO, USA

Introduction: Previous studies investigating the development of sleep have traditionally removed unweaned pups from the home cage while recording sleep with "hard-wired" systems. Limitations of this method include decreased session recording time and stress. The method proposed allow continuous wireless recording of preweaned pups without removal from the dam. This limits maternal separation and allows for a more accurate representation of the development of sleep/wake cycles in the rat.
Methods: Two animals from separate litters were implanted with a DSI radiotelemetry device at P10 for recording continuous EEG, EMG, and body temperature. The telemetry device was placed subcutaneously in the abdomen. For EEG recording, fine-wire electrodes were secured to the soft scull using 1/16" 000 screws and dental acrylic. For EMG recording, fine wires from the telemetry device was carefully placed in the nuchal muscle bilaterally. Tissue adhesive was used to close the scalp and abdomen. The pups were immediately placed in their home cage, and the respective litters were culled to three pups each, including the telemetry animals. The animals were weighed daily, and were recorded until P20. The data was separated into 4 hour per day samples, and scored manually using 30-second epochs. Scoring was based on traditional EEG, EMG, and behavioral criteria for AS, Wake, and Quiet Sleep.
Results: Both animals maintained weight within 5 grams of their littermates. Neither of the animals was rejected by the dam. AS was scorable at P11, and peaked with it accounting for 68% of state. By P19, AS occupied 18% of state scored, which approaches adult levels.
Conclusion: Radiotelemetry allows for the continuous recording of multiple variables from preweaned rat pups. The ability to gather continuous data allows for a more accurate measure of sleep in developing animals, and can be useful in studies investigating the effects of sleep deprivation on the developing CNS.

1039

VALIDATION OF AN AUTOMATIC DETECTION SYSTEM FOR BREATHING EVENTS DURING SLEEP

Dorffner G,[1] Woertz M,[2] Anderer P,[3] Gruber G,[4] Parapatics S[4]
(1) Medical University Vienna, Vienna, AE, Austria, (2) Austrian Research Institute for Artificial Intelligence, Vienna, AE, Austria, (3) Medical University of Vienna, Vienna, AE (Europe), Austria, (4) The Siesta Group, AE (Europe)

Introduction: The study investigates the validity of a recently developed automatic detection system for breathing disturbances in sleep. The quality of the automatic detection software, which is part of the Somnolyzer24x7 framework, was determined by using correlation and the Bland-Altman analysis (Lancet, 1986). Results are based on data recorded in the SIESTA project.
Methods: The detection algorithm for respiratory events uses 4 polysomnographic (PSG) signals: oxygen saturation, nasal airflow, movement of the chest wall and of the abdomen. Intervals of decreased airflow are calculated based on the determination of single inspiration and expiration maxima. For both effort signals, intervals with possible events are extracted similarly. An expert system is finally used for the detection of apnea and hypopnea events. For the present comparison, PSGs of 51 apnea patients (44 males and 7 females, aged 51+/-10 years) were investigated. The visual apnea/hypopnea scoring was done according to the AASM criteria (Sleep, 1999).
Results: The human scored AHI was 45+/-31 for the adaptation night and 41+/-26 for the second night. The automatic detection resulted in an AHI of 42+/-26 and 41+/-22. The correlation between human and automatic indices were r=0.94 and r=0.92 for the first and second night, respectively. Bland-Altman analysis showed neglectable bias (2.7 and 0.5 for first and second nights, respectively) and the plots used to visualize individual differences suggested equivalence of human scoring and the automatic detection.
Conclusion: The high correlation coefficients as well as the inspection of the Bland-Altman plots in 102 PSGs of patients with apneas proved the validity of the Somnolyzer 24x7 detection and thus justifies the usage of the automatic method in clinical studies. Due to the modular detection process, the automatic detection system can be adapted for different criteria (e.g. AASM 2001, Medicare, etc.)
Support (optional): Research supported by Austrian Industrial Research Promotion Fund (Project 806765). The Austrian Research Institute for Artificial Intelligence is supported by the Austrian Federal Ministry of Education, Science and Culture and the Austrian Federal Ministry of Transport, Innovation and Technology.

1040

FEASIBILITY OF USING ACTIGRAPHY TO OBJECTIVELY MEASURE SLEEP IN ADOLESCENTS AND ADULTS DIAGNOSED WITH DIABETES MELLITUS

Perfect M,[1] Curcio J,[2] Lyle-Lahroud T,[3] Elkins G[4]
(1) University of Arizona, Tucson, AZ, USA, (2) University of Arizona, AZ, USA, (3) Texas Children's Hospital, TX, USA, (4) Baylor University, TX, USA

Introduction: Very few investigations have utilized actigraphy with diabetics. Preliminary findings from our lab suggested that individuals with DM exhibit poor sleep hygiene. We address clinical and methodological issues that were made salient when manual scoring of actigraph data in the context of a randomized clinical pilot study.
Methods: Twenty participants with DM, were enrolled in an ongoing intervention study targeting stress and sleep, wore a wrist actigraph for approximately a week. The PI and/or trained research team members set rest intervals (in pairs) according to known times for "lights out" and waking up for each participant.
Results: Participants (30% Non-White; 3 males) had a mean age of 34.99 (11.89). They wore the devices about 95% of the time and used the event marker to denote removal of the device. Some participants´ habits presented challenges, including: night-to-night sleep intra-variability (e.g., one person´s mean WASO was 32.35 and the SD was 24.72); falling asleep for varying durations before the official "time in bed" period; and irregular patterns of awakenings and/or activity during

the middle of the night. Lessons learned included the need to request better documentation of activities during periods of little movement and clarifying instructions for participants to press the event marker to signal "lights out" rather than when they were getting ready to go to bed.
Conclusion: Findings support the feasibility of using actigraphy with diabetic adolescents and adults. In addition to diary methods, research should be conducted to determine potential contextual factors that influence recorded movement. Software features, which may be available depending on the company, that may facilitate data interpretation include: algorithms for shorter rest intervals, options to set napping intervals distinct from nighttime rest intervals; and statistical analysis capabilities to assess the influence of daily rest-activity patterns on each respective night´s sleep quantity and quality.
Support (optional): Supported by Scott & White Memorial Fund.

1041

ANALYSIS OF AMBULATORY HOME SLEEP STUDIES IN SEVERE HEART FAILURE PATIENTS

Amir O,[1] Amos Y,[2] Mintz S,[3] Reiseld D[4]
(1) Carmel medical center, Herzelya, Israel, (2) WideMed LTD, Hertzelya, Israel, (3) WideMed LTD, Israel, (4) WideMed LTS, Hertzelyia, Israel

Introduction: Previous studies showing that sleep apnea is associated with poor prognosis in heart failure (HF) patients were performed in sleep labs and may represent referral bias.

Feasibility of ambulatory home monitoring sleep study for severe systolic HF patients was evaluated; prevalence of SDB and arrhythmogenic consequences of apnea were examined.
Methods: 60 patients (52 males, 65±13 years) with advanced systolic HF were included. Mean NYHA classification: 3; LVEF: 25±8%; ischemic cardiomyopathy was the etiology in 38 (63%) patients. Beta blockers were used in 56 (93%) patients.

All patients were home sleep monitored for a full night. WideMed's Morpheus system was used for scoring and analysis and the results were manually validated.
Results: All patients completed full night recordings without reporting any major discomfort. Complete signal recordings were achieved in 56 patients (93%). Total sleep time was 5±1 hours. Mean AHI was 35±19; most events were central (central AHI was 20±11). Cheyne-Stokes breathing was present in 56 (93%) patients. One patient had no apneas, 8 patients had mild apnea (AHI: 5-14), 18 had moderate apnea (AHI:15-29), and 33 showed severe apnea (AHI >30).
In 48 patients significant amount of apneas (at least 10%) were associated with heart rate increase of at least 10%. Average number of premature beats per sleep hour was 191±363; almost half of these were related to apnea/hypopnea events (44% ±26%).
Conclusion: 1. Home monitoring of severe HF patients is feasible and well accepted by these patients.
2. Prevalence of sleep apnea and Cheyne stokes respiration was higher than previously reported. This may be attributed to the severity of HF in the examined patients.
3. Significant cardiac rhythm changes were associated with sleep apnea.

1042

SLEEP MOVEMENT MICROANALYSIS

Woodward S,[1] Arsenault N,[2] Lynch J,[3] Nguyen T,[4] Voelker K,[3] Leskin L,[3] Leskin G,[5] Sheikh J[6]
(1) Department of Veterans Affairs, Palo Alto, CA, USA, (2) Department of Veterans Affairs, Menlo Park, CA, USA, (3) Stanford University, Menlo Park, CA, USA, (4) Stanford Univerity, Menlo Park, CA, USA, (5) Palo Alto VA Health Care System, Menlo Park, CA, USA, (6) Stanford University, Stanford, CA, USA

Introduction: In this presentation, we consider the ability of the mattress actigraphy to transduce two previously unexamined classes of body movement. These are brief low-amplitude thoracic twitches, and slow position shifts probably associated with progressive atonia.
Methods: Movement data were derived from 66 nights of laboratory sleep obtained from 48 adult subjects. Voltage outputs from three single-axis DC accelerometers underlying the thorax were recorded continuously at 600 Hz. Post-processing involved exclusion of all large-amplitude movements associated with position adjustments, leaving only "movement-free" sleep as defined by conventional methods. Thoracic twitches were then defined as 1) exceeding by three standard deviations the magnitude of concurrent respiratory movement and 2) being one second or less in duration. They were counted per epoch. Slow position shifts were quantified as the aggregate change in DC level over all thoracic sensors for any "movement free" period of at least 10 minutes duration. The whole-period value was then assigned to each included epoch. Movement records were precisely co-registered with sleep staging based upon EEG, EOG, and EMG.
Results: Thoracic twitch counts exhibited a large main effect of stage ($F(1,65) = 135.6$, $p < 0.00001$). They did not distinguish sleep from wake, but were lower in stage four sleep. Slow position shifts also exhibited a large main effect of stage ($F(1,63) = 184.3$, $p < 0.00001$ – two nights lacked scoreable aggregate slope). Slow position shift were larger in stages wake, 1, and REM than in Stages 2, 3, and 4.
Conclusion: "Movement free" periods of sleep contain both very small and very slow movement phenomena that are systematically variable over sleep stage. The relative absence of twitches in stage 4 sleep is consistent with earlier videographic findings. Slow position shifts are distributed in a manner consistent with evolving skeletal muscle atonia.
Support (optional): This work was supported by NIH/NIMH grant MH64724 to Javaid Sheikh and by the Department of Veterans Affairs.

1043

AN IMPROVED, NON-INVASIVE, HIGH-THROUGHPUT SYSTEM TO MONITOR SLEEP AND WAKE IN MICE

Donohue K, Medonza D, Crane E, O'Hara B
University of Kentucky, Lexington, KY, USA

Introduction: This work evaluates a cost effective, non-invasive, high-throughput system for detecting sleep-wake states in mice using a single piezoelectric sensor covering the cage bottom. Previous work collected data with similar sensors and developed a neural network classifier based on ad hoc features related to breath-motion regularities. The resulting classifier matched hand-scored sleep-wake classifications, and simultaneous EEG/EMG scored data, on the order of 90-95% (Flores AE, *et al.*, 2007), but was difficult to set-up and utilize on a continual basis.
Methods: This new re-designed system is now significantly less complex, with a classification system that uses a linear classifier with 6 features directly extracted from the power spectrum, autocorrelation, and generalized spectrum (autocorrelation of complex spectrum). System variability was also reduced by complete re-design of all

hardware including the amplifier system, piezoelectric films, protective coatings, and cage structures. This system was tested on C57BL/6J, DBA/2J, CAST/Ei, and F1 hybrids. Automated classification of sleep vs. wake was compared to both visual scoring of piezo signals and to independent sleep-wake assessment made by human observers. EEG/EMG comparisons are currently underway.
Results: From visual inspection, the waveforms from the new system show a more consistent and uniform pattern, especially during sleep, when an approximately 3Hz pattern typically predominates (reflecting the average 3Hz respiratory rate for sleeping mice). While quiet wake may sometimes appear similar, there is almost always at least some grooming or postural adjustments that decreases regularity. Accuracy of the automated classification of sleep vs. wake relative to human observations was 94%. No attempt was made to distinguish Slow-wave-sleep vs. REM sleep, although this may be possible in the future, along with other behavioral assessments.
Conclusion: This new automated system can be an effective high-throughput sleep screen, and is currently being utilized in collaborations with the Tennessee-Mouse-Genome-Consortium to identify genes and gene alleles that influence sleep.
Support (optional): This work is supported by a DoD AFOSR award - FA9550-05-1-0464, and by an NSF Functional Genomics Infrastructure Award - EPS-0132295.

1044

SYMPTOM PATTERN OF SLEEP-DISORDER COMPLAINT INFLUENCES PHYSICIAN REFERRAL

Bailes S,[1] Baltzan M,[2] Rizzo D,[1] Fichten C,[3] Sully J,[2] Libman E[1]
(1) Sir Mortimer B. Davis - Jewish General Hopital - Montreal, Montreal, Quebec, Canada, (2) Mount Sinai Hospital, Montreal, Montreal, Quebec, Canada, (3) Dawson College, Montreal, Quebec, Canada

Introduction: Older adults are under-referred to sleep clinics. To explore reasons for this, we surveyed (1) primary care patients to inquire about which sleep disorder-related symptoms they recently discussed with their family doctors, and (2) first-time sleep clinic patients to discover what symptom presentation resulted in a "successful" referral.
Methods: The Primary Care Sample comprised 191 older family practice patients and the Sleep Clinic Sample comprised 117 consecutive new patients.

Participants completed the Sleep Study Checklist (SSC) in their respective waiting areas. The SSC includes 21 symptoms of sleep disorder, insomnia, fatigue, sleepiness, psychological and health functioning. Respondents rate symptom severity and check which had been discussed with their family practice physician in the past year (Primary Care Sample) or their referring physician (Sleep Clinic Sample). All Family Practice participants were offered a sleep evaluation, including questionnaires, medical assessment, and polysomnography. Sleep Clinic subjects were awaiting their first appointment at the clinic. According to their participation, Primary Care subjects were designated: Refusers (completed SSC, refused further evaluation), Drop-outs (completed some evaluation steps, but not PSG), Completers (completed all evaluation steps).
Results: Approximately 35% of the Primary Care Sample endorsed sleep disorder-related symptoms, but few had discussed these with their doctor within the past year. Significantly more Completers had discussed sleep disorder symptoms than Refusers or Drop-outs. The discussed symptoms of the Sleep Clinic Sample were much more focussed on sleep apnea-related symptoms (snoring, breathing interruption, non-refreshing sleep, daytime sleepiness, fatigue) than those of the Completers, who discussed a wider range of symptoms (insomnia, body pain, nocturnal urination and anxiety). On PSG, Completers had a high rate of apnea diagnosis (84%).
Conclusion: • Sleep Clinic patients are more focussed in their presentation of apnea-related symptoms.
• Completers present a wider range of symptoms, possibly distracting from a sleep clinic referral.
Support (optional): Canadian Institutes of Health Research

1045

KATRINA: CHANGE IN SLEEP RELATED COMPLAINTS AND COMPLAINERS

Sharon D,[1] Mack C,[2] Hymmel B[3]
(1) Comprehensive Sleep Medicine Center, Destrehan, LA, USA, (2) Comprhensive Sleep Medicine Center of the Gulf Coast, Destrehan, LA, USA, (3) Comprehensive Sleep Medicine Center of the Gulf Coast, Destrehan, LA, USA

Introduction: Natural disasters cause a significant disruption of day to day life in the affected areas. On August 29, 2005 the Katrina storm hit the Gulf Coast, causing loss of lives, extensive damage, transforming hundred of thousands of residents in evacuees. We hypothesized that following such a disaster more patients will complaining of increasing difficulty initiating and/or maintaining sleep, immediately after the disaster.
Methods: A retrospective review of the main patient complaint, as provided to the author during an initial sleep medicine evaluation was conducted. Four groups were generated: group A January 1, 2005 to August 28, 2005; group B: January 1, 2006 to August 31, 2006; Group C: May 1, 2005 to August 28, 2005; group D:. September 5, 2005 – December 31, 2005 The main complaints were divided across four categories: 1: OSA related complaints such as snoring, breathing pauses during sleep, or CPAP loss; 2: insomnia related complaints such as difficulty achieving and maintaining sleep; 3: complaints of excessive waketime sleepiness; 4: complaints suggesting movement disorders or parasomnias.
Results: Table 1 shows the demographic data. An overall decrease in the number of patients presenting to the sleep center has been noted. Among the presenting patients, a reversal of the gender distribution occurred after the storm. Before the storm males accounted for 47% (group A) and 44% (group C) and after the storm males accounted for 62% (group B) and 55% (group D) of the patients presenting to the sleep medicine specialist.
Table 2 shows the distribution of the primary complaint among the groups. Complaints related to the ability to initiate and maintain sleep showed a slight tendency for increase after the storm, while complaints of excessive daytime sleepiness and fatigue decreased.
Conclusion: Our data shows an increase in the number of male patients and insomnia complaints after Katrina, despite an overall decrease in initial sleep medicine evaluations. This increase might be a result of existential concerns raised by the evacuee situation. The task of debris cleaning in a polluted environment might have contributed to the increase in male patients. This review included only a small number of patients. A broader review including all of the sleep centers in the affected and the surrounding areas is needed to provide clearer information about changes in sleep complaints after a natural disaster.
Support (optional): None

1046

CPAP COMPLIANCE: DEVELOPING A MODEL FOR CARE IN AN AASM ACCREDITED SLEEP CENTER

Matadeen-Ali C,[1] Patel P,[2] Weiss M,[3] Davidson C,[3] Havaligi N,[4] Ramachandran S[2]
(1) Sleep Wellness Center of Pottstown, Pottstown, PA, Pottstown, PA, USA, (2) Sleep wellness Center of Pottstown, Pottstown, PA, USA, (3) Sleep Wellness Center of Pottstown, PA, USA, (4) Drexel University, Philadelphia, PA, USA

Introduction: Nasal CPAP is effective in treating OSAS, however resistance and intolerance to CPAP poses limitations to its use. Although education has been shown to affect CPAP usage, a structured approach to the management of OSAS in a community setting to affect CPAP compliance has not been previously reported. The aim of the study was to determine the impact of a goal driven protocol on CPAP compliance in a recently accredited AASM center.
Methods: 64 consecutive patients with OSAS were studied. All subjects were initially evaluated by a board certified sleep specialist and subsequently followed by a certified respiratory therapist. Subjects were educated about OSAS and received printed AASM brochures on sleep apnea. The educational program was reinforced by technologists prior to their sleep studies. CPAP desensitization and mask fittings were conducted if indicated. This was followed by a specialized CPAP clinic where patients watched a video, were fitted with masks and received their CPAP with downloadable compliance cards. All patients had open access to the center and were seen on follow up at 1 month and compliance data collected.

Results: 51 patients (80%) used CPAP for > 4 hrs/night. Subjects were 38 males, 13 females, mean age 56.9± 10.55 years, BMI 36.8± 9.1, ESS 12± 5 and AHI 30± 25. 13 (20%) patients used CPAP for < 4hrs/night. Subjects were 8 males, 5 females, mean age 55± 19.93 years, BMI 32.8± 6.6, ESS 11± 5 and AHI 21± 17. Subjects in both groups were similar for age, BMI, ESS and AHI (p>0.05).
Conclusion: Patient demographics, severity of disease or extent of daytime sleepiness does not influence compliance. Access to specialized services with a structured management protocol for OSAS and close follow up in an AASM accredited center improves CPAP compliance and is a model for development in sleep centers.

1047

MARKOV STATE TRANSITION MODELS FOR THE PREDICTION OF CHANGES IN SLEEP STRUCTURE INDUCED BY AIRCRAFT NOISE

Basner M,[1] Siebert U[2]
(1) German Aerospace Center (DLR), Cologne, Germany, (2) Department of Public Health, Medical Decision Making and Health Technology Assessment, UMIT, Hall i. Tirol, Austria

Introduction: This investigation quantitatively assessed the effects of the introduction of a noise-free period at Frankfurt Airport between 11 pm and 5 am on sleep structure.
Methods: A six state (Wake, S1, S2, S3, S4 and REM) Markov state transition sleep model was built. Transition probabilities between states were calculated for both noise-free and noise conditions with autoregressive multinomial logistic regression based on polysomnographic laboratory studies, where 125 healthy subjects were investigated for 13 consecutive nights. First-order Monte Carlo simulation trials were performed for modelling a noise-free night and three noise scenarios: (1) traffic at Frankfurt Airport on 16 August 2005, (2) as (1), but flights between 11 pm and 5 am cancelled and (3) as (2), with flights between 11 pm and 5 am from (1) rescheduled to periods before 11 pm and after 5 am.
Results: The results of the models indicate that there will be a small benefit for airport residents compared to the current situation without a ban of air traffic in terms of sleep structure even if all traffic is rescheduled to periods before 11 pm and after 5 am (average time spent awake -3.2%, S1 -4.6%, S2 -0.9%, S3 +3%, S4 +9.2%, REM +0.6%, number of sleep stage changes -2.5%). This benefit is likely to be outweighed by the increase in air traffic during shoulder hours, especially for those who choose to or have to go to bed before 10:30 pm or after 1 am.
Conclusion: Alternative strategies might be necessary to both guarantee undisturbed sleep of airport residents and to minimize economic and legal disadvantages accompanied by a ban of air traffic between 11 pm and 5 am. The models developed in this investigation may serve as a valuable tool for optimizing air traffic patterns at airports, and therefore guide political decision making.
Support (optional): This work was partially financed by the HGF-Virtual Institute "Transportation Noise Effects on Sleep and Performance" (grant #VH-VI-111). The data used for the analysis were financed within the DLR/HGF-project "Quiet Air Traffic".

1048

INADEQUACY OF DME SUPPLIER PATIENT EDUCATION AND TRAINING IN PAP THERAPY FOR SLEEP APNEA.

Hazel K,[1] Taskar V,[1] Glasscock D,[2] Stocks J[1]
(1) University of Texas Health Center at Tyler, Tyler, TX, USA, (2) University of Texas Health Center at Tyler, TX, USA

Introduction: Compliance with PAP in OSA is well known to depend upon patient education as well as comfort and effectiveness. Because of the lack of re-imbursement the responsibility for education is often diverted to DME suppliers.
Methods: To measure the clinical efficacy of this behavior and to address expected inadequacies a PAP clinic was established and patients surveyed. This activity was conducted without charge. Patients from the Center for Sleep Disorders were referred as a) newly diagnosed with sleep apnea and b) patients with admitted PAP non-compliance and/or intolerance. Disease severity and risk was reviewed with the patient. Patients were shown and fitted for various PAP masks. Patients were given the opportunity to choose among various PAP mask styles. Specific comfort complaints and patient concerns were addressed in the PAP clinic and when necessary individual DME suppliers were contacted. A survey of specific problems was conducted.
Results: 127 patients were evaluated and 92 surveys completed. 32 visits were for initial set up (mask fit and education). 27 visits were for mask intolerance. Additional complaints included: pressure intolerance, sinus/ear difficulties, intolerance to bilevel PAP therapy. We identified 20 different DME companies. 22% of the surveyed patients reported never having been told about equipment maintenance. 12 were no longer using PAP therapy. 8 were never offered different masks, 11 were not given a choice of machines. Only 3 were using the same mask they had used during their sleep study. Lack of humidification was not a cause for non-compliance. Patient dissatisfaction was associated with a perception of inadequate follow up.
Conclusion: Patient education and training for PAP therapy in sleep apnea must remain the responsibility of the prescribing medical care provider not the DME equipment supplier. Reimbursement for such clinical activity is warranted given that clinical efficacy is dependent upon compliance.

1049

SLEEP HABITS IN MEDICAL PROFESSIONALS

Hurlburt K,[1] Simon R,[2] Blackwelder T[3]
(1) St. Mary Medical Center, Walla Walla, WA, USA, (2) Walla Walla, WA, USA, (3) Worldclass CME, Walla Walla, WA, USA

Introduction: Participants at a yearly CME program on Sleep have been given surveys about their sleep habits the last 3 years. Data from those surveys is presented here.
Methods: An anonymous survey has been administered to 4 consecutive groups of physicians, nurses, and allied health professionals at a national CME program. The survey consists of 24 questions and an Epworth Sleepiness Scale.
Results: Results between the 4 data sets shows no clinical difference in sleep habits between the groups. There is no clinical difference in average hours of sleep between medical professionals and the general public. There were no differences between men and women in average hours of sleep (men = 6.7 hours, women =6.8 hours). There was no clinical difference in hours of sleep based on occupation - Specialist MD (Sleep) 6.84 hours, Primary Care MD 6.65 hours, Sleep Technologist 6.64 hours, Registered Nurse 6.94, Other (Psychologist, Dentist, etc.) 6.69 hours. There is a trend for higher BMI´s having lower hours of sleep per night.

The average Epworth Sleepiness Scale score was 6.55 (S.D. = 4.1009). This compares to Johns original normal controls with an average of 5.9 (S.D. = 2.2). There was a slight negative correlation between Epworth and average hours of sleep, but this was not statistically significant.

Only 16% of the respondents reported that their personal physician asked them anything about their sleep, and only 12% were specifically asked about snoring. When asked if they had driven while drowsy in the past year, 69% answered yes, and when asked if they had actually fallen asleep while driving in the past year, 27% answered yes.
Conclusion: The sleep habits of medical professionals, including sleep professionals, are no better than those of the general population.

1050

A CONCEPTUAL MODEL OF SLEEP QUALITY IN OLDER ADULTS LIVING IN THE COMMUNITY

Liao W,[1] Tzeng Y,[2] Hsu H,[3] Tzeng Y,[4] Lai T,[2] Hwang S[5]
(1) Chun Shan Medical University, Taichung, Taiwan, (2) Chun Shan Medical University, Taiwan, (3) Chang Gung Institute of Technology, Taiwan, Taiwan, (4) National Taichung Institute of Technology, Taiwan, (5) Chang Gung Institute of Technology, Taiwan

Introduction: Poor sleep is a common complaint among elders and often has impact on an individual´s quality of life.
Methods: To investigate how personal, physical, psycho-social and environmental dimensions are related to the overall sleep quality, a cross-sectional design with face-to-face interview was conducted in community dwelling elders (N=259, mean ages 76.0±6.4 years) by using the Pittsburgh Sleep Quality Index (PSQI), the Hospital Anxiety and Depression Scale (HADS), the Ford Insomnia Stress Response Test (FIRST), and the Barthal Activity of Daily Living (ADL) Index. A conceptual framework and bivariate correlations guided a series of multiple regressions to identify the best predictors for sleep quality.
Results: Most of subjects were male (59.5%), lived with spouse and offspring (68.0%), had at least one kind of chronic disease but in stable condition (92.3%), and can perform ADL independently (88.4%). The leading exercise and leisure activities were walking (60.2%) and watching TV (52.5%), respectively. However, only 32.0% of them had regular exercise. Mean global PSQI score was 7.5±4.2, and 60.6% of subjects were identified as poor sleepers (PSQI>5). Variation of perceived sleep quality among individuals was high. Anxiety (beta=.377), depression (beta=.252) (psychological dimension), disease numbers (beta=.166) (physical dimension), noise (environmental dimension), napping (beta=.114), leisure activities (beta=-.123), exercise (.094) (social dimension), and ADL (beta=.095) (personal dimension) were the best predictors for sleep quality, which were accounted for 47.2% of variance of sleep quality in older adults living in the community.
Conclusion: This conceptual model of sleep quality provides a comprehensive framwork for managing sleep in community dwelling elders. Health providers can enhance sleep quality for the elderly by facilitating their ADL status, social activities, mental well-beings, and sleep environment.
Support (optional): N/A

1051

CONTINUOUS POSITIVE AIRWAY PRESSURE TREATMENT FOR OBSTRUCTIVE SLEEP APNEA IS NOT AN EFFECTIVE OPTION IN PUBLIC HEALTH CARE IN BRAZIL

Varela M,[1] Varela M,[2] Potasz C,[3] Junqueira O,[4] Oliveira M,[4] Carvalho L,[4] Carvalho J,[2] Prado L,[4] Prado G[5]
(1) University of Sao Paulo (UNIFESP), São Paulo, Brazil, (2) Federal University of Sao Paulo (UNIFESP), São Paulo, Brazil, (3) Universidade Federal de São Paulo, São Paulo, Brazil, (4) Federal University of Sao Paulo, São Paulo, Brazil, (5) Federal University of São Paulo, São paulo, Brazil

Introduction: Obstructive Sleep Apnea Syndrome (OSA) is a disorder characterized by repeated cessations of breathing during sleep, which can result in serious consequences affecting cardiovascular, physiological, neurocognitive, emotional, and psychosocial functioning. Continuous Positive Airway Pressure (CPAP) is the treatment of choice for OSA. In Brazilian Health Care Public System only recently CPAP has been used as an OSA treatment. The present study aims to characterize OSA patients, to verify adherence to treatment, how long they are using CPAP, and the conditions for treatment effectiveness.
Methods: Retrospective Study. We randomly selected 105 patients with confirmed OSA diagnosis from the Outpatient Clinic Neuro-Sono (UNIFESP), a public health care unit, and analyzed their medical file.
Results: 105 patients (ranging 18-86 years old) received a diagnosis of OSA based on PSG. Among these patients, 26 patients were diagnosed with mild OSA, 24 with moderate and 50 with severe. 49 patients received prescription to use CPAP; however, only 5 patients were using it for at least 3 months. Preliminary results shows that among the main reasons for non effectiveness of CPAP treatment are the prevalence of low-income family patients and a series of psychosocial features supporting no adherence.
Conclusion: Given the importance of CPAP treatment for OSA patients, the results of the current study suggested the importance of investigating social and private reasons to non effectiveness of CPAP treatment in Brazilian Health Care Public System.

1052

SLEEP PATTERNS IN INNER CITY CHILDBEARING WOMEN

Caldwell B
University of Medicine and Dentistry of New Jersey, Newark, NJ, USA

Introduction: Sleep disturbance is common among women of childbearing; however, little is known about the characteristics of sleep patterns of childbearing women living in inner cities.
The purpose of this study was to examine the relationship between sleep patterns and stress, mood disturbance and traumatic symptoms in inner city childbearing women.
Methods: The design was exploratory observational. One hundred twenty-nine inner city non-preganant women of childbearing age were recruited from an urban medical center. Participants wore wrist actigraphs and completed sleep logs for three day period. They completed the Pittsburgh Sleep Quality Index, Beck Depression Inventory, Beck Anxiety Inventory, Posttraumatic Stress Scale and Life Events Scale.
Results: Self-reported sleep was moderately associated with psychological symptoms, including anxiety, depression and psychological trauma symptoms. Negative life events were highly correlated with the psychological variables. Sleep disturbance explained 14.4% of the variance in PTSD symptom severity score, 15.6% in depression and 21.5% in anxiety. The mean PSQI score of 6.81 suggests on average, that the participants are reporting less than adequate sleep

quality.Objective and subjective sleep efficiencies were 84.8% and 82.7% respectively, compared to the 96% normative value for 20 to 50 year olds found in the literature.
Conclusion: To our knowledge, this is the first study to examine objective and subjective sleep patterns of inner city minority childbearing women and the relationship to psychological symptoms. The findings provide direction when constructing intervention studies for vulnerable groups of childbearing women. Because of the co-occurring psychological symptoms, clinical intervention studies will need to measure and evaluate the outcomes of the both the sleep and a cluster of psychological variables.
Support (optional): The study was funded by the University of Medicine & Dentistry of New Jersey School of Nursing and the Foundation of UMDNJ.

1053

DIFFERENCES IN PATIENT REFERRAL PATTERNS FOR SUSPECTED SLEEP APNEA BETWEEN SLEEP SPECIALISTS AND NON-SLEEP SPECIALISTS

Paruthi S, O'Brien L, Wiebelhaus J, Consens F
University of Michigan, Ann Arbor, MI, USA

Introduction: Non-sleep specialists may have difficulty recognizing and referring appropriate patients with sleep complaints for evaluation with overnight polysomnograms (PSG). The University of Michigan maintains an open access sleep center where non-specialists can directly refer patients with a clinical suspicion of sleep-disordered breathing. We sought to determine the characteristics of patients referred by non-sleep specialists and sleep specialists.
Methods: A retrospective database review of diagnostic polysomnograms performed at the University of Michigan Sleep Disorders Center on patients ≥18 years of age between April and December 2006.
Results: A total of 1235 PSGs were included in the analysis, with non-sleep specialists referring 741 (60%) of patients. Unsurprisingly, the vast majority of polysomnograms ordered by both groups of physicians were full-night diagnostic evaluations (89% for sleep specialists and 76% for non-sleep specialists). Non-sleep specialists were more likely to request a split-night protocol than sleep specialists (24% vs. 8.5% respectively; $p<0.0001$). Patients referred by non-sleep specialists had a significantly higher body mass index and were older than those referred by sleep center physicians (33.6±7.8 vs. 32.5±8.0kg/m2; $p=0.025$ and 49.1± 13.7years vs. 47.4± 14.3 years; $p=0.036$). A similar proportion of males were referred by physicians in each group (52% vs. 54% for non-sleep and sleep specialists respectively). Patients referred by both physician groups were equally likely to have a final diagnosis consistent with obstructive sleep apnea (80% of those referred by a non-sleep specialist compared to 77% referred by a sleep specialist).
Conclusion: Despite our findings suggesting that physicians without specialist training in sleep medicine are more likely to refer older and heavier patients for evaluation, the frequency of a positive polysomnogram was similar between physician groups.

1054

LATERAL VENTRICULAR PERFUSION OF SALUBRINAL, WHICH ARRESTS PROTEIN TRANSLATION, PROMOTES SWS IN RATS

Methippara M,[1] Kumar S,[2] Noor Alam M,[3] Szymusiak R,[4] McGinty D[4]
(1) Veterans Administration of Greater Los Angeles HealthCare System, North Hills, CA, USA, (2) Patna University, India, (3) Veterans Administration of Greater Los Angeles HealthCare System, CA, USA, (4) University of California, Los Angeles, CA, USA

Introduction: Sleep is associated with increased brain protein synthesis. Sleep deprivation increases neocortical expression of PERK, an enzyme inducing arrest of protein translation. We have shown that hypothalamic administration of a protein synthesis inhibitor increases sleep. We hypothesized that brain protein synthesis is an endpoint of sleep, and that molecules signaling interruption of protein synthesis will facilitate sleep-promoting mechanisms. Arrest of protein translation is brought about particularly through phosphorylation of a key translational control protein, eIF2α. We hypothesized that p- eIF2α, or a downstream signal of arrest of protein synthesis would directly facilitate sleep. Salubrinal (SAL) increases p- eIF2α by preventing its dephosphorylation. Thus, we predicted that SAL administration would increase sleep.
Methods: Seven male Sprague-Dawley rats were implanted with EEG and EMG electrodes and guide cannula directed at the lateral ventricle. A week after surgery, microinjection cannulae were inserted and sleep recordings started 18 hrs later. In random order, 100 μM of SAL or artificial CSF were perfused (0.2 μL/min) for 12 hrs followed by 12 hrs of ACSF perfusion, beginning at ZT 12. Significance of treatment effects was analyzed with paired t test.
Results: In the first 3 hrs of perfusion, 100 μM of SAL significantly ($p < 0.05$) reduced active wake (SAL: 37.3 ± 7.9 vs ACSF: 60.7 ± 5.9) and increased SWS 2 (SAL: 34.9 ± 4.1 vs ACSF: 14.6 ± 3.2) without affecting other stages. There were significant ($p < 0.05$) increases in the number of episodes of SWS2 (SAL: 51.0 ±10.9 vs ACSF: 25.3± 3.0) and REM (SAL: 10.4 ± 2.5 vs ACSF: 5.7±1.2). Episode durations were not changed.
Conclusion: The findings are consistent with the previous reports of sleep promotion by protein synthesis inhibitors, supporting a hypothesis that signals associated with protein synthesis arrest facilitate sleep.
Support (optional): This work was supported by the grants: MH 47480, NS 050939

1055

MUTAGENESIS SCREEN TO DISCOVER MICE WITH HIGH REM SLEEP TIME

Williams D,[1] Dugovic C,[2] Laposky A,[3] Losee-Olson S,[1] Owens-Ream J,[1] Turek F[1]
(1) Northwestern University, Evanston, IL, USA, (2) Johnson & Johnson PRD LLC, San Diego, CA, USA, (3) Evanston, IL, USA

Introduction: The major regulatory genes involved in sleep regulation have not been identified. We have conducted a forward genetics approach (ENU mutagenesis) in mice (C57BL/6J) to screen for unique sleep-wake phenotypes. Here we report on one line that demonstrated high active sleep (AS) as neonates and high REM sleep as adults.
Methods: The initial screen for sleep phenotypes was conducted by measuring EMG activity in 9-10 day old neonatal mice. One line was selected from a founder animal (1G3158) with a high percentage of AS (79%) compared to the distribution of pup-tested mice (N=4824, mean±SD; 55±13%). After the fourth generation of this line, we began to screen sleep in adult (3-4 months of age) mice. Male mice were implanted with EEG/EMG electrodes followed by 48-hours of baseline recording under a LD 14:10 cycle.
Results: Out of 311 G5-G7 adult mice tested, 76 were selected for high REM sleep time (>70 minutes per 24-hour period). The selected mutants had an average of 77±7 minutes of REM sleep compared to 60±7 minutes in wild-type littermates (N=235). The increase in REM sleep was due to an increased number of REM sleep bouts (mutants, 65±9 vs. littermates, 49±8, $p<.001$). There was no difference in average REM bout duration between groups. Interestingly, absolute EEG theta (6-10 Hz) power during REM was significantly reduced in mutant mice (mutants, 114±86 vs. littermates, 162±109 uV2/Hz, $p<.001$). It is important to note that REM sleep amount in the mutagenized population (N=311, 64±10 minutes) was significantly greater compared to a distribution of separate C57BL/6J wild-type animals (N=48, 57±10 minutes) ($p<.001$).
Conclusion: This semi-dominant or dominant mutation leads to an increase in AS in neonates and to an increase in REM sleep in adult male mice. This mutant line of animals can now be used to identify the mutant gene responsible for increased REM sleep.
Support (optional): This research was supported by a grant from the Defense Advanced Research Projects Agency (DARPA) and the Army Research Office (ARO), award number DAAD19-02-1-0038.

1056

CORTICAL GENE EXPRESSION DURING SLEEP, WAKEFULNESS, AND SLEEP DEPRIVATION: A PROTEOMIC APPROACH

Cirelli C,[1] Luebke A,[2] Tononi G[3]
(1) Madison, WI, USA, (2) University of Wisconsin/Madison, WI, USA, (3) University of Wisconsin/Madison, Madison, WI, USA

Introduction: Hundreds of mRNAs are changing in the brain between sleep and wakefulness, and after sleep deprivation. Since proteins carry out most of the cellular functions, however, the direct measurement of protein levels is a better determinant of the overall functional state of the sleeping and awake brain. Proteomic profiling using surface-enhanced laser desorption/ionization time-of-flight mass spectrometry (SELDI-TOF-MS) is an emerging technique to identify new biomarkers in biological tissues. Here we used Proteinchip arrays and SELDI-TOF-MS to determine changes in protein expression in the cerebral cortex of sleeping, spontaneously awake, and sleep deprived rats.
Methods: Rats (male WHY, 12-14 week old) were sacrificed after 6h of sleep (S, n=18), 6h of spontaneous wakefulness (W, n=14), 6h of sleep deprivation (short-SD, n=18), 7d of sleep deprivation by the disk-over-water method (long-SD, n=22), 7d of sleep restriction (yoked controls of long-SD rats, n=22). Proteomic spectra of cortical samples were generated by Proteinchip arrays (CM10, Q10, IMAC30, and H50, Ciphergen) and SELDI-TOF-MS.
Results: Overall, using 4 different types of Proteinchip arrays, 1055 protein peaks were consistently detected in cortical samples. Fifty-eight protein peaks (2.6-31.6 kDa) were identified as differentially expressed between S, W, and short-SD rats (Mann Whitney U test, $p<0.05$), of which 48 were "sleep" peaks (S>W and S>SD) and 10 were "waking"peaks (S. Thirty-one protein peaks (2-20.6 kDa) were identified as specifically expressed in long-SD rats (Mann Whitney U test, $p<0.05$), of which 23 were upregulated (long-SD>W and long-SD>short-SD) and 8 downregulated. Preliminary clustering analysis showed that long-SD clustered away from both SD and W (% of correct separation, long-SD vs SD, long-SD = 93%, SD = :75%; long-SD vs W, long-SD = 93%, W = :92%). Peak identification is in progress.
Conclusion: Protein peaks identified through proteomic analysis of cortical samples may identify biomarkers of sleep and sleep deprivation.
Support (optional): Supported by DoD SBIR 48019-LS-SB1.

1057

INCREASE OF CYTOKINE-IMMUNOREACTIVE CELLS IN THE OLFACTORY BULB OF MICE AFTER INTRANASAL INOCULATION WITH INFLUENZA A VIRUS

Leyva-Grado V,[1] Wu M,[1] Churchill L,[1] Majde J,[1] Krueger J[2]
(1) Washington State University, Pullman, WA, USA, (2) Pullman, WA, USA

Introduction: Tumor necrosis factor alpha (TNFá), interleukin 1 beta (IL1â) and type I interferon (IFN) are cytokines produced in response to an influenza infection and are sleep regulatory substances. We previously demonstrated that within 15 h after intranasal inoculation with influenza, viral RNA (negative and positive strands) and cytokine mRNA levels increase in the olfactory bulb (OB). In this study we evaluate whether viral and cytokine immunoreactivity (IR) increases in the OB and which cell types are involved.
Methods: Mature C57BL/6 male mice received an intranasal (IN) inoculation with the H1N1 PR8 strain of influenza, either live (n=6) or boiled virus (n=6). Mice were anesthetized and perfused with 4% paraformaldehyde at 15 h post-inoculation to collect the brains. Brains were post-fixed and frozen prior to microtome sectioning. Immunohistochemistry for viral antigens, TNFá, IL-1â and the interferon-induced enzyme, 2´, 5´-oligoadenylate synthetase (OAS), was performed in OB sections using DAB as a chromophore. Additionally, double labeling for the viral antigens and cytokines was performed using specific cell markers for neuronal nuclear protein (NeuN), microglia-like cells (F4/80) and astrocytes [glial fibrillary acidic protein (GFAP)].
Results: The number of morphologically glia-like IL1â- and OAS-IR cells increased in the OB glomerular layer of mice inoculated with live virus in comparison with boiled virus controls. In the adjacent external plexiform layer, increases were observed in the number of neuron-like IL1â- and TNFá-IR cells as well as the number of glia-like OAS-IR cells. Using double labeling, the viral antigen co-localized to cells expressing F4/80 and GFAP. IL1â was observed in cells that expressed NeuN, and also in cells that expressed GFAP. TNFá co-localized to cells expressing NeuN.
Conclusion: Virus and somnogenic cytokines are rapidly expressed in the OB after intranasal influenza infection and may be important in influenza virus-induced increases in NREM sleep.
Support (optional): NIH HD36520 to Krueger JM and National Autonomous University of Mexico.

1058

SLEEP LOSS AFFECTS MICRORNA EXPRESSION IN THE RAT HYPOTHALAMUS

Davis C,[1] Bohnet S,[1] Krueger J[2]
(1) Washington State University, Pullman, WA, USA, (2) Pullman, WA, USA

Introduction: MicroRNAs (miRNAs) are regulators of mRNA translation. They are small (~22 nucleotide) strands with the capacity to hybridize with mRNA leading to degradation of mRNA or inhibition of mRNA translation by several different mechanisms. There is much evidence indicating that protein and gene expression changes across the sleep/wake cycle. Given that the hypothalamus is involved in sleep regulation, we hypothesized that sleep loss would affect miRNA levels in the hypothalamus.
Methods: Male Sprague-Dawley rats 275-325 g were sleep deprived for 8 hrs using gentle handling. Immediately following sleep deprivation, rats were decapitated; the hypothalamus was extracted and flash-frozen in liquid nitrogen. Control rats were sacrificed at the same time, but were not deprived of sleep. RNA isolation, fractionation, labeling and array hybridization was executed in accordance with the manufacturer´s protocol for mirVana Bioarrays (Ambion).
Results: miR-146a, miR-181a, miR-429 and several members of the miR-34 family exhibited increases compared with levels found in hypothalami from controls.
Conclusion: These findings suggest that miRNAs may be one mechanism underlying state-dependent gene changes in the brain. For instance, sequence alignment analyses predict that miR-34 sub-types target the interleukin-1 receptor antagonist. Interleukin-1 beta is a sleep regulatory substance that increases with sleep deprivation. Current results also add to our previous findings that sleep loss changes miRNA expression in the hippocampus and suppresses many miRNAs in the frontal cortex (Davis *et al.*, 2006, Society for Neurosci. Mtg, program # 14.13).
Support (optional): This research was supported by grants NS25378 and NS31453 from NINDS.

1059

LET-7 MICRORNA EXPRESSION IN BRAIN TISSUES FROM SLEEP DEPRIVED RATS VERIFIED BY STRAND-ELONGATION PCR

Meyerson J,[1] Davis C,[1] Bohnet S,[1] Krueger J[2]
(1) Washington State University, Pullman, WA, USA, (2) Pullman, WA, USA

Introduction: MicroRNAs are small 19-21 nucleotide RNA molecules that have an essential role in regulating mRNA degradation and protein translation. MicroRNA/mRNA complexes are found at the synapse and many are activity-dependent. This led us to hypothesize that miRNAs play a role in sleep-related neural plasticity.
Methods: Based on previous microarray results (Davis *et al.*, 2006, Society for Neurosci. Mtg, program # 14.13), we determined the levels of Let-7 microRNAs in two groups of male Sprague-Dawley rats; cage controls and rats sleep deprived for 8 hours by gentle brushstrokes. Rats were euthanized and the hippocampus and prefrontal cortex were extracted and flash-frozen in liquid nitrogen. We subsequently isolated microRNA and performed strand-elongation PCR to measure levels of Let-7 subtypes.
Results: Let-7 subtypes manifest tissue-specific bidirectional expression dynamics relative to 5S ribosomal RNA levels. Specifically, Let-7B and Let-7D microRNAs were increased in the hippocampus after 8 hours of sleep deprivation, while Let-7C in the prefrontal cortex decreased after sleep loss.
Conclusion: These data suggest that regulation of individual Let-7 miRNAs are tissue specific and are responsive to changes in sleep. Bioinformatic analyses predict that Let-7 miRNAs regulate the translation of Sleep Regulatory Substances such as: Tumor Necrosis Factor, Interleukin, and NFKappaB, because their sequences are complementary to the UTRs of at least one of the Let-7 subtypes. Target mRNA for Let-7 miRNAs may also have a role in plasticity of cells affecting regulators of axonal guidance and spine growth.
Support (optional): This work was supported be NIH grants NS25378 and NS31453

1060

INCREASED SLEEP IN A DROSOPHILA MODEL OF FRAGILE X SYNDROME

Bushey D,[1] Huber R,[1] Tononi G,[2] Cirelli C[1]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) University of Wisconsin, Madison, WI, USA

Introduction: Inheriting a mutation in the Fragile X (FraX) mental retardation (*FMR1*) gene is the most common cause of mental retardation in human populations. FraX patients show abnormal dendritic spine morphology, with more long and thin spines. *FMR1* knockout mice show mild learning deficits, hyperactivity, and dendritic abnormalities. They also show defects in synaptic plasticity, with normal or reduced long-term potentiation and enhanced long-term depression, the latter due to increased activity of group I metabotropic glutamate receptors (mGluR). A *Drosophila* model for FraX was recently established, based on loss-of-function mutations of *dfmr1*, the single homolog of *FMR1*. *dfmr1* mutant flies also show abnormal synaptic branching and memory deficits, and the latter can be rescued pharmacologically by mGluR antagonists. *dfmr1* mutant flies show abnormal circadian rhythms, but their sleep/waking pattern has never been analyzed. Here, we studied sleep duration and intensity and the response to sleep deprivation in *dfmr1* mutant flies and their wild-type siblings.
Methods: Four *dfmr1* alleles were tested: *dfmr1*$^{+}$ (wild-type), *EP3517*, Δ*50M*, and Δ*113M*. *EP3517* is a hypomorphic mutation, while Δ*50M* and Δ*113M* are deletions that extend into *dfmr1* and result in a complete loss of gene function (amorph). The results between amorph alleles did not differ in sleep amount and were therefore combined. Locomotor activity, sleep, and sleep intensity were measured as previously described.
Results: The sleep phenotype did not differ between homozygous *EP3517* flies and their wild-type siblings. Homozygous Δ*50M* (n=11) or Δ*113M* (n=7) flies slept significantly longer (1052±52 min of sleep/24-h) than siblings that had these alleles in combination with *EP3517* (heterozygous) or were homozygous for *EP3517* (n=128, 889±15, $p<0.0001$). The number of brief awakenings (BA) was lower in mutant flies than in controls (N. of BA/h of sleep, amorph, 0.096±0.02; control, 0.16±0.02, $p<0.05$). On average, the mutants had less sleep episodes (21 bout/24-h) compared to controls (29 bout/24-h $p<0.05$) while the mean sleep duration of each episode increased (min, mutant 47; control 34; $p<0.05$). The amount of waking locomotor activity was increased in Δ*50M* and Δ*113M* homozygotes compared to *EP3517* siblings (activity counts/min, amorph, 1.7±0.2; control, 1.4±0.05; $p<0.005$).
Conclusion: A complete loss of *dfmr1* function increases the total daily sleep amount, and consolidates sleep, as indicated by the decrease in BA and the increase in the duration of sleep episodes.
Support (optional): Supported by NIGMS (R01 GM075315).

1061

USING SMALL INTERFERING RNA TO KNOCKDOWN DIFFERENT SLEEP RELATED GENES IN RATS

Chen L,[1] Basheer R,[2] Bolortuya Y,[1] Thakkar M,[3] McCarley R[1]
(1) Harvard Medical School & VA Boston Healthcare System, Brockton, MA, USA, (2) Harvard Medical School & VA Boston Healthcare System, West Roxbury, MA, USA, (3) University of Missouri-Columbia, Columbia, MO, USA

Introduction: Recently we reported reversible siRNA knockdown of prepro-orexin in the perifornical hypothalamus (PFH; Chen, EJN, 2006). To further investigate the broad applicability of this technique, we used siRNA targeted against orexin type I receptor (Ox1R) in the locus coeruleus (LC), orexin type II receptor (Ox2R) in the PFH, glutamic acid decarboxylase 67 (GAD67) and vesicular GABA transporter (vGAT) in the basal forebrain (BF).
Methods: A cocktail of siRNAs targeting Ox1R or Ox2R or their scrambled controls were microinjected bilaterally into LC and PFH respectively. For rats treated with GAD67 or vGAT, siRNAs were unilaterally injected into BF with controls on the contralateral side. Simultaneous analysis of the mRNA levels of the target gene and a colocalized non-targeted gene (tyrosine hydroxylase with Ox1R, GAD65 with GAD67, GAD67 with vGAT) using real-time PCR was done to confirm specificity of the siRNA knockdown. Sleep recordings were also performed.
Results: Ox1R siNRAs induced 26.2% knockdown without non-specifically affecting tyrosine hydroxylase (N=11, $P<0.05$). Furthermore, two injections of Ox1R siRNA on successive days induced a persistent increase in REM sleep in the dark period for 2 days (N=3). The same administration regimen of Ox2R siRNAs moderately increased knockdown when compared with single injection effects (73.9% vs. 64.7%, N=4, behavioral analysis pending). siRNAs against GAD67 in BF (N=6) led to decreased expression of GAD67 and GAD65 as well as the PCR normalizers indicating general transcription suppression. vGAT siRNA induced 29.6% KD of vGAT mRNA (N=6) but did not suppress GAD67. Analysis of sleep effects is ongoing.
Conclusion: Microinjection of siRNAs is a simple and specific approach to induce targeted gene knockdown. Multiple factors, such as the number of injections, or the target gene selection, may affect the degree or specificity of the knockdown. It is possible to observe behavioral effects even after a modest knockdown.
Support (optional): NIMH grants 062522, 01798 and Dept. Vet. Aff.

1062

FREQUENCY ANALYSIS OF THE POLYMORPHISM G619A OF THE AA-NAT GENE IN A SAMPLE OF THE BRAZILIAN POPULATION AND ITS RELATIONSHIP WITH CIRCADIAN PHENOTYPES

Pereira D,[1] Pedrazzoli M,[1] Koike B,[1] Louzada F,[2] Benedito-Silva A,[3] Remesar-Lopez A,[3] Tufik S[1]
(1) Universidade Federal de São Paulo, São Paulo, Brazil, (2) Universidade Federal do Paraná, Paraná, (3) Universidade Federal de Sao Paulo, São Paulo, Brazil

Introduction: Genes involved in melatonin synthesis, such as Aa-nat, may be important for our understanding of diurnal preference and circadian rhythm disturbances in humans. In Japan, Hohjoh et al reported an association of the G619A polymorphism in the Aa-nat gene with Delayed Sleep Phase Syndrome (DSPS). The present study sought to analyze G619A polymorphism frequency in a Brazilian sample, including DSPS patients.
Methods: Based on the diurnal preference determination questionnaire Horne-Ostberg, 161 volunteers were grouped into morning, intermediate and evening preference category. A total of 373 volunteers did not answer the questionnaire but took part in the study as a sample of general population. Seventeen DSPS patients diagnosed in the Sleep Institute at Universidade Federal de São Paulo Brazil, using the international sleep disorder classification, participated in this study. The G619A polymorphism was genotyped by PCR-RFLP.
Results: The allelic frequencies in the sample were in Hardy-Weinberg equillibrium ($X^2 = 0.018$, df=2, $p > 0.05$). Only two heterozygous (G619A) individuals were found in this study, one of them with Japanese ancestry, thus showing that there is no allelic variation for G619A polymorphism in our sample of Brazilians.
Conclusion: It has been reported a higher frequency of 619A allele of

the Aa-nat gene in DSPS patients in a Japanese sample. We did not find this association in our study, nor did we find a variation of this polymorphism in the Brazilian population. A possible explanation for the differences in our results is the ethnic origin. Brazilians have mainly an European/Portuguese-Brazilian Native genetic background. Our sample contained a high proportion of Caucasians, whereas all subjects in the Hohjoh et al study were Japanese. It is now very important to analyze different background ethnicities to validate G619A polymorphism in different populations. Perhaps in seeking the effects of this Aa-nat G619A polymorphism in different populations, we may determine whether it affects the melatonin secretion timing curve and the circadian rhythm.
Support (optional): FAPESP (grant #98/14303-3) and AFIP

1063

ASSOCIATION OF SEROTONIN TRANSPORTER (5HTT) GENE POLYMORPHISM WITH AMOUNT OF SLOW-WAVE SLEEP IN HUMAN SUBJECTS

Linn S, McClure T, Monaghan K, Bluhm D, Watson K, Roth T, Richardson G
Henry Ford Hospital, Detroit, MI, USA

Introduction: Functional polymorphisms of the serotonin transporter gene have been linked to a number of behavioral traits and psychiatric diagnoses thought to be related to serotonin neurotransmission, although many of these results have not been consistent. More recently, polymorphisms of the 5HTT gene and its promoter have been implicated as risk factors in sudden infant death syndrome (SIDS). While sleep regulation is a common feature in all the presumptive associations, there are as yet no data on the relationship between genetic variation in the serotonin transporter and normal sleep in humans.
Methods: As part of a study of PSG and endocrine correlates of insomnia, 54 subjects (32f; age 19-50, mean 29.9y) screened for psychiatric and medical disease underwent genotyping for functional polymorphisms of the 5HTT promoter (5HTTPR). PSG data were collected on a standard schedule on two successive nights and scored by a single scorer blind to genotype. Only data from the second night were analyzed to avoid first-night effects.
Results: Overall genotype frequency was comparable to that reported for population-based samples (L/L 44%; L/S 46%; S/S 10%). Analysis of PSG results showed a significant effect of genotype on slow-wave sleep (SWS). The presence of the S allele (L/S + S/S) was associated with significantly more SWS (74.5 minutes vs 47.5 minutes, $F=8.95$, $p<.01$), and the effect of genotype remained when analysis controlled for age and sex ($F=11.9$, $p<.01$). Trends towards increased sleep efficiency and decreased Stage 1 and 2 NREM sleep were not statistically significant in the combined model.
Conclusion: Through decreased activity of the promoter, the 5HTTPR short allele results in increased serotonergic neurotransmission. The finding of increased SWS is consistent with results manipulating serotonin neurotransmission pharmacologically in humans. These results demonstrate that genetic factors that affect serotonergic neurotransmission have substantial effects on basal expression of sleep states.
Support (optional): Supported by MH63968 (GSR).

1064

AN IN-SILICO ANALYSIS OF GENES IN THE QTL FOR SLEEP HOMEOSTASIS IN MICE

Mackiewicz M, Pack A
University of Pennsylvania, Philadelphia, PA, USA

Introduction: Increases in EEG delta power that occur in recovery sleep following sleep deprivation are a measure of the homeostatic drive for sleep. Study of the increase in delta power following sleep deprivation in recombinant inbred strains of mice (C57/B6/JxDBA2/J) identified a region (Dps1) on chromosome 13 that contains genes that modified accumulation of delta power (1). We performed comprehensive annotations of genes in the Dps1 region, established their polymorphisms, and determined expression patterns in sleep and wakefulness. We identified potential candidate genes that may underlie the accumulation of delta power after sleep deprivation.
Methods: Using the Ensembl Genome Browser (release 39) we mapped the relevant markers to chromosome 13, and determined the number and location of genes in the Dps1 region. The number and distribution of SNPs in C57/B6/J and DBA2/J mice were also established using the SNP database (NCBI; version 36.1). We identified non-synonymous changes in coding and differences in promoter regions in both strains of mice for all genes within Dps1. The expression of these genes in sleep and wakefulness in the brain of C57/B6/J mice was established by microarrays. The "top candidate genes" to explain Dps1 QTL were selected based on the SNP and gene expression cirteria.
Results: There are 78 genes in the Dps1 region. Using an in-silico strategy we identified the Homer1 gene as a potential candidate. Homer 1 is up-regulated in the brain during prolonged wakefulness. A dominant negative form of Homer reduces the binding of mGLUR to signaling molecules reducing glutamate signaling. There are SNP differences between inbred mice in the promoter region of the Homer 1 gene.
Conclusion: These changes likely impact the binding of transcription factors and lead to differential expression of Homer 1 among mouse strains.
(1) Franken *et al.*, J. Neurosci 21:2610-2621, 2001
Support (optional): NHLBI grant HL60287

1065

MACROMOLECULE BIOSYNTHESIS - A KEY FUNCTION OF SLEEP

Mackiewicz M,[1] Shockley K,[2] Romer M,[1] Galante R,[1] Zimmerman J,[1] Naidoo N,[1] Churchill G,[2] Pack A[1]
(1) University of Pennsylvania, Philadelphia, PA, USA, (2) The Jackson Laboratory, Bar Harbor, MA, USA

Introduction: Microarray-based expression is widely used to quantify gene expression levels on a high-throughput basis. Genomic approaches have been successfully applied to studies of gene expression in the central nervous system during sleep and wakefulness; however, the temporal dimention to gene expression has not been thoroughly studied. We therefore sought to identify dynamic changes in gene expression associated with different durations of sleep and extended wakefulness. We proposed that determining genes which change expression during sleep can point to possible function(s) of sleep.
Methods: Experiments were performed on males mice (C57/BL6). Animals were subjected to 3, 6, 9 and 12 hrs of total sleep deprivation (n=5 in each time point). Sleeping mice were left undisturbed, and were sacrificed at the same diurnal time points as sleep deprived mice. Transcript levels in the cerebral cortex and hypothalamus were assayed by microarrays using the GeneChip Mouse Genome 430 2.0 array (Affymetrix).

Results: There were significant differences in gene expression between behavioral states; we identified 3988 genes in the cerebral cortex and 823 genes in the hypothalamus with altered expression patterns between behavioral states. Gene transcription is remarkably active during sleep, as 2090 genes in the cerebral cortex and 409 genes in the hypothalamus were defined as sleep-specific. The largest classes of over-represented genes increasing expression with sleep were those involved in biosynthesis and transport. In both the cerebral cortex and hypothalamus, there was up-regulation of multiple genes encoding enzymes involved in cholesterol synthesis and proteins of lipid transport. There was up-regulation during sleep of genes involved in synthesis of proteins, heme, maintenance of vesicle pools, as well as antioxidants and genes encoding proteins of energy-regulating pathways.
Conclusion: We postulate that during sleep there is a rebuilding of multiple key cellular components in preparation for subsequent wakefulness.
Support (optional): NIA grant AG17628 and NHLBI grant HL60287.

1066

GENOMIC APPROACHES TO IDENTIFY SLEEP GENES - QTL MAPPING OF MULTIPLE SLEEP-WAKE TRAITS

Zhou L,[1] Chung B,[1] Dugovic C,[2] Vitaterna M,[1] Laposky A,[1] Kasarskis A,[3] Schadt E,[3] Turek F[1]
(1) Northwestern University, Evanston, IL, USA, (2) Johnson & Johnson PRD LLC, San Diego, CA, USA, (3) Rosetta Inpharmatics LLC - Merck Research Laboratories, Seattle, WA, USA

Introduction: Although there is considerable evidence supporting a strong genetic basis for sleep-wake cycle traits and some sleep disorders, the molecular mechanisms underlying the various characteristics of the sleep-wake cycle are largely unknown. We are using quantitative trait loci (QTL) analysis as a tool in the genetic dissection of a number of different sleep-wake traits.
Methods: To find regulatory genes involved in the control of the sleep-wake cycle, mapping of QTLs for 50 sleep-wake traits was carried out for 75-N2 mice. QTLs were identified for baseline sleep-wake traits over the entire 24 hour day, as well as for different phases of the cycle, including the light phase (ZT 0-14), dark phase (ZT 14-24) and the middle of the dark phase when variability between animals in the amount of wake is highest (ZT 16-20). The parental strains were a line of C57BL/6J (B6) animals carrying a mutant gene that increases wake time, and BALB/cbyJ (BALB) animals.
Results: We identified 41 QTLs for 27 sleep-wake phenotypes measured over the entire day. 30 QTLs were identified for sleep-wake traits during the dark phase, and 32 QTLs were identified for the ZT 16-20 time period. Surprisingly, no QTLs were identified for the light phase. Comparison among the three sets of QTLs (entire day, dark phase and for ZT16-20) showed that 8 QTLs were linked to the same sleep-wake traits during the three different phases. Besides these 8 common QTLs, 7 other QTLs were linked to sleep-wake traits for both the 24 hour and dark phase time periods, while 7 other QTLs were found for traits during the dark phase and ZT 12-16.
Conclusion: These preliminary results indicate that different genetic factors regulate different aspects of sleep and wake. The lack of QTLs for sleep-wake traits during the day suggests the possibility that bright light during the normal sleep phase of the nocturnal mouse may be masking the expression of genetic differences during this time interval. These QTL´s can now be used for identifying genes and the molecular pathways involved in the regulation of the sleep-wake cycle.
Support (optional): This research was supported by Merck & Co., Inc. and a grant from the Defense Advanced Research Projects Agency (DARPA) and the Army Research Office (ARO), award number DAAD19-02-1-0038.

1067

INTEGRATING QTLS OF N2 MICE AND GENE EXPRESSION MICROARRAY DATA OF PARENTAL STRAINS TO IDENTIFY SLEEP GENES

Yang H,[1] Zhou L,[1] Shimomura K,[2] Kasarskis A,[3] Schadt E,[3] Winrow C,[4] Renger J,[4] Turek F[1]
(1) Northwestern University, Evanston, IL, USA, (2) Northwestern University, IL, USA, (3) Rosetta Inpharmatics LLC - Merck Research Laboratories, Seattle, WA, USA, (4) Merck Research Laboratories, San Diego, CA, USA

Introduction: Diversity in gene expression undoubtedly is one of the mechanisms that accounts for differences in sleep phenotypes between strains of inbred mice. Microarray technology is a powerful tool for monitoring differences in gene expression as it can test for the simultaneous expression of thousands of genes. However, one disadvantage in using microarrays to look for expression differences between strains is that thousands of genes can be differentially expressed in any given tissue (e.g. brain) between any two strains, making it difficult to narrow down the genes responsible for regulating any particular behavior, such as sleep. Here we present an approach that integrates QTL analysis from a cross between two strains with microarray data from the parental strains as a way to select candidate genes that may be involved in sleep regulation.
Methods: Microarray gene expression was carried out for the expression of approximately 44,000 transcripts from three different brain regions of inbred C57BL/6J (B6) mice (N=12) and inbred BALB/cbyJ (BALB) mice (N=10) sacrificed in the middle of the light phase. The brain regions were the frontal cortex, thalamus and hypothalamus. Genome-wide QTL mapping for 50 sleep-wake phenotypes was conducted using high density SNP data for 75 animals from a B6/BALB cross in which the F1 animals were mated with B6 animals. Based on 24 hr sleep-wake patterns, we found 41 QTLs for 27 sleep-wake phenotypes. The GeneNetwork database was used to test whether candidate genes are potentially cis-regulated, i.e. for genes whose expression controlling loci overlap with the physical location of the gene.
Results: There was an overlap of 1,033 genes that were differentially regulated between the strains in all three brain regions. 129 of these genes were found to fall within the QTLs for sleep-wake traits in the N2 animals. Using information in the GeneNetwork database, 28 genes were found to be potentially cis-regulated, making them candidates for sleep-wake regulation. These 28 genes were within 11 QTLs mapping to the following sleep-wake traits: relative power of wake band 1 or 3, relative power of NREM band 1, 2 or 3, relative power of REM band 2 or 3, number of wake bouts, number of REM bouts, duration of NREM bouts and duration of total sleep bout. These 28 genes can now be tested for allele specific expression analysis between the strains to determine if differences in expression are associated with differences in sleep-wake traits.
Conclusion: By integrating QTLs and gene expression microarray data it was possible to select 28 candidate genes that could have a causal relationship to sleep regulation from a total of approximately 1,033 genes that were expressed differentially in the brains of the two parental lines.
Support (optional): This research was supported by Merck & Co., Inc. and a grant from the Defense Advanced Research Projects Agency (DARPA) and the Army Research Office (ARO), award number DAAD19-02-1-0038.

1068

USE OF HAPLOTYPE ANALYSIS AND ALLELE SPECIFIC EXPRESSION ANALYSIS TO REDUCE THE SIZE OF QTLS FOR SLEEP-WAKE TRAITS

Yang H,[1] Zhou L,[1] Preuss F,[2] Shimomura K,[2] Kasarskis A,[3] Schadt E,[3] Winrow C,[4] Renger J,[4] Turek F[1]
(1) Northwestern University, Evanston, IL, USA, (2) Northwestern University, IL, USA, (3) Rosetta Inpharmatics LLC - Merck Research Laboratories, Seattle, WA, USA, (4) Merck Research Laboratories, San Diego, CA, USA

Introduction: Via QTL mapping we have identified multiple genomic regions related to different sleep wake traits. A common obstacle in identifying a responsible gene(s) for a given phenotype within a QTL is that these regions commonly encode hundreds of genes. In order to more narrowly define the region of interest we used interval-specific haplotype analysis combined with allele specific expression analysis, to greatly reduce the number of candidate genes within QTL regions for a number of sleep-wake traits.
Methods: 75 C57BL/6J x BALB/cbyJ N2 animals were analyzed for 50 sleep-wake traits. We applied interval specific haplotype analysis onto 7 sleep-wake QTLs which mapped to the same genomic regions for traits linked to the same QTL when analyzed throughout the entire 24 hr day, as well as during just the dark period. Haplotype analysis takes advantage of the fact that regions of identity by descent between two strains are unlikely to encode the genetic polymorphisms giving rise to the QTL, and therefore can be neglected, whereas regions where two strains contain alleles from different ancestral sources are more likely to encode the causal genes. Following the haplotype analysis, the remaining candidate genes within a QTL were tested for allele specific expression level differences comparing paternal (C57BL/6J) and maternal (BALB/cbyJ) mRNA transcripts of F1 animals. Allele specific expression analysis was conducted using mRNA extracted from different brain regions, including the midbrain, thalamus and frontal cortex, for the same QTL candidate gene to detect any potential tissue specific expression differences.
Results: We obtained 7 stable QTLs for 7 different sleep traits. By comparing high-density SNP markers for "SNP rich" and "SNP desert" regions between BALB/cbyJ and C57BL/6J mice, we were able to reduce the size of the candidate regions for all 7 QTLs to differing degrees. For example, a QTL for the number of wake bouts included 32 Megabases, whereas after haplotype analyses the region was reduced to 7.5 megabases. A different QTL for NREM sleep delta power was only marginally reduced by haplotype analysis. However, this QTL was reduced from 214 to 7 genes by using public database information (e.g. from Ensembl, MGI and GeneNetwork) to identify potential cis-regulated genes highly expressed in the brain in combination with allelic specific expression differences of the cis-regulated genes.
Conclusion: Integrating haplotype analysis, database searching and allele specific expression analysis is an effective strategy for reducing the number of candidate genes within large QTLs. As an example, we were able to reduce a QTL that initially contained hundreds of genes, to a subgroup of 7 potential candidate genes that regulate NREM sleep delta power.
Support (optional): This research was supported by Merck & Co., Inc. and a grant from the Defense Advanced Research Projects Agency (DARPA) and the Army Research Office (ARO), award number DAAD19-02-1-0038.

1069

GHRH, GHRH-R AND PIT-1 MRNAS HAVE DIURNAL RHYTHMS IN RAT CORTEX

Jimenez L,[1] Bohnet S,[1] Krueger J[2]
(1) Washington State University, Pullman, WA, USA, (2) Pullman, WA, USA

Introduction: Growth hormone releasing hormone (GHRH) is a sleep regulatory substance; it promotes NREMS where as its inhibition reduces sleep. The GHRH receptor (R) and GHRH are present in the hypothalamus, pituitary, and cerebral cortex. Pit-1 is in the pituitary. We hypothesized that components of the somatotropic axis are in the cortex and vary with the sleep/wake cycle because direct application of GHRH to the cortex enhances EEG delta power. To test this hypothesis, we evaluated the time course for levels of GHRH, GHRH-R, and Pit-1 mRNAs in the cortex.
Methods: Rats were on a 12:12 hour light dark cycle. Cerebral cortex tissue samples were collected every 3 hours. Total RNA was extracted using Trizol RNA isolation, and cDNA was synthesized using Thermoscript Reverse Transcriptase protocol. Real-time Polymerase chain reaction (PCR) was used to measure GHRH, GHRH-R, Pit-1, and cyclophillin mRNA´s. One-way analysis of variance (ANOVA) was used to analyze data. mRNA´s were compared to cyclophillin mRNA across the 24 hour period. Pit-1 was sequenced using an ABI automated cycle sequencer.
Results: GHRH mRNA increased during the light period with a peak at dark onset; during the dark period the expression levels were low and constant. The cortical Pit-1 sequence was identical to that of pituitary Pit-1. Pit-1 mRNA peaked in the middle of the light cycle. During the dark period Pit-1 mRNA levels were low and did not vary. GHRH-R mRNA levels did not change.
Conclusion: GHRH and Pit-1 mRNAs displayed distinct diurnal variations in the cortex. The variation of cortical GHRH mRNA is consistent with the idea that GHRH plays a role in EEG delta power. The role, if any, of Pit-1 in cortical functions remains unknown.
Support (optional): This work was supported by NIH NS27250.

1070

TRANSCRIPTOME-WIDE EXPRESSION PROFILING FOR THE IDENTIFICATION OF SLEEP/WAKE GENE NETWORKS

Winrow C,[1] Kasarskis A,[2] Williams D,[3] Owens-Ream J,[3] Dugovic C,[4] Schadt E,[5] Laponsky A,[6] Turek F,[3] Renger J[1]
(1) Merck Research Laboratories, West Point, PA, USA, (2) Rosetta Inpharmatics, LLC, Merck & Co., Inc., Seattle, WA, USA, (3) Northwestern University, Evanston, IL, USA, (4) Johnson & Johnson PRD LLC, San Diego, CA, USA, (5) Genetics Department, Rosetta Inpharmatics, LLC, Merck & Co., Inc., Seattle, WA, USA, (6) Nortwestern University, Evanston, IL, USA

Introduction: In this study, gene expression analysis across the murine transcriptome was performed to identify networks of genes involved in regulating sleep and wake. This approach was combined with an integrated pathway analysis to identify links between gene networks governing sleep and other neurological processes and pathology.
Methods: Subsequent to ENU-mutagenesis on a C57BL/6J background we used multi-day sleep recording to identify a group of high wake mice (avg. wake time= 815±7 minutes, n=12) and a group of low wake mice (avg. wake time= 664±13 minutes, n=12). Brains were dissected and mRNA was extracted from 3 discrete regions (frontal cortex, thalamus and hypothalamus). Following labeling, these samples were hybridized to microarrays representing over 40,000 annotated gene transcripts. Analysis was performed using the Rosetta Resolver

Bioinformatics Portal and integrated pathway analysis methods.
Results: Robust gene signatures for each individual region (frontal cortex, thalamus and hypothalamus) were obtained with a low false positive rate, validating this approach. A substantial number of previously uncharacterized regionally restricted genes were identified. Comparisons between the low wake cohort and the high wake cohort showed significant differences in gene expression. In the high wake animals, there were 308 signature genes in frontal cortex, 201 signature genes in thalamus and 25 signature genes in hypothalamus. In the low wake animals, there were 455 signature genes in frontal cortex, 203 signature genes in thalamus and 40 signature genes in hypothalamus. Pathway analysis demonstrated the involvement of many signature genes in neurological processes and/or pathologies.
Conclusion: Transcriptional profiling identified regionally enriched and distributed gene expression across frontal cortex, thalamus and hypothalamus, and enabled the detection of signature genes between low wake and high wake groups of mice.
Support (optional): This project was supported by Merck & Co., Inc and the Defense Advanced Research Program Agency (DARPA).

1071

COMBINING QTL MAPPING WITH EXPRESSION PROFILING TO IDENTIFY GENES REGULATING SLEEP BEHAVIOR IN MICE

Winrow C,[1] Kasarskis A,[2] Schadt E,[3] Laponsky A,[4] Williams D,[5] Owens-Ream J,[5] Zhou L,[5] Turek F,[5] Renger J[1]
(1) Sleep Research, Merck Research Laboratories, West Point, PA, USA, (2) Rosetta Inpharmatics, LLC, Merck & Co., Inc., Seattle, WA, USA, (3) Genetics Department, Rosetta Inpharmatics, LLC, Merck & Co., Inc., Seattle, WA, USA, (4) Nortwestern University, Evanston, IL, USA, (5) Northwestern University, Evanston, IL, USA

Introduction: DNA variations across mouse strains allow for the identification of genes that may be responsible for causing the observed sleep differences between different inbred mouse strains. In this study we used sleep phenotyping, single nucleotide polymorphism (SNP) genotyping and transcriptional profiling to identify pathways linked with the sleep differences between the BALB/cByJ and C57BL/6J mouse strains.
Methods: Multi-day sleep recordings were obtained from 100 N2 animals generated by crossing BALB/cByJ and C57BL/6J inbred strains. Sleep scoring and characterization of >40 sleep parameters was performed. Brains were harvested and mRNA was extracted from 3 different regions (frontal cortex, thalamus and hypothalamus). These samples were hybridized to microarrays representing over 40,000 annotated gene transcripts. Genomic DNA was collected from each animal to analyze over 2500 individual polymorphisms across the murine genome that are polymorphic between BALB/cByJ and C57BL/6J.
Results: Transcriptional profiling showed unique and overlapping genes expressed in frontal cortex, thalamus and hypothalamus. Although we confirmed expression of several genes known to be in these areas, many genes had not been previously characterized in these brain regions. Genome-wide linkage analysis was carried out using a high-density panel of SNPs to map quantitative trait loci (QTL) for the individual sleep parameters as well as the gene expression traits. Pathway analysis performed by integrating the sleep and expression QTL highlighted the overlap of candidate regions with indications in addition to sleep.
Conclusion: The combination of expression profiling, SNP genotyping and quantitative phenotyping enabled the identification of distinct chromosomal loci and associated genes associated with observed sleep differences between C57BL/6J and BALB/cByJ inbred mouse strains.
Support (optional): This project was supported by Merck & Co., Inc and the Defense Advanced Research Program Agency (DARPA).

1072

LAMININ ALPHA1 AFFECTS HYPOTHALAMUS FORMATION AND HYPOCRETIN CELL LOCATION IN ZEBRAFISH

Gaus S,[1] Faraco J,[2] Renier C,[2] Mignot E[1]
(1) Stanford University, Palo Alto, CA, USA, (2) Stanford University, CA, USA

Introduction: Hypocretin (hcrt) is an important modulator of sleep and wakefulness; disruption of the hcrt system causes narcolepsy. We are using forward genetics to discover novel functional regulators of hcrt and other sleep-related neurochemical systems. Our model, zebrafish (Danio rerio), expresses hcrt mRNA in a pattern and location similar to that observed in mammals.
Methods: From a pilot in situ hybridization (ISH) wholemount screen of approximately 200 F2 families from a three-generation ENU mutagenesis, we isolated a family with aberrant hcrt expression. The mutant phenotype is being characterized by microscopic observation, ISH, and immunostaining at multiple developmental timepoints. To determine which gene was mutated, we employed positional cloning, complementarity testing, and morpholino knock-down techniques.
Results: We isolated a mutant, initially called scatterbrain (F2W315), which displays displaced hcrt-expressing cells. The phenotype is recessive and fully penetrant. While initial body morphology is normal, by 24-48 hours post fertilization, the midbrain-hindbrain boundary, tectal ventricle, and lens are affected. Expression of several neurotransmitters, including histamine and melanin-concentrating hormone, appears normal, but expression of others is abnormal: hcrt and isotocin (oxytocin) appear scattered. Positional cloning localized this mutation to laminin alpha1 on chromosome 24, confirmed by complementation crosses (30%) and morpholino injections (62%). Sequencing is underway to determine the actual mutation, expected to be a point mutation (typically observed in ENU mutagenesis). Further phenotype characterization is also ongoing.
Conclusion: Zebrafish can be used as a genetic model to study hypocretin cell development. The existence of this scattered-pattern mutation indicates that hcrt expression is likely cell-autonomous. Laminin, a secreted basement membrane protein which mediates developmental cell attachment, migration, and organization, is required for organizing subregions of the hypothalamus, including cells expressing hcrt. This forward genetic approach has potential applications to human disorders, including complex syndromes in which narcolepsy is associated with other defects.
Support (optional): NIH NS23724 and HHMI

1073

INCREASES IN AROUSAL AFTER ESTROGEN TREATMENT ARE ACCOMPANIED BY LOWERED A2A RECEPTOR MRNA EXPRESSION IN THE VENTROLATERAL PREOPTIC AREA

Ribeiro A,[1] Pfaff D,[2] Devidze N[2]
(1) New York, NY, USA, (2) Rockefeller University, New York, NY, USA

Introduction: Estradiol (E2) modulates lipocalin-type prostaglandin D synthase (L-PGDS) expression in a region-dependent manner in mouse brain (Mong *et al.* 2003). This links sex hormones with sleep-wake cycle regulation. The somnogenic effects of PGD2 are thought to be mediated via increases in adenosine, and a select group of sleep-active VLPO neurons are directly activated by adenosine 2A (A2A) agonists. We hypothesize that increased arousal after E2 treatment is mediated by

a reduction of L-PGDS and lowered A2A receptor expression in the VLPO.
To test this hypothesis, arousal responses in ovariectomized (OVX) mice treated with 3 doses of E2 were studied, followed by quantitative reverse-transcriptase polymerase chain reaction (Q-RT-PCR) to determine A2A mRNA expression in VLPO extracts from oil- or E2-treated mice.
Methods: 48 OVX Swiss-Webster mice were implanted with E2 (0.125, 1.25 or 50 µg) or oil (control) capsules, and were placed in running wheels (RW) under a 12:12h light–dark cycle. RW activity was continuously recorded for 3 weeks, after which all animals were sacrificed, their brains quickly excised and the VLPO was dissected. Following RNA isolation, mRNA was reverse-transcribed and cDNA was used to quantitatively determine the amount of A2A and 18S mRNA present in each microdissected VLPO extract. Ct values were analyzed using rest software developed by Pfaffl *et al.* (2005 version).
Results: Average RW activity was increased during the dark period by 61, 140 and 44% after 0.125 ($p<0.01$), 1.25 ($p<0.001$) and 50 µg E2, respectively. These changes in RW activity were accompanied by decreases in A2A mRNA levels in VLPO extracts by a factor of 1.89 ± 1.14, 1.09 ± 3.20 and 1.58 ± 0.61 ($p<0.001$) after 0.125, 1.25 and 50 µg E2, respectively.
Conclusion: The present findings support the hypothesis that increases in arousal following E2 are mediated via lowered L-PGDS and A2A-receptor signaling in VLPO.
Support (optional): This work was funded by NIH grant HD05751.

1074

UNCOVERING THE NEXT GENERATION OF SLEEP TARGETS – APPLICATION OF LASER CAPTURE MICRODISSECTION AND GENE EXPRESSION ANALYSIS

Rigby A,[1] Serikawa K,[2] Stone D,[3] McWhorter M,[2] Koblan K,[4] Renger J,[5] Winrow C[6]
(1) Sleep Research, Merck Research Laboratories, West Point, PA, USA, West Point, PA, USA, (2) Gene Expression Laboratory, Rosetta/Merck Research Laboratories, Seattle, WA, USA, WA, USA, (3) Molecular Profiling, Merck Research Laboratories, West Point, PA, USA, PA, USA, (4) Merck Research Laboratories, Neuroscience, Philadelphia, PA, USA, (5) Merck and Co., Inc., West Point, PA, USA, (6) Merck Research Laboratories, San Diego, CA, USA

Introduction: Elucidation of gene expression changes in brain regions implicated in sleep regulation could provide a better understanding of sleep and wake circuitry and yield novel sleep targets for drug development. Laser capture microdissection (LCM) was used to isolate discrete brain regions and even individual neurons from rodent brains obtained at different circadian time points. RNA was extracted from the collected neurons and gene expression was interrogated using microarrays and quantitative RT-PCR.
Methods: Animals were sacrificed at defined time points within the sleep cycle (n=4 for each time point) and LCM was performed to isolate LC, SCN, VTA, VLPO, GCL and other regions. RNA from each region was extracted, analyzed and amplified for gene expression studies using Taqman or microarrays representing over 40,000 annotated gene transcripts. Data was analyzed using the Rosetta Resolver Portal and integrated pathway analysis methods.
Results: Taqman analysis revealed regional and circadian-related differences in gene expression of specific genes including Per1, Per2, Bmal1, TH and RevErbA. Robust gene expression signatures were obtained for each region using microarrays for global expression profiling. Unclassified agglomerative analysis showed that individual brain regions from multiple animals clustered together. Interestingly, overlapping and distinct circadian expression signatures were detected between brain regions. In particular, strong circadian differences were observed in VLPO and VTA, including many genes not previously known to be under circadian control. Pathway analysis demonstrated the involvement of signature genes in a range of neurological processes and/or pathologies.
Conclusion: LCM provides specificity and exclusivity in extracting distinct brain nuclei, and generates high quality RNA with sufficient yields for gene analysis. This approach sensitively detects both regional and circadian variations in gene expression. The combination of LCM, expression profiling and pathway analysis allows the dissection of CNS circuitry thereby enabling the identification of novel targets for development.
Support (optional): This project was supported by Merck & Co., Inc.

1075

GENE EXPRESSION PATTERNS IN THE LOCUS COERULEUS DURING SLEEP/WAKEFULNESS: MICROARRAY ANALYSIS

Gerashchenko D,[1] Thompson C,[2] Wisor J,[1] Ng L,[2] Smith K,[2] Jones A,[2] Kilduff T,[1] Lein E[2]
(1) Biosciences Division, SRI International, Menlo Park, CA, USA, (2) Allen Institute for Brain Science, Seattle, WA, USA

Introduction: Noradrenergic locus coeruleus (LC) neurons play an important role in arousal regulation. Firing of noradrenergic LC neurons is high during wakefulness, progressively decreases during slow wave sleep, and becomes practically silent during paradoxical sleep. It is expected that state-associated changes in LC activity are associated with corresponding changes in gene expression in LC neurons. Identification of gene expression patterns in LC neurons could help to understand mechanisms of sleep/wake regulation. In the current study, we studied gene expression profile in the LC by identifying the genes whose expression is enriched in the LC region and by doing microarray analysis of gene expression in the LC during different sleep/wake states.
Methods: The Allen Brain Atlas was used to find genes that are expressed more strongly in the LC than in the surrounding brain areas. Digitized intensity of in situ hybridization signal in the LC was divided by the intensity of signal in the pontine area, and the genes with highest ratios were selected. For microarray analysis, LC samples were collected by laser-capture microdissection in mice in the following 5 groups: 1) 6 h of sleep deprivation (SD) from ZT0-ZT6, 2) SD control (ZT6), 3) 6 h SD followed by 4 h recovery sleep (RS) (ZT10), 4) RS control (ZT10), 5) spontaneous waking (ZT18). cDNA synthesis, cRNA amplification and hybridization on chips were done according to standard CodeLink protocols. Data were analyzed using ANOVA.
Results: Approximately 2000 genes that are enriched in the LC were selected from the Allen Brain Atlas based on the highest expression ratios of LC /brainstem in situ hybridization signal. According to the gene ontology classification, a large number of these genes are involved in cellular physiological processes. The microarray results showed that the largest number of genes that strongly changed their expression was observed in the SD group. Most of differentially expressed genes that were also present on the list of genes enriched in the LC belonged to either SD group (*dexi, epdr2, cul4a, prnp, neurl*) or spontaneous waking group (*prnp, lrrn6c, nrg1, pgrmc1, neurl*).
Conclusion: Gene expression results of the present experiment are consistent with an important role of the LC in arousal regulation. Along with our companion abstract (Thompson *et al.*), these results indicate that SD has a stronger effect on gene expression than does RS or time of day, at least in the cortex and LC.
Support (optional): Supported by the Department of Defense USAMRAA award W81XWH-06-1-0131 and NIH 5RO1HL59658.

1076

LOSS OF FUNCTIONAL HOMER LEADS TO SLEEP FRAGMENTATION IN DROSOPHILA

Naidoo N,[1] Ferber M,[1] Worley P,[2] Pack A[1]
(1) University of Pennsylvania, Philadelphia, PA, USA, (2) Johns Hopkins University, Baltimore, MD, USA

Introduction: Microarray studies in rodents and Drosophila indicate that expression of the synaptic scaffolding protein Homer is altered with sleep and wake. Using Drosophila as a model organism we determined the role of Homer in sleep- wake behavior.
Methods: Sleep-wake behavior was determined in young (5-7 day old) male and female Homer ^{R102} transgenic flies (n = 200) maintained in 12:12 light: dark conditions. Canton-S (CS) flies were used as background controls (n=200). Using the 5 minutes of inactivity definition of sleep we determined the following parameters: % time active and sleeping, number of sleep and wake bouts, mean length of sleep and wake bout, maximum length of the sleep and wake bout, number of activity counts per bout.
Results: While we observe no change in the % time sleeping and the % time active between Homer mutant flies and the background CS flies, Homer mutant flies do display a greater number of both sleep and wake bouts than the control background strain and also exhibit shorter sleep and wake bouts. There are significant differences in wake bout number (Homer 32, CS 15, $p<0.01$), wake bout length (Homer 12 minutes, CS 26 minutes, $p = 0.02$), sleep bout length (Homer 40 min, CS 104 min, $p<0.01$) and number of sleep bouts (Homer 32; CS 14, $p<0.01$) in both male and female Homer ^{R102} mutant flies compared with CS flies.
Conclusion: Disruption of sleep architecture occurs in key human diseases such as narcolepsy, in which there is behavioral state instability, and in sleep-maintenance insomnia during sleep. With the exception of the orexin/hypocretin system not much is known about the molecules that may contribute to behavioral state stability. The scaffolding protein Homer that is required to maintain both sleep and wake state stability in Drosophila appears to be one such molecule.
Support (optional): Supported by NIH grant AG17628.

1077

CHANGES IN LIFE SPAN IN HYPERKINETIC SHORT SLEEPING MUTANT FLIES

Bushey D,[1] Hughes K,[2] Tononi G,[3] Cirelli C[1]
(1) University of Wisconsin-Madison, Madison, WI, USA, (2) University of Illinois at Urbana-Champaign, Urbana, IL, USA, (3) University of Wisconsin, Madison, WI, USA

Introduction: We recently isolated *Minisleep,* a short sleeping mutant line carrying a mutation in *Shaker*, a gene coding for the alpha subunit of a voltage-dependent potassium channel. *Minisleep* and other *Shaker* short sleeping mutants are short-lived relative to their genetic controls, which are normal sleepers. *Hyperkinetic* (*Hk*) codes for the beta (modulatory) subunit of *Shaker* and strong hypomorph *Hk* mutations (Hk^{1} and Hk^{Y}) also cause reduced sleep. Here we tested whether *Hk* mutations also reduce life span. Moreover, in both *Hk* and their wild-type siblings, we measured whether sleep duration and/or fragmentation can affect survival, and if they change with aging.
Methods: *Hk* mutants were outcrossed into the Canton-S background for over 3 generation. Within 24 h after eclosure, mutants were separated from wild-type siblings using an ether-induced leg-shaking phenotype caused by *Hk* mutations. Using the Drosophila activity monitor system, sleep and locomotor activity from individual males (n ≥199/line) were measured at 20°C in 1-min bins until death. Flies were transferred into new tubes containing fresh food every week.
Results: Hk^{1} and Hk^{Y} are short-lived relative to their wild-type siblings (lifespan in days ±SE, mutant/control; Hk^{1} 66 ±1.5/93 ±1.8; Hk^{Y} 70 ±1.4/94 ±2.1; Wilcoxon test, $p<0.0001$). A proportional hazards regression analysis showed that, in both Hk^{1} and their wild-type siblings, daily sleep amount (first 28 days of life) was negatively correlated with life span. Moreover, after correcting for differences in total sleep, flies with longer average duration of sleep episodes had lower survival. In Hk^{Y} mutants, instead, more frequent brief awakenings were associated with reduced lifespan, while none of the sleep parameters correlated with lifespan in their wild-type siblings. The activity index, a measure of locomotor activity during waking, did not affect lifespan in any of the lines examined. Moreover, in all lines, aging did not affect daily sleep amount, nor the mean number of brief awakenings or the mean duration of sleep episodes.
Conclusion: Like *Shaker* short sleeping mutants, *Hk* short sleeping mutants also have reduced life span. Sleep amount and sleep fragmentation can effect survival in both mutant and wild-type flies, but the effects are complex and dependent on the specific fly line. In the 4 tested lines, sleep duration and sleep fragmentation did not change with aging.
Support (optional): NIGMS (R01 GM075315)

1078

DISSECTION OF DIFFERENTIALLY EXPRESSED GENES AND PATHWAYS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME BEFORE AND AFTER CPAP TREATMENT

Lee P, Chen J, Yu C, Yang P
National Taiwan University Hospital, Taipei, Taiwan

Introduction: The aim of this study are (1) To genome-wide profile the gene expression patterns of peripheral blood mononuclear cell (PBMC) in patients with obstructive sleep apnea (OSA) and the changes of gene expressions before and after CPAP treatment (2) To correlate the altered gene expression with the severity of the disease and outcome of OSA patients
Methods: We selected 12 patients with severe OSA and 12 healthy control subjects as the study subjects. Twelve patients with severe OSA were treated with CPAP for 4 weeks. All patients had blood sampled at 5 AM just before waking up and RNA was then isolated from PBMC to perform oligo-micorarray. We used oligo microarray to genome-wide profile the gene expression patterns in OSA patients and the changes of gene expressions before and after CPAP treatment. The oligo-micorarray data was processed with CRSD database. Two-way hierarchical clustering method was performed to interpret the correlation between genes of control subjects and OSA patients and changes before and after CPAP treatment. RT-PCR was employed to confirm the selected genes (genes of interest) and investigate the correlation with clinical outcome. Genes of interest were also analyzed to determine transcriptional factor and pathway involved.
Results: There were totally 36 chips including 12 controls, 12 diseases and 12 treatments. The gene patterns were significantly different between control subjects and OSA patients. CPAP treatment could alter the gene expression patterns. From profiled changes of gene patterns before and after CPAP treatment, 26 genes and four pathways were identified as genes and pathways of interest. These four pathways included apoptosis, oxidative phosphorylation, cell adhesion and activation and metabolism.
Conclusion: The gene expression pattern was different between control subjects and OSA patients. CPAP treatment could alter the gene expression patterns in OSA patients.

1079

CATECHOLAMINE CAN ATTENUATE HYPOXIA-INDUCED TNF- α EXPRESSION IN PERIPHERAL BLOOD MONOCYTES AND U937

Lee P
National Taiwan University Hospital, Taipei, Taiwan

Introduction: Obstructive sleep apnea can result in intermittent hypoxia and sympathetic hyperactivity. Several cytokines, especially TNF-α, were reported to increase in the in OSA patients. In vivo studies showed catecholamine could potentiate lipopolysaccharide-induced TNF-α expression. Therefore, the objectives of this study were to prove our hypothesis that catecholamine could potentiate hypoxia-induced TNF-α expression and to explore the potential therapeutic effects of α or β agonist/antagonists.
Methods: We used the human peripheral blood monocyte and monocyte cell line U937 as target cells. The CD14+ monocytes were isolated by positive selection with magnetic beads. In hypoxic condition, we used 0.1% O2 and 5% CO2 at a controlled incubator and maintained PO2 of the medium around 33 mmHg the. In nomoxic condition, we used 21% O2 and 5% CO2 and PO2 in the medium was around 154 mmHg. Both monocyte and U937 were treated with catecholamine, α; and β agonists/antagonists for 12 hours at normoxic and hypoxic conditions. The supernatant and cells were harvested at 0, 0.5, 1, 3, 6 and 12hr after drug treat. The supernatant was harvested for ELISA and cells were harvested for PCR to assess the TNF-α expression. The TNF-α expression in hypoxic condition was compared to normoxic condition.
Results: In hypoxia, both epinephrine and norepinephrine could attenuate the TNF-α expression in both human monocytes and U937. The dose-dependent attenuation peaked at 3hr after drug treat. Both α and β agonist also could decrease the hypoxia-induced TNF-α expression. However, catecholamine, α and β agonist didn't affect TNF-α expression at normoxia.
Conclusion: Catecholamines and could attenuate the TNF-α expression at hypoxia but not at normoxia. The result would help us with treating OSA patients with cardiovascular disease.

1080

ATTACHMENT ANXIETY, RELATIONSHIP CONTEXT, AND SLEEP IN MAJOR DEPRESSION

Troxel W,[1] Cyranowski J,[2] Hall M,[2] Frank E,[1] Buysse D[1]
(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) University of Pittsburgh, PA, USA

Introduction: Sleep is a physiologically vulnerable state that optimally occurs when one feels sufficiently secure to down-regulate vigilance-- a felt experience that is largely derived from the social context. However, scant research has investigated the impact of close relationship quality on sleep. We investigated whether an index of relationship quality (attachment anxiety) and measures of relationship context (marital and bed-partner status) correlate with sleep.
Methods: We measured sleep using polysomnography (PSG) and subjective sleep quality in 118 women (mean age = 38.01, SD = 10.34) with recurrent major depression. Participants reported their marital and bed-partner status. A categorical measure of attachment anxiety (high versus low) was derived from Bartholomew and Horowitz´s Relationship Questionnaire (1991). All analyses statistically adjusted for age, severity of depressive symptoms, and length of time between psychosocial and sleep assessments.
Results: There were no significant main or interaction effects of any of the relationship measures on subjective sleep quality. Women with a bed-partner had better PSG-assessed sleep efficiency ($F = 10.40$, $p < .01$) and increased REM density ($F = 3.82$, $p < .05$) compared to women without a bed-partner. Marital status was associated with sleep efficiency ($F = 3.41$, $p < .05$), although post-hoc comparisons were non-significant. Attachment anxiety interacted with marital status on the percentage of Stage 3-4 sleep ($F = 7.28$, $p´s < .05$), such that anxiously attached women who were previously married showed the least amount (as confirmed by confidence intervals).
Conclusion: Depressed women who exhibit an anxious attachment style and have experienced a marital rupture show reduced Stage 3-4 sleep, which may signal a concomitant reduction in restorative cognitive and metabolic processes. Relationship quality and context are important correlates of sleep. These results provide a more nuanced approach to considering qualitative and structural aspects of relationships that may influence sleep.

1081

BENEFITS OF PHYSICAL ACTIVITY ON SLEEP

Tatum J,[1] Taylor D,[2] Bramoweth A,[1] Gardner C,[1] Williams J,[1] Zimmerman M,[1] Roane B,[1] Grieser E[1]
(1) University of North Texas, Denton, TX, USA, (2) University of North Texas, TX, USA

Introduction: Studies have shown that people who exercise showed physical and psychological benefits (e.g., reduced stress and anxiety) (King, Taylor & Haskell 1993). Additional benefits of exercise are found in the improvement of sleep quality (Tworoger *et al.*, 2002). However, few studies have explored what type of physical activity is needed to affect these changes. The present study examined the relationship between sleep quality and type of exercise (e.g., walking, stretching and strength training) and exercise frequency.
Methods: Undergraduate students (N=367) who were enrolled in psychology classes completed a health survey that included questions about their exercise and sleep habits in exchange for extra credit.
Results: The primary measure analyzed was the Pittsburgh Sleep Quality Index (PSQI). Preliminary analyses of the sleep data show that as exercise frequency (e.g., # of times per week) increased, enthusiasm also increased ($p<.01$). When specific types of exercise were examined, only increased walking frequency was associated with better sleep as a whole ($p<.05$). Post hoc analyses for the individual parameters of sleep showed that increased walking frequency was associated with less wake time after sleep onset ($p<.05$), less discomfort due to feeling too hot at night ($p<.05$), and increased enthusiasm for daily activities ($p<.01$).
Conclusion: Preliminary data show a promising effect of low intensity exercise, especially walking, on sleep quality.

1082

TOO MUCH OF A GOOD THING? REM SLEEP THETA ACTIVITY PREDICTS TWO-WAY ACTIVE AVOIDANCE (TWAA) PERFORMANCE AND INCREASES PRIOR TO MALADAPTIVE LEARNING IN RATS

Fogel S,[1] Smith C,[2] Beninger R[3]
(1) Queen's University at Kingston, City of Kawartha Lakes, Ontario, Canada, (2) Trent University, Peterborough, Ontario, Canada, (3) Queen's University at Kingston, Kingston, Ontario, Canada

Introduction: REM sleep increases following learning in the TWAA task in specific time periods termed REM sleep windows. Hippocampal theta predominates REM sleep. Theta rhythms are considered to be a mechanism for inducing hippocampal long-term potentiation. This study investigated if theta during REM is related to memory consolidation for TWAA learning.
Methods: Twenty male Sprague-Dawley rats (250-300g) were implanted with four EEG and two EMG electrodes. After recovery, 3 days of acclimatization, and 24 hours of baseline recording, animals were trained on the TWAA task for 100 trials (50 trials/day) from 9-10AM and re-tested for 25 trials on day 3. EEG was recorded for 23 hours after training on both training day 1 (TD1) and TD2. Rats in the learning (L) group (n=10) avoided the footshock on 70% of the last 20 test trails. The remaining rats (n=10) were assigned to the non-learning (NL) group.
Results: The L-group had an increase in correct avoidances over 5 blocks of 25 trials ($F(4,36)=9.54$, $p< 0.00001$). Surprisingly, the NL-group had significantly more failures to cross on the last block of trials ($Z(19)=2.12$, $p=0.034$). TWAA performance was negatively correlated with theta from hr 17-20 on the baseline day during REM sleep ($r(17)=-0.81$, $p<0.005$) and wake ($r(17)=-0.77$, $p<0.005$), but not during SWS. REM theta increased during hr 17-20 on TD2 in the NL-group ($F(1,16)=8.88$, $p=0.009$) but not on the baseline or TD1, or during SWS or wake.
Conclusion: Theta during hr 17-20 on the baseline day predicted performance, and increased in hr 17-20 on TD2 for non-learning rats. Surprisingly, the NL-group began to fail to escape from the footshock on the test day after the increase in theta was observed. Failures to cross may be indicative of learned-helplessness. The results suggest that theta was a good predictor of maladaptive learning and increased prior to the development of escape failures.
Support (optional): Supported by grants from the Natural Sciences and Engineering Research Council of Canada to CTS and RJB

1083

REM SLEEP DURATION PREDICTS TWO-WAY SHUTTLE ACTIVE AVOIDANCE (TWAA) LEARNING AND INCREASES 17 - 20 HOURS FOLLOWING LEARNING IN RATS

Fogel S,[1] Smith C,[2] Beninger R[3]
(1) Queen's University at Kingston, City of Kawartha Lakes, Ontario, Canada, (2) Trent University, Peterborough, Ontario, Canada, (3) Queen's University at Kingston, Kingston, Ontario, Canada

Introduction: REM sleep increases following learning in the TWAA

task. Subsequent memory impairment is observed if REM sleep deprivation is applied during periods of increased REM. These post-training intervals have been termed REM sleep windows. Little is known about the relation between baseline sleep characteristics and learning in rats. Human studies have demonstrated that sleep parameters can predict learning potential as measured by IQ tests. This study investigated the ability to predict the level of learning from individual differences in sleep in rats.
Methods: Twenty male Sprague-Dawley rats (250-300g) were implanted with four EEG and two EMG electrodes. After recovery, 3 days of acclimatization, and 24 hours of baseline recording, animals were trained on the TWAA task for 100 trials (50 trials/day) from 9-10AM and re-tested for 25 trials on day 3. EEG was recorded for 23 hours after training on both training day 1 (TD1) and TD2. Rats in the learning (L) group (n=10) avoided the footshock on 70% of the last 20 test trails. The remaining rats (n=10) were assigned to the non-learning (NL) group.
Results: The L-group had an increase in correct avoidances over 5 blocks of 25 trials ($F(4,36)=9.54$, $p<0.00001$). There was no change in correct avoidances in the NL-group. TWAA performance correlated with the %REM sleep from hr 17-20 of the 24-hr period prior to training ($r(15)=.48$, $p=0.05$) and with the number of REM periods ($r(15)=.54$, $p=.026$). The %REM sleep was higher in the L-group ($F(5,85)=3.21$, $p=0.01$) on TD1 during hr 17-20 following training (post-hoc $t(17)=3.21$, $p=0.005$).
Conclusion: REM sleep during hr 17-20 on the baseline day predicted TWAA performance. Learning-dependent increases in REM sleep were observed when REM sleep already predominated. Results suggest that the duration of REM sleep is a good predictor of learning and increased in a learning-dependent manner during specific post-training windows of time.
Support (optional): Supported by grants from the Natural Sciences and Engineering Research Council of Canada to CTS and RJB

1084

STAGE 2 SLEEP SPINDLES, MOTOR LEARNING, AND AGING

Peters K,[1] Ray L,[1] Smith V,[2] Smith C[1]
(1) Trent University, Peterborough, Ontario, Canada, (2) Trent University, Ontario, Canada

Introduction: Previous studies have established a relationship between sleep spindles and memory consolidation. The majority of these studies, however, have involved young adults. The objective of this investigation was to compare the changes in spindle density following motor learning in younger and older adults.
Methods: In-home sleep recordings were performed on 14 younger (17-24 yrs) and 14 older adults (62-79 yrs) for three consecutive nights. The first night was discarded, while the second and third nights served as the baseline and post-acquisition nights respectively. Stage 2 spindle density was determined by dividing the number of Stage 2 spindles by the number of minutes of Stage 2 sleep. Subjects performed the pursuit rotor on two occasions: between the baseline and post-acquisition nights and one week later. For behavioural data, a 2(Session: Acquisition, Retest) x 2(Group: Younger; Older) ANOVA was conducted to assess changes in performance on the pursuit rotor task. For sleep data, a 2(Night: Baseline, Post-Acquisition) x 2(Group: Younger, Older) ANOVA was conducted to assess changes in Stage 2 spindle density.
Results: Regarding pursuit rotor performance, the session by group interaction was significant [$F(1,26)=7.73$, $p=.010$]. The magnitude of learning across sessions was greater in the younger adults [$t(13)=9.08$, $p<.001$] than in the older adults [$t(13)=2.85$, $p=.014$]. For Stage 2 spindle density, the night by group interaction was significant [$F(1,26) = 5.30$, $p = .030$]. The increase in spindle density was significant in the younger subjects [$t(13)=3.30$, $p= .006$] but not the older subjects [$t(13)=.33$, $p=.747$].
Conclusion: The results of this investigation suggest that differences in motor learning across sessions in younger and older adults may be related to the changes in sleep architecture that occur following initial acquisition in these two age groups.
Support (optional): Canadian Institutes of Health Research and the Alzheimer Society of Canada

1085

EFFECTS OF 40-HOUR SLEEP DEPRIVATION ON SHORT-TERM MEMORY IN A CONSTANT ROUTINE PROTOCOL

Anders D,[1] Vollenweider S,[1] Quervain D,[2] Wirz-Justice A,[3] Krauchi K[3]
(1) Psychiatric University Clinics, Basel, AE (Europe), Switzerland, (2) University of Zurich, AE (Europe), (3) Psychiatric University Clinics, AE (Europe)

Introduction: Circadian and homeostatic aspects of sleepiness regulation can influence the outcome of diverse neurocognitive performance tests. We investigated the influence of these components on short-term memory during 40-hour of sleep deprivation.
Methods: Twelve healthy women (luteal phase; age: 20-31yr) completed a stringently controlled 40-hour constant routine protocol. Core body temperature (CBT) was continuously measured, subjective sleepiness was rated on the Karolinska Sleepiness Scale at half-hourly intervals and performance in a forward digit span (F) and backward digit span (B) test was evaluated two-hourly.
Results: Sleepiness ratings were highest during the CBT minimum and remained at a higher level on the 2nd day compared with the 1st day (sleep deprivation effect). Performance of F showed a circadian trough 6h after the CBT minimum on day 2 (27.5h after lights on) but not on day 1 (3.5h after lights on). Performance of B showed a narrow circadian trough 2h after the CBT minimum (23.5h after lights on). This ruled out detection of a potential circadian trough 24h earlier (sleep phase). No significant differences in F and B occurred between day 1 and 2 (no sleep deprivation effect).
Conclusion: There is a circadian component in the performance of F that is visible only on the 2nd day when sleep pressure is high. Sleep deprivation-induced sleepiness alone seems to play a minor role in this test of short-term memory - only its interaction with the circadian trough worsens short-term memory. The circadian modulation of a less complex task (F) seems to be larger than that of a more complex one (B). Furthermore, the results do not support a direct effect of CBT on F and B performance.
Support (optional): Research supported by SNF Grant #3100A0-102182 to K.K. and the Gottlieb Daimler and Karl Benz Foundation.

1086

IN OLD RATS PREHABILITATION EXERCISE ACCELERATES THE RECOVERY OF SLEEP-WAKE PATTERNS AFTER SURGERY

Blanco-Centuiron C,[1] Culley D,[2] Crosby G,[2] Priyattam S[1]
(1) Sleep Research Society, West Roxbury, MA, USA, (2) Harvard University, Boston, MA, USA

Introduction: Following general anesthesia the elderly recover significantly slower compared to young individuals. Exercise has been shown to improve the quality of life in the elderly, and elderly individuals who exercise prior to surgery recover faster. Here we investigate whether prehabilitation exercise could improve the recovery of the sleep-wake pattern in old rats.

Methods: Male F344 rats were anesthetized with isoflourane (1-2.5%, 2 L/min) and implanted with epidural sleep electrodes. To assess the effect of aging on the time course of sleep recovery following surgery, four young (3 months) and five old (22 months) rats were continuously recorded for three weeks after surgery. Another group of four 22 months-old rats were also recorded for three weeks but were previously exercised for eight consecutive weeks. Exercise consisted of walking at a slow pace (2 m/min) for 50 min at night onset. Young and old non-exercised rats were gently kept awake while their counterparts exercised. Sleep recorded over a 24h period during the 2nd, 7th, 14th and 21st days after surgery was selected for analysis.
Results: On the 2nd day after surgery, sleep was abnormal with all groups having an inverted diurnal rhythm of sleep and wake. On the 7th day, sleep in young and old exercised rats was not different from days14 and 21 post–surgery, but old non-exercised rats still showed a disturbed sleep-wake pattern during the day and night. By the 14th day sleep in these rats had also returned to normal.
Conclusion: Exercise in old rats shortened the recovery from anesthesia and surgery. Recovery of sleep in old exercised rats was similar to that of young non-exercised rats. Since sleep recovered faster in old rats we conclude that exercise induces plasticity in the old brain which could also allow faster recovery of cognitive function.
Support (optional): VA Research Service and NIH grants (MH55772, NS30140, NS52287, AG20253, GM077057)

1087

SLEEP-DEPENDENT PERCEPTUAL LEARNING WITH AND WITHOUT DISTRACTORS.

Mednick S,[1] Serences J[2]
(1) University of California, San Diego, la jolla, CA, USA, (2) Salk Institute for Biological Studies, la jolla, CA, USA

Introduction: Does sleep-dependent improvement on a visual search task depend on the presence of distractors?
Methods: We investigated this question by testing two groups of subjects in three sessions across two days. The Night first group was tested at 7PM on Day 1, and 9AM and 7PM on Day 2. The Day first group was tested at 9AM and 7PM on Day 1, and 9AM on Day 2. Subjects detected targets (oriented gabors) that appeared alone in the periphery (distractor absent condition), or embedded in a field of distractors (distractor present condition), followed by a mask. Both distractors and mask were made of two superimposed oriented gabors. Performance was measured as the target contrast that led to 80% correct in a staircase procedure.
Results: Learning was shown after a night of sleep in the Night first group only. This sleep-dependent learning was found when distractors were present, whereas sleep did not affect learning in the absence of distractors. Repeated within-day testing in the Day first group led to "perceptual maintenance". Subsequent sleep, however, did not produce normal sleep-dependent learning.
Conclusion: Our results suggest that improvement on these visual search tasks depends on inter-session sleep only in the presence of distractors. We hypothesize that the presence of distractors increases the complexity of the stimulus, thus the brain may enlist sleep for increasingly complex information consolidation.
Support (optional): F32 EY015564-01

1088

DECREASES IN STAGE 2 SLEEP FOLLOWING ACQUISITION OF A DECLARATIVE TASK USING A RETROACTIVE INTERFERENCE PARADIGM

Moran C, McGilvray M, Peters K, Smith C
Trent University, Peterborough, Ontario, Canada

Introduction: The protective effect of sleep on declarative memory from associative interference has recently been reported. The present study examined the changes in sleep states associated with acquisition of lists of two word pairs, separated by 12 hours that either included a night of sleep or a period of waking.
Methods: Female adults were asked to learn a paired associate list (A-B). Training continued until 100% recall was obtained. After 12 hours which either included sleep (SLP, n=10) or an equal period of awake (AW, n=10), participants were given a second list of paired associates (A-C). Then, after a 15 minute distractor task, participants were asked to recall both list A-B and A-C (Test1). SLP subjects were sleep recorded for 3 consecutive nights, an acclimatization night (discarded), a baseline night, and a post-training sleep night. All participants were given a second retest 1 week later (Test 2).
Results: Behavioural: The SLP group had superior memory recall for the A-B list compared to the AW group at both Test 1 and Test 2. [$F(1,18) = 13.58$, $p < .002$]. Sleep Recording: Comparison of times spent in each of the sleep stages between baseline and post-training night showed no differences in Stages 1, Stages 3/4, or REM. However, there was a significant drop in the number of minutes of Stage 2 sleep from Baseline to Post-training night [$t(9) = 2.269$, $p < .05$].
Conclusion: The post-training time that included a night of sleep was clearly more beneficial to memory consolidation, despite interference, than an equal amount of time spent awake. The decreases in Stage 2 sleep were not predicted, but suggest, in the absence of any other sleep changes, that reductions in certain sleep stages are also part of the complex consolidation process which takes place over the night of sleep following declarative task acquisition.
Support (optional): The Natural Sciences and Engineering Research Council of Canada (NSERC)

1089

DECREASES IN NUMBER OF SLEEP SPINDLES FOLLOWING ACQUISITION OF A DECLARATIVE TASK USING A RETROACTIVE INTERFERENCE PARADIGM

McGilvray M,[1] Moran C,[1] Peters K,[1] Smith C[2]
(1) Trent University, Ontario, Canada, (2) Trent University, Peterborough, Ontario, Canada

Introduction: The protective effect of sleep on declarative memory from associative interference has been reported. The present study examined the changes in number and density of NREM sleep spindles in participants following acquisition of lists of word pairs.
Methods: Female adults were asked to learn a paired associate list (A-B). Training continued until 100% recall was obtained. After 12 hours which either included sleep (SLP, n=10) or an equal period of awake (AW, n=10), participants were given a second list of paired associates (A-C). Then after a 15 minute distractor task, participants were asked to recall both list A-B and A-C (Test 1). SLP subjects were sleep recorded for 3 consecutive nights, an acclimatization night (discarded), a baseline night, and a post-training night. All participants were given a retest 1 week later (Test 2). Spindles were counted manually at both Central (C3, C4) and Frontal (F3, F4) sites.
Results: Behaviour and Sleep State Changes: The SLP group had superior memory recall ($p < .002$) and showed a reduction in minutes of

Stage 2 from baseline to post-training night ($p < .05$) (See accompanying abstract).
Sleep Spindles: The total number of Stage 2 sleep spindles at F3, F4 was significantly decreased from baseline to post-training night [$t(9) = 2.97$, $p<.02$]. On the other hand, there was no change in the number of Stage 2 spindles observed at the central sites. The same pattern was seen for total NREM sleep. There was a very modest increase in number of spindles during Stage 3/4 ($p < .08$) at the central sites.
Conclusion: The post-training time that included a night of sleep was clearly more beneficial to memory consolidation than an equal time awake. The results are unique in reporting reductions in numbers of sleep spindles at frontal sites following successful declarative task acquisition.
Support (optional): Natural Sciences and Engineering Research Council of Canada (NSERC)

1090

IMPACT OF REM SLEEP DEPRIVATION AND DREAMING ON EMOTIONAL ADAPTATION TO NEGATIVE STIMULI

Lara-Carrasco J,[1] Nielsen T,[1] Paquette T,[2] Solomonova E,[3] Stenstrom P,[1] Levrier K,[4] Maliha G,[4] Dallaire S[4]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) Centre d'étude du sommeil, Hôpital du Sacré-Coeur, Montreal, Quebec, Canada, (3) McGill University, Montreal, Quebec, Canada, (4) Universite de Montreal, Quebec, Canada

Introduction: While REM sleep and dreaming are widely associated with emotional adaptation (EA) in clinical studies, experiments using emotional induction have produced contradictory results. We assessed the impact of REM sleep deprivation and dream emotions on EA to standardized, negative picture stimuli.
Methods: 28 subjects (21 W; 25.39±4.65 yrs) slept one adaptation and one experimental night after randomization to high (HRSD; N=15) or low REM sleep deprivation (LRSD; N=13) groups. Awakenings were forced after 5 min into successive REMPs for HRSD and after 25 min for LRSD. One hr prior to sleep, subjects viewed sets of 36 neutral and 36 negative pictures and evaluated emotions with: 1-9 scales measuring valence (negative-to-positive) and arousal (weak-to-strong), and 1-5 scales measuring intensities of 9 emotions. The task was repeated 1 hr after morning awakening. EA% change scores were calculated for valence ((morning-evening)/9*100) and intensity ((evening-morning)/9*100). Subjects rated dreams collected after experimental awakenings for emotions using the same scales. Four oneway ANOVAs for valence and intensity of neutral and negative pictures assessed HRSD vs. LRSD differences on EA% scores. Subjects were also split into high-EA (HEA) and low-EA (LEA) groups and compared. MANOVAs with 9 dream emotion scales as dependent variables assessed HEA vs. LEA dream differences.
Results: HRSD and LRSD groups differed only by a trend ($F(1, 26)=2.39$, $p=.134$) showing greater EA-arousal to negative pictures for HRSD (15.31% vs. 2.85%). A multivariate trend for dream emotions distinguished LEA and HEA groups split on EA-valence, negative pictures (Trace=.52, $F(9, 17)=2.05$, $p=.09$). Sadness was the only univariate effect ($F(1,25)=15.32$, $p<.006$) with less sadness for HEA dreams (1.07 vs. 2.01).
Conclusion: Findings replicate earlier work using negative pictures but go further to suggest that dreaming itself may play a role in the process of regulating negative emotions across the night.
Support (optional): Canadian Institutes of Health Research

1091

WOMEN WITH VASOSPASTIC SYNDROME EXHIBIT DIFFICULTIES INITIATING SLEEP AND TURN THEIR EXPERIENCED ANGER INWARDS

Von Arb M,[1] Gompper B,[1] Fontana P,[1] Vollenweider S,[2] OrgüL S,[3] Flammer J,[3] Zemp Stutz E,[4] Krauchi K[1]
(1) Psychiatric University Clinics, Basel, AE (Europe), Switzerland, (2) Psychiatric University Clinic Basel, Basel, AE (Europe), Switzerland, (3) University Eye Clinic Basel, Basel, AE (Europe), Switzerland, (4) Institute of Social and Preventive Medicine University of Basel, AE (Europe)

Introduction: Primary vasospastic syndrome (VS) is a functional disorder of vascular regulation in otherwise healthy subjects, mostly in women, with cold hands and feet as leading symptoms. Epidemiological, ambulatory and controlled laboratory studies show evidence for a close relationship between VS and difficulties initiating sleep. Anger/aggression problematic is known to correlate with vascular dysregulation as well as with sleep disturbances. The aim of the study is to elucidate whether women with VS exhibit a higher level of anger/aggression than controls.
Methods: 146 women were recruited from participants of a larger survey in a random population sample of Basel-Stadt (Kräuchi *et al.*, APSS, 2005) filling in detailed postal questionnaires on sleep behavior, thermal discomfort, anger and anger expression. Women with VS and controls (CON) were classified using questionnaire-derived scores (feeling of cold hands and feet, finger color changes). Anger/aggression scores were derived from the state-trait-anger-expression-inventory (STAXI) used for dispositional state (S-A), trait anger (T-A), and for anger expression. Anger expression consists of three subscales: Anger-In (A-I), Anger-Out (A-O), and Anger-Control (A-C).
Results: In comparison to controls (N=84), women with VS (N=62) showed significantly higher VS –scores (2.85±0.06 vs. 1.60±0.03units) and increased sleep onset latency (SOL; 23.2±2.3 vs. 14.7±1.6min) ($p<0.05$, t-test). S-A, T-A, A-O and A-C did not differ between the groups, however, VS showed significantly higher values of A-I than CON (15.5±0.6 vs. 13.7±0.5units). Multivariate backward stepwise regression analysis controlling for BMI, age and smoking revealed high VS -score as the most significant predictor for high A-I. In turn, among these variables, high A-I is the best predictor for long SOL.
Conclusion: In this sample, high VS –score is not only associated with long SOL but also with high A-I, indicating a possible role of anger/aggression problematic in the genesis of VS and difficulties initiating sleep.
Support (optional): "Research supported by the SNF Grant # 3100A0-102182 to K.K. and the Schwickert-Stiftung"

1092

A DAYTIME NAP FACILITATES RELATIONAL MEMORY

Lau H,[1] Fishbein W[2]
(1) City University of New York System, New York, NY, USA, (2) City University of New York System, NY, USA

Introduction: Sleep has been shown to facilitate consolidation of declarative memory. Furthermore, hippocampal processes during wakefulness appear to play a critical role in extracting relational information common to distinct memory traces in animal and human studies. The same hippocampal processes are hypothesized to be operative during sleep as well. The present study investigated the effect of a daytime nap on performance of a relational memory task.
Methods: Participants learned two lists of face-object photograph pairs (AB and BC tasks) separately. The objects (B) were common to both

lists but paired with two different faces. After either a daytime nap or a period of wakefulness, participants were tested on a force-choice task (AC task), in which they had to associate faces previously paired with the same object, followed by retests of AB and BC tasks.
Results: An ANCOVA, with the average score of AB and BC tasks at baseline as the covariate, revealed that the nap group (n = 18) performed better on the AC task than the wake group (n = 17) (F = 4.502, p = 0.042). A repeated-measures ANOVA on average performance on AB and BC tasks found near significant interaction between condition (nap/wake) and time of test (baseline/test)(P < 0.09).
Conclusion: The results suggest sleep facilitates processes that reorganize and form relational links among discrete memory traces that share common elements.

1093

SEX DREAMS: WHAT DO MEN AND WOMEN DREAM ABOUT?

Zadra A
Universite de Montreal, Montreal, Quebec, Canada

Introduction: Given the longstanding clinical and popular interest in sexual dreams, it is surprising that only two studies, both completed over 40 years ago, have described the relative frequency and content sexual dreams. The aim of the present study was to conduct a detailed investigation of the actual nature and content of sexual dreams across a large sample of dream reports from men and women.
Methods: Participants were 109 women (mean age = 29.8 ± 12.2 years) and 64 men (mean age = 30.4 ±14.2 years). They recorded their home dreams in a daily sleep log for 2 to 4 weeks. Dream reports were scored on a variety of scales including the nature of sexual activity, characters, setting and affect.
Results: Participants reported a mean of 20.6±10.8 dreams for a total of 3564 dream reports. 45% of the men and 41% of the women reported one or more sexual dreams for a total of 292 sexual dreams, or 8.2% of all reports. Sexual intercourse was the most common type of sexual content, followed by sexual propositions, kissing, and fantasies. Masturbation accounted for approximately 6% of both male and female´s sexual dreams and an orgasm was experienced in approximately 4% of all sexual dreams. Negative affect characterized 15% and 20% of men and women´s sexual dreams, respectively. Men´s sexual dreams were more likely to take place in public or unknown settings, to have the dreamer initiate sexual contact, and to involve unknown characters or multiple partners.
Conclusion: Approximately 8% of everyday dream reports from both men and women contain some form of sexually-related activity. Viewed in the context of the continuity hypothesis of dreaming, gender differences in the content of everyday sexual dreams may reflect people´s waking needs, experiences, attitudes and concerns with respect to sexuality.
Support (optional): Research supported by a grant from the Social Sciences and Humanities Research Council of Canada.

1094

INTERACTIVITY IN A VIRTUAL MAZE TASK ENHANCES DELAYED INCORPORATIONS OF MAZE FEATURES INTO DREAM CONTENT

Nielsen T,[1] Saucier S,[2] Stenstrom P,[3] Lara-Carrasco J,[4] Solomonova E[5]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) Universite de Montreal, Quebec, Canada, (3) Université de Montréal, Quebec, Canada, (4) L'hôpital du Sacré-Coeur de Montréal, Montreal, Quebec, Canada, (5) McGill University, Quebec, Canada

Introduction: Salient spatial or social events influence dream content occurring the next night (day-residue effect) and about a week later (dream-lag effect). Using a virtual maze task, we studied the effects of a spatial stimulus on both of these effects by varying two stimulus attributes: interactivity (active, passive) and visual display (virtual reality: VR, television: TV).
Methods: 57 healthy subjects (45W; 24.46±3.25 yrs) underwent a 20-min 3D maze task in one of 4 conditions: 1) VR-Act (n=15): interacted with the maze using VR goggles; 2) VR-Pas (n=14): passively viewed the maze using VR goggles; 3) TV-Act (n=15): interacted with the maze on TV and using a mouse; 4) TV-Pas (n=13): passively viewed the maze on TV. Subjects then rated task-related sense of presence and cybersickness. For 14 days, subjects recorded dreams and rated each (9-pt scale) for incorporations of maze elements. To maximize N, scores were averaged over 2 successive days, producing 7 post-maze time periods per subject: D1-2, D3-4, D5-6, D7-8, D9-10, D11-12 and D13-14. Mean incorporation was also calculated (D1-14). 2 X 2 ANOVAs (interactivity X display type), assessed changes in incorporation by condition; polynomial curve-fitting assessed fluctuations over time.
Results: An Interactivity main effect (F(1,53)=3.9493, p=0.052) revealed higher D1-14 for Active (M=2.10 „b 1.42) than for Passive (M=1.50, b 0.64) groups. Bimodal polynomials with approximate circaseptan morphology characterized both VR-Act (3rd-order; Rsq=.989) and TV-Act (4th-order; Rsq=.962) groups. VR-Act peaks were D1-2 and D9-10; TV-Act peaks were D3-4 and D11-12. Lagged cross-correlation between the two curves (r=.566, p<.05) suggested a 1-day delay of the entire circaseptan process for TV-Act. The latter was also associated with more cybersickness symptoms (p<.07). Day-residues (D1-2) only were found for Passive conditions.
Conclusion: Interactivity facilitates delayed dream incorporations with an approximate circaseptan morphology. However, overstimulation (producing cybersickness) may delay this process.
Support (optional): Canadian Institutes for Health Research and the Natural Sciences and Engineering Research Council of Canada

1095

INTRODUCTION OF THE RAT-PSYCHOMOTOR VIGILANCE TASK (RPVT): VIGILANCE IMPAIRMENTS PRODUCED BY ADENOSINE PERFUSION IN THE BASAL FOREBRAIN.

Christie M,[1] Chen L,[1] Bolortuya Y,[1] Lee E,[2] McCarley R,[3] Strecker R[1]
(1) Harvard Medical School & VA Boston Healthcare System, Brockton, MA, USA, (2) Bio-Pharmaceutical, SK Corporation, Brockton, MA, USA, (3) VAMC and Havard Medical School, Brockton, MA, USA

Introduction: The consequences of sleep loss on vigilance/sustained attention are well documented. Sleep disturbance from disease, vocational demands, or experimental design result in a marked impairment in tasks requiring sustained attention. Parallel work has provided substantial evidence that adenosine (AD) is a mediator of the homeostatic sleep drive. For example, AD infused into the basal forebrain (BF) increases sleep, whereas A1 receptor antagonists promote wakefulness. In order to address the role of BF AD in attention deficits caused by sleep disruption we infused AD into the BF of rats trained to perform a novel animal analogue of the widely used human psychomotor vigilance task.
Methods: The rPVT is an animal analogue of the human psychomotor vigilance task (PVT), widely used in sleep research to assay attention. Rats were trained to respond to short (0.5s), but unpredictable, light flashes at a central location with a nose-poke into the water delivery port mounted directly below the light. As in the human PVT, response latency is the primary measure of performance; other measures include: premature response errors (responding during the inter-trial interval),

and omissions (`lapses´ in the human literature). 300μM of AD or aCSF vehicle were bilaterally perfused via microdialysis for two hours immediately prior to rPVT task performance.
Results: Response latencies were significantly slower in the session immediately after AD perfusion when compared to both baseline (no drug) and sessions following aCSF perfusion. Similarly, omissions increased after AD sessions, but not after baseline or aCSF sessions. In contrast the number of premature response errors decreased markedly after AD sessions, but not after baseline or aCSF sessions. The behavioral effects observed will be compared to similar effects produced by sleep deprivation, and to the increase in sleep produced by the AD perfusion in the BF.
Conclusion: Elevation of AD in the BF induces vigilance deficits analogous to those induced by sleep disruption in both rats and humans. The combined data suggest that AD elevation in the BF produces an increase in sleepiness.
Support (optional): This research was supported by NIH HL060292, NIMH 39683, NIMH 40999, Dept. of Vet. Aff.

1096

DAYTIME NAPS, MOTOR MEMORY CONSOLIDATION AND REGIONALLY SPECIFIC SLEEP SPINDLES

Nishida M,[1] Walker M[2]
(1) Beth Israel Deaconess Medical Center, Boston, MA, USA, (2) Harvard University, Boston, MA, USA

Introduction: Increasing evidence demonstrates that motor-skill memories improve across a night of sleep, and that non-rapid eye movement (NREM) sleep commonly plays a role in orchestrating these consolidation enhancements. Here we show the benefit of a daytime nap on motor memory consolidation and its relationship not simply with global sleep-stage measures, but unique characteristics of sleep spindles at regionally specific locations, mapping to the corresponding memory representation.
Methods: Two groups of subjects trained on a motor-skill task using their left hand – a paradigm known to result in overnight plastic changes in the contralateral, right motor cortex (Walker *et al.* 2005). Both groups trained in the morning and were tested 8hr later, with one group obtaining a 60-90 minute intervening midday nap (PSG monitored), while the other group remained awake.
Results: At testing, subjects that did not nap showed no significant performance improvement, yet those that did nap expressed a highly significant 15% consolidation enhancement ($p<0.001$). Within the nap group, the amount of offline improvement showed a significant correlation with the global measure of stage 2-NREM sleep ($r=0.55$). However, topographical sleep spindle analysis revealed more precise correlations. Specifically, when spindle activity (density and spectral power) at the central electrode of the non-learning hemisphere (left) was subtracted from that in the learning hemisphere (right), representing the homeostatic difference following learning, strong positive relationships with offline memory improvement emerged ($r=0.64$) – correlations that were not evident for either hemisphere alone.
Conclusion: These results demonstrate that motor memories are dynamically facilitated across daytime naps; enhancements that are uniquely associated with electrophysiological spindle events expressed at local, anatomically discrete locations of the brain, where sleep-dependent plastic changes have previously been discovered (Walker *et al.* 2005).
Support (optional): NIMH, AASM

1097

EMOTIONAL MEMORY TRADE-OFFS OCCUR PREFERENTIALLY DURING SLEEP

Payne J,[1] Stickgold R,[2] Walker M,[2] Kensinger E[3]
(1) Harvard University, Cambridge, MA, USA, (2) Harvard University, Boston, MA, USA, (3) Boston College, Chestnut Hill, MA, USA

Introduction: People often remember central, emotional information at the expense of background details. An example of this trade-off is the "weapon focus effect", where victims vividly remember an assailant´s weapon but have little memory for the scene´s background. However, it is unknown how this effect develops over time, or whether a period of sleep would effect the consolidation of these memories differently than a period spent awake.
Methods: Seventy-two participants studied scenes containing a negative or neutral object embedded in a background scene. These scenes were studied at 9AM or 9PM. Memory for objects and backgrounds was tested (1) after 12 daytime hrs spent awake, (2) after 12 hr including a night of sleep, or (3) in the morning or evening, just 30 minutes after training.
Results: Emotional items were better remembered after sleep than wake ($p < .01$). Measures of forgetting showed a 10% deterioration of emotional items after sleep, which was no different than that occurring after just 30 minutes (also 10%), indicating that there was no further loss of memory in the sleep condition; however, after 12 hr of wake, these items deteriorated by nearly 25%, a value that was significantly greater than that seen in the 30-min and sleep conditions ($ps < .05$). Across all groups, emotional objects were well remembered at the expense of background details. But importantly, this trade-off was more pronounced after sleep than after an equivalent period of wake ($p < .05$).
Conclusion: We demonstrate that human emotional memory develops differentially across time delays containing sleep and wake. Sleep appears to facilitate the process of emotional memory enhancement, and to strengthen the trade-off of memory for central emotional objects over their background details. Thus, sleep may act to selectively enhance those aspects of a memory that are of greatest apparent value to the organism.
Support (optional): This study was supported by the Harvard Mind, Brain and Behavior Interfaculty Initiative (MBB) to JDP, NIMH 48832 to RS, and the National Science Foundation to EK.

1098

"DEPRESSIVE" RAT´S LEARNING UNDER THE ACTION OF AMITRIPTYLINE

Maisuradze L,[1] Gogichadze M,[1] Mgaloblishvili-Nemsadze M,[1] Lortkipanidze N,[1] Darchia N,[1] Gvilia I,[1] Emukhvari N,[2] Oniani N,[2] Basishvili T[2]
(1) I.Beritashvili Institute of Physiology, Dept. Neurobiology of Sleep and Wakefulness Cycle, Tbilisi, Georgia, (2) I.Beritashvili Institute of Physiology, Tbilisi, Georgia

Introduction: Although numerous comprehensive studies have been devoted to investigate REM-sleep involving in memory processing, conflicting evidences are still exhibited. More or less consensus is that REM-sleep reductions with amitriptyline (AM) impair memory processing. Since AM is widely used in the treatment of depression, the goal of the present work was to determine an influence of AM on the learning in "depressive" rats.
Methods: Twenty four adult male Albino "depressive" rats (weight 230-300 g) were selected according to the Porsolt Method. The animals were trained in one-session (120 trials) two-way active avoidance (AA) test. Before an acquisition the experimental rats (n=12) were

intraperitoneally injected with AM (5 mg/kg) while the controls (n=12) - with Ringer solution. After 24 hour, the animals of both groups were re-tested for retention. The learning criterion was considered as nine correct responses, i.e. avoidance reaction only on acoustic stimuli, of ten consecutive trials. The results were analyzed by t test.
Results: AM-treated rats were quick learners and proved to be superior to the controls; they required significantly less trials (44.25;SD=2) to achieve the learning criterion as compared to control (91.5;SD=19.4) animals. In the re-testing session the both group reached the criterion faster than in the learning session; the number of the trials required for the criterion achievement decreased in control (17;SD=3.2) and AM-injected (14.25;SD=1.4) rats. Although control animals reached the criterion slowly, group difference between experimental and control rats in the amount of trials in retention was not statistically significant.
Conclusion: AM does not disturb AA learning and retention in "depressive" rats; the facilitation of acquisition in AM-receiving group may be explained by an enhancement of the exploratory activity and decrease of fear reaction that were observed in the open-field test. We suggest that REM-sleep reduction seen with AM is not related to memory impairment.

1099

THE CONCEPT OF NORMAL SLEEP HELD BY THE GENERAL PUBLIC

Lack L
Flinders University of South Australia, Adelaide, South Australia, Australia

Introduction: Unrealistic expectations about sleep may contribute to the development of insomnia and are addressed in cognitive/behavior therapy for insomnia. If, for example, one strongly believed that 7-8 hours of solid sleep were necessary for good health, then perceived awakenings would increase psychophysiological activation and insomnia. Therefore, it is important to assess whether the general public´s concept of healthy sleep is realistic.
Methods: A sample of convenience was obtained (N=250, mean age = 38.5(14.4) years) quasi randomly with the aid of trained student assistants. Interviewees were asked to plot the sleep pattern across a typical night of sleep for a healthy, young adult. With pen or pencil they plotted a continuous curve from lights out time to final out-of-bed time as the X axis. Wakefulness and sleep at varying depths was the Y axis. The continuous curve for each participant was then digitised with one of four different values (0=wake, 1=light sleep, 2=moderate, 3=deep sleep) at 15 half-hourly time points. Mean curves for the whole sample and separately for the older participants (>40 years age, N=101) were calculated. The number of intermediate peaks (a lightening of sleep followed by subsequent deepening before awakening) was also calculated.
Results: The mean curve for the total sample showed a highly significant ($F=132$, $p<.0001$) U-shape with nadir at moderate to deep sleep midway through the sleep period. Seventy percent showed the U-shape curve with no intermediate peaks. Only 4% indicated an actual awakening before final awakening. The older group showed almost an identical pattern with only 2% indicating an awakening in healthy sleep.
Conclusion: The predominant public conception of healthy sleep is that of an uninterrupted deep sleep. Perceived awakenings would be anxiety producing and lead to insomnia. Therefore, public education about the normality of light sleep phases and awakenings may be protective against the development of insomnia.

1100

HUMAN RELATIONAL LEARNING: GIVE IT TIME, AND SLEEP.

Ellenbogen J,[1] Hu P,[1] Payne J,[2] Walker M[1]
(1) Harvard University, Boston, MA, USA, (2) Harvard University, Cambridge, MA, USA

Introduction: Human relational memory – the ability to extract and generalize across existing stores of information – is a fundamental cognitive faculty. Little is known, however, about how and when this `inferential knowledge´ emerges. Here we explore the hypothesis that human relational learning develops offline, specifically during sleep.
Methods: Fifty-six healthy young participants initially learned five pairs of items in random order, on pair at a time, called `premise-pairs´ (i.e. A>B, B>C, C>D, D>E, E>F). Unknown to the subjects, the premise pairs contained an embedded meta-structure (i.e. A>B>C>D>E>F). Following an offline delay of either 20-min, 12-hr (wake or sleep), or 24-hr, knowledge of the hierarchy was tested, including inferential judgments for novel pairs (e.g. B>D, C>E, B>E).
Results: All groups performed similarly on premise-pair retention (all > 85%), which are considered the building blocks of the meta-structure. There was a striking dissociation, however, in subjects´ ability to make inferential judgments: the 20-min group showed no evidence of inferential ability (52%; i.e. chance), while the 12-hr and 24-hr groups displayed highly significant inferential ability (both >75%; $p<0.001$). Most interestingly, if the 12-hr period contained sleep, rather than wake, relational memory for the most distant and difficult inferences received an additional boost (i.e.B>E pair; Sleep=93%, Wake=69%, $p=0.03$).
Conclusion: Here we demonstrate that human relational learning specifically develops during offline time delays. Furthermore, sleep appears to preferentially facilitate this process, enhancing and binding hierarchical memory, thereby allowing superior performance (+35% advantage) for the most difficult inferential judgments.
Support (optional): This study was supported by the National Institutes of Health (NIH) and the American Academy of Sleep Medicine (AASM).

1101

EFFECTS OF SLEEP INERTIA ON FINE MOTOR PERFORMANCE

Hageman J, Christou E, Rodgers J, Wright K
University of Colorado at Boulder, Boulder, CO, USA

Introduction: Steadiness and accuracy of fine motor control have important safety implications for personnel required to perform immediately upon awakening, such as medical personnel using surgical instruments or security personnel firing a weapon. We tested the hypothesis that sleep inertia would impair fine motor function.
Methods: Sixteen healthy, drug free, right-handed subjects (13 women, 3 men) aged 21.8±3.8 (Mean±SD) were tested in the laboratory on two occasions approximately one week apart. Participants were randomly assigned to nap and no-nap conditions and tested using a repeated measures, counterbalanced, within subject research design. Sleep was scored from C3xA1. Subjects performed two fine motor control tasks using a force transducer (Entran Sensors and Electronics model ELW-D1-20L, Fairfield, NJ) held between the right index finger and thumb. The first task required subjects to match a target force for 2-min and the second task required subjects to pinch the force transducer to match a trace of a parabola drawn on an oscilloscope screen. Steadiness was assessed by the coefficient of variation of force during the matching task and pinch force accuracy was assessed by the deviation from target force for both force tasks. Statistics used included repeated measures

ANOVA with Hunyh-Feldt correction for sphericity and modified Bonferonni correction for planned comparisons.
Results: Performance testing began on average 73±16 sec after EEG verified awakening. Sleep inertia significantly impaired finger movement precision. Specifically, we found significant reductions in steadiness and pinch force accuracy immediately upon awakening from sleep (all p<0.018). Steadiness and accuracy improved across time such that fine motor performance was not significantly different between the nap and the no-nap conditions 15 min after awakening.
Conclusion: Sleep inertia impaired fine motor performance indicating that central and/or peripheral mechanisms that control fine motor function are altered upon awakening from sleep.
Support (optional): Research Supported in part by NIH AG024621, NIH AG024662 and by a grant from the Undergraduate Research Opportunities Program and the Howard Hughes Medical Institute in collaboration with the Biological Sciences Initiative at the University of Colorado at Boulder.

1102

DOES ONE WEEK OF SLEEP EXTENSION IMPACT EATING BEHAVIOR IN HEALTHY YOUNG ADULTS?

Peszka J,[1] Harsh J,[2] Mastin D[3]
(1) Hendrix College, Conway, AR, USA, (2) University of Southern Mississippi, Hattiesburg, MS, USA, (3) University of Arkansas at Little Rock, Little Rock, AR, USA

Introduction: There is growing evidence of a relationship between obesity and curtailed sleep possibly mediated in a number of ways including shortened sleep leading to increased eating. Eating behavior in free-running humans is influenced by a variety of factors; however, it has not been shown experimentally that prior sleep or sleepiness are related to actual food intake. We examined whether one week of extended sleep can produce declines in eating in healthy young adults.
Methods: 32 healthy university students (19-24 yrs) trained by a registered dietician kept daily food and sleep diaries for three weeks during summer break. Baseline sleepiness (Epworth Sleepiness Scale) and hunger (Three Factor Eating Questionnaire) were assessed. Participants slept and ate normally for weeks 1 and 3 and remained in bed at night 2 additional hours during week 2. Sleepy (ESS≥11) and nonsleepy (ESS≤ 8) participants who extended sleep for at least 30 minutes per night (N=16) were used in the analyses.
Results: Baseline sleepiness was positively correlated with baseline average daily caloric (r(14)=.425;p<.05) and carbohydrate consumption (r(14)=.559;p<.05) but not hunger; these relationships were replicated in week 3. Participants significantly extended sleep from 7.2 to 8.5 hours per night during week 2, and returned to normal sleep during week 3 (F(2,42)=73.55; p<.05). A 2X3 ANOVA showed no significant interaction between sleepiness (sleepy and nonsleepy) and sleep duration (weeks 1,2,3). Participants ate significantly fewer calories during sleep extension compared to weeks 1 and 3 (294 and 291 fewer calories/day respectively). Sleepy participants consumed more calories compared to nonsleepy participants, although this effect only approached significance (p=.067).
Conclusion: We suggest voluntary curtailment of sleep below sleep need leading to daytime sleepiness may be related to increased food consumption. Extending sleep as little as 30 minutes per night could produce significant declines in food intake.

1103

TYPE A PERSONALITY AND RESILIENCE TO NEUROBEHAVIORAL IMPAIRMENT FROM SLEEP LOSS

Sherman M, Webber S, Tucker A, Belenky G, Van Dongen H
Washington State University, Spokane, WA, USA

Introduction: There is a trend to extend daytime activities into the night to gain productive time (“colonization of the night”, Melbin, 1987). Type A individuals are, by definition, especially prone to such behavior. Generally, though, people differ considerably in the extent to which they can maintain optimal performance during extended wakefulness. We examined whether Type A individuals are more likely than others to be resilient to neurobehavioral performance deficits from loss of sleep.
Methods: 20 healthy adults (ages 22–40y; 11 females) spent eleven consecutive days in a sleep laboratory. They were exposed to three 36h total sleep deprivation periods, each preceded and followed by two extended nighttime sleep periods (12h TIB). During two of the sleep deprivation periods, subjects completed a 30min neurobehavioral performance battery every 2h. The battery included the Karolinska Sleepiness Scale (KSS), which yielded a subjective sleepiness score, and the Psychomotor Vigilance Test (PVT), for which the number of lapses (RT>500ms) was determined. These data were averaged within subjects across the last 24h of each sleep deprivation. Prior to the experiment, subjects filled out the Survey of Work Styles, which yielded their overall Type A scores. The relationship between these and subjects´ KSS and PVT responses was assessed with mixed-effects analysis of covariance.
Results: Means and standard deviations for Type A scores in this sample were almost identical to published norms. No significant relationships were found between Type A scores and KSS scores (F[1,20]=1.66; P=0.21) or PVT lapses (F[1,20]=0.24; P=0.63).
Conclusion: There was no evidence that Type A personality is associated with resilience to neurobehavioral impairment from sleep loss. Thus, while extending wakefulness into the night may be particularly attractive for Type A persons to gain productive time, in general these individuals are not invulnerable to performance deficits resulting from sleep loss.
Support (optional): NIH grants HL70154 and RR00040; congressionally directed funding W81XWH-01-0099.

1104

BODY IMAGE IN DREAMS OF WOMEN DURING PREGNANCY

Sabourin C,[1] Dimillo J,[2] De Koninck J[1]
(1) University of Ottawa, Ottawa, Ontario, Canada, (2) University of Ottawa, Ontario, Canada

Introduction: Recently, there has been a growing interest in the relationship between dream content and a personality dimension reflecting “thin” and “thick” boundaries (Hartmann, 1998). We attempted to further explore this phenomenon by investigating dreams during pregnancy. As this period leads to major physical changes and is known to be psychologically challenging (Johnson, Burrows, & Williamson, 2004), we hypothesized that dreams of pregnant women, compared to those of non-pregnant women, would reflect these upheavals and would contain more elements suggesting fragility of body boundaries.
Methods: Twenty-eight participants (14 pregnant women, 14 non-pregnant women) completed a morning dream diary during a ten-day period. Twenty-five dreams were randomly selected for each group. All dreams were coded by two raters using a body image scale devised by Fisher (1986) measuring two categories of elements: (1) Barrier elements, reflecting body boundaries´ definiteness (e.g., enclosing

structures, containers, coverings) and (2) Penetration elements, reflecting body boundaries´ fragility (e.g., damaged or destroyed objects, body openings). Interrater reliability was .70 to .78 for both scales.
Results: Of the 50 dreams reported by both groups, 37 (74%) contained penetration elements, and all dreams contained barrier elements. As expected, the dreams of pregnant women contained significantly more penetration elements than the dreams of non-pregnant women ($p<.001$). No difference was observed between groups for barrier elements. Furthermore, these results were not dependent on the length of the dreams reported in each group.
Conclusion: These results support the notion that dream content is guided by the dreamer´s dominant emotions and concerns, such as body changes in the context of pregnancy.

1105
THE RELATION OF SLEEP TO SERIAL REACTION TIME LEARNING
Porte H, Bussard M
Cornell University, Ithaca, NY, USA

Introduction: The putative relationship of sleep to memory consolidation has been studied extensively. Results have sometimes appeared to conflict. It is generally accepted, however, that Stage 2 sleep as defined by the presence of full-fledged sleep spindles or K complexes may support the consolidation or enhancement of certain kinds of motor procedural learning. The relation of sleep to classically defined serial reaction time (SRT) learning--both implicit and explicit--remains to be elucidated. The present study investigates the role of sleep in consolidating or enhancing procedural (implicit) SRT learning vs. conscious (explicit) SRT learning. The study addresses two questions: First: Does sleep positively affect either motor procedural or explicit SRT learning? Second: Is sleep systematically affected by either implicit or explicit SRT learning?
Methods: The SRT task as used by Reber & Squire to dissociate implicit from explicit learning in temporal lobe amnesics was adapted according to the subsequent design of Schendan and colleagues. To adjust for the capabilities of normal college student subjects the task was initially piloted with subjects who did not sleep in the lab. Experimental subjects were then randomly assigned to "implicit" or to "explicit" SRT conditions. After one baseline night of sleep, subjects returned to the lab to complete either the implicit or the explicit SRT task, followed by a night of undisturbed sleep and retesting in the morning.
Results: The cognitive agility of college student subjects necessitated a number of test protocol adaptations in order to reliably dissociate explicit from implicit SRT learning. With test conditions revised accordingly, preliminary results from sleep subjects suggest that a night of undisturbed sleep enhances both nonspecific and targeted implicit SRT learning. Results for the explicit SRT condition, and any effects of learning on parameters of sleep, remain to be analyzed.
Conclusion: Preliminary data analysis suggests that sleep may enhance implicit SRT learning.

1106
DOES INTROVERSION/EXTRAVERSION PREDICT RESILIENCE TO COGNITIVE IMPAIRMENT FROM SLEEP LOSS?
Webber S, Sherman M, Tucker A, Belenky G, Van Dongen H
Washington State University, Spokane, WA, USA

Introduction: It has been demonstrated that inter-individual differences in resilience to cognitive impairment from sleep deprivation constitute a trait, and several groups have begun searching for predictors of this trait. However, the identification of predictive markers is hampered by a lack of knowledge about the underlying mechanisms. Without theoretical guidance and statistical safeguards, searches for predictors risk becoming "fishing expeditions" with increased likelihood for chance findings. Replication is therefore especially important in this context. Here we investigate the replicability of the recent claim that introversion/extraversion predicts responses to sleep deprivation on the Psychomotor Vigilance Test (PVT).
Methods: 20 healthy adults (ages 22–40y; 11 females) spent eleven consecutive days in a sleep laboratory. They were exposed to three 36h total sleep deprivation periods, each preceded and followed by two extended nighttime sleep periods (12h TIB). During two of the sleep deprivation periods, every 2h subjects completed a 30min neurobehavioral performance battery which included a 10min PVT. The number of lapses (RT>500ms) for every test bout was averaged within subjects across the last 24h of each sleep deprivation period. Prior to the experiment, subjects filled out the Eysenck Personality Inventory (EPI) and the Myers Briggs Type Indicator (MBTI), which both yielded an introversion/extraversion personality score. The relationship between subjects´ scores and their PVT responses to sleep deprivation was assessed with mixed-effects analysis of covariance.
Results: No significant relationships were observed between PVT lapses and introversion/extraversion on the EPI ($F[1,20]=0.19$; $P=0.66$) or the MBTI ($F[1,20]=0.04$; $P=0.84$).
Conclusion: The recent finding that introversion/extraversion predicts resilience to cognitive impairment from sleep loss was not replicated in our study (despite ample statistical power). This highlights the importance of examining the generalizability of candidate predictors for resilience to sleep deprivation.
Support (optional): NIH grants HL70154 and RR00040; congressionally directed funding W81XWH-01-0099.

1107
DYSFUNCTIONAL SLEEP COGNITION AND VULNERABILITY TO STRESS-RELATED SLEEP DISTURBANCE
Chou C,[1] Yang C,[2] Chen J[3]
(1) National Cheng-Chi University, Department of Psychology, Taipei, Taiwan, Taipei City, Taiwan, (2) National Cheng-Chi University, The Research Center for Mind, Brain, and Learning, Taipei, Taiwan, Taipei City, Taiwan, (3) National Cheng-Chi University, Taipei City, Taiwan

Introduction: Dysfunctional sleep cognition has been shown to be a contributing factor in chronic insomnia. Its effect on the sleep of individuals without insomnia is less studied. The vulnerability to stress-related sleep disturbance is proposed to be an individual trait that sets the stage for the development of insomnia. The aim of the present study is to explore the association between dysfunctional sleep cognition and trait vulnerability to sleep disturbance, in order to understand the role of sleep cognition in the predisposing trait of insomnia.
Methods: Participants consist of 364 college students without reported insomnia. The Ford Insomnia Response to Stress Test (FIRST) and the

10-item version of the Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-10) were administered.
Results: The total score of the DBAS-10 correlated moderately with the FIRST score (r=.38). Nine DBAS-10 items correlated with the FIRST score. The beliefs about control and predictability over sleep showed higher correlations with the FIRST score, as indicated by item 10 (r=.42), item 8 (r=.28), and item 5 (r=.23). The beliefs about negative consequences of poor sleep is also associated with the FIRST, as indicated by item 7 (r=.25), item 7 (r=.22), item 9 (r=.22), and item 3 (r=.22). The dysfunctional beliefs about sleep needs (item 1: r=.14) and sleep-promoting practices (item 4: r=.13; item 2: r=.09) yielded non-significant to low correlations with the FIRST score.
Conclusion: The beliefs about the need to control and predict sleep as well as the consequences of poor sleep may have developed quite early along with the trait vulnerable to the development of insomnia. The dysfunctional cognitions about sleep need and sleep-promoting practices did not correlate well with stress-related insomnia, and may develop later on in the process of becoming chronic insomnia.
Support (optional): This study is partially supported by the National Science Council of Taiwan (Grant No. NSC95-2413-H-004-020-MY3).

1108

THE IMPACT OF PRE-SLEEP LEARNING ON PAIRED ASSOCIATE WORD RECALL IN 8TH GRADE GIRLS

Colrain I,[1] Reeve L[2]
(1) SRI International, Menlo Park, CA, USA, (2) The Girls' Middle School, Mountain View, CA, USA

Introduction: There is growing evidence that procedural memory recall is enhanced if learning is timed to occur before a period of sleep. Good sleep habits have also been correlated with academic performance in middle-school aged children. The present study tested the hypothesis that pre-sleep learning would enhance long-term recall of paired associates.
Methods: 35 8th grade girls (aged between 12 and 14 yrs) from the Girls' Middle School, were given 10 minutes to learn lists of 20 unrelated word pairs under two conditions: immediately prior to sleep (S) and early in the morning (W). Recall tests were taken at 10 minutes and approximately 9 hours after learning (i.e. the following morning for S, and the late afternoon for W). Order of conditions was counterbalanced. Subjects were retested on both lists without prior warning approximately 1 week later. Short-term and long-term forgetting scores were computed.
Results: Data were obtained from 26 girls where the time difference between the 9-hour and 10-minute tests varied by less than 2 hours between S and W. Two-factor (condition x time) ANOVA of the forgetting scores indicated a significant effect of time ($p < .001$), with more long-term than short term forgetting; and a significant condition by time interaction ($p < .01$). Post-hoc t-tests indicated that short-term forgetting was significantly less in S (W 2.2± 3.3 vs. S 0.4 ± 3.7 words, $p < .05$), but long-term forgetting was less in W (W 7.8 ± 5.4 vs. S 10.5 ± 4.9 words, $p < .05$). Evaluation of long-term forgetting in all 35 subjects confirmed this effect (W 7.7 ± 5.5 vs. S 9.8 ± 5.4 words, $p < .01$)
Conclusion: The data indicate that in 12-14 year-old girls, pre-sleep learning of word pairs is associated with less forgetting when recall is 8-10 hours post-learning, but more forgetting long-term.

1109

THE EXPRESSION OF HIPPOCAMPALLY DEPENDENT LEARNING IN NREM SLEEP AND ITS RELATION TO SLEEP MENTATION: TRACE VS. DELAY CONDITIONING

Wamsley E,[1] Antrobus J[2]
(1) The City College of New York; now at The Center for Sleep and Cognition, Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA, USA, (2) The City College of New York, New York, NY, USA

Introduction: Though substantial evidence indicates that consolidation of declarative memories is facilitated by hippocampally mediated "replay" of experience during NREM , little empirical work has addressed the speculation that dreaming may represent a cognitive component of this processing. Here, we experimentally induced hippocampus-dependent memory reactivation during NREM and observed the effects of this manipulation on EEG and heart-rate conditioned responses (CRs), as well as on reports of sleep mentation.
Methods: "Trace" conditioning, where the CS and UCS are separated by a temporal gap, is a hippocampally dependent task which provides a simple model of declarative memory. In contrast, "Delay" conditioning proceeds independently of hippocampal involvement. Prior to sleep, subjects underwent either Trace or Delay differential auditory fear conditioning. The conditioned stimulus cue (CS+) and a control cue (CS-) were then presented to subjects during stage 2 NREM sleep. Mentation reports were elicited following each cue presentation. It was hypothesized that both Delay and Trace participants would exhibit CRs during sleep. Furthermore, it was hypothesized that in Trace, but not Delay participants, physiological CRs would be accompanied by concomitant effects within sleep mentation reports.
Results: Both Delay-conditioned and Trace-conditioned participants exhibited conditioned responses (CRs) during post-training sleep. Brief (<5 sec) EEG arousals were more likely to occur in response to the CS+ than to the CS- in both Trace and Delay participants (main effect of cue type: $F1,35=6.21$, $p=.02$). Trace participants also exhibited conditioned K-complex responses ($t17=2.05$, $p=.05$). In Trace-conditioned participants, where CRs were hippocampally-mediated, emotional valence of mentation reports was significantly more negative in response to the CS+ as compared to the CS- cue, on early trials ($t17=2.66$, $p=.02$).
Conclusion: These findings support the hypothesis that hippocampally dependent declarative learning can be accessed during NREM sleep, and suggest that hippocampally mediated memory reactivation directly influences qualitative characteristics of ongoing sleep mentation.

1110

DREAMS AND SLEEP PATTERN IN WOMEN WITH BULIMIA NERVOSA

Anelli M,[1] Fantini M,[1] Erzegovesi S,[2] Bellodi L,[2] Ferini-Strambi L[1]
(1) Sleep Disorder Center, Department of Neurology, Università Vita-Salute San Raffaele, Milan, Italy, (2) Eating Disorder Center, Department of Psychiatry, Università Vita-Salute San Raffaele, Milan, Milan, Italy

Introduction: Few studies have investigated the dream content in eating disorders, mainly in a descriptive fashion. The aim of the present study was to quantitatively assess the dream characteristics and sleep pattern in patients with Bulimia Nervosa compared to healthy control subjects.
Methods: Twenty female patients diagnosed with BN according to DSM-IV (mean age: 21.7±7.0yrs., range:16-46yrs.) and 20 age and sex-matched control subjects entered the study. Subjects were asked to recall most recent dreams; verbatim dream descriptions were recorded and

scored according to the Hall and Van De Castle method (1966). Coded dreams were processed by dreamSAT software and differences in dream categories were evaluated by means of Cohen´s "h" statistic. Furthermore, the two groups were asked to fill the Typical Dreams Questionnaire, the Pittsburgh Sleep Quality Index and the Composite Scale of Morningness.
Results: A total of 104 and 150 dreams were collected in BN and controls, respectively. BN patients had more "dream with male characters" (70%vs.53%, p=0.002) and lesser "dreams with friend characters" (22%vs.43%, p<0.01) than controls. BN patients had fewer "dreams with friendly interactions" (42%vs.61%, p=0.006) but also lesser "dreams with at least one aggression" (22%vs.44%, p=0.005). Fewer BN patients had "dreams with at least one sexuality element" (4%vs.11%, p<0.03). Eating themes were present in more than one third of BN dreams (31.7%) and only in 7.3% of controls (p<0.0001). Among typical dreams, "to eat some delicious food" and "to be suffocated or fail to breath" were more frequently reported in BN than controls (p=0.001 and p=0.018) as well as that of "a person now dead being alive" (p=0.003). BN group reported a more disturbed sleep (PSQI:8.8±4.8vs.4.4±2.9;p=0.012) with poorer habitual sleep efficiency (0.8±01.1vs.0.4±0.8;p=0.005), more frequent hypnotic use on the previous month (1.2±1.3vs.0.05±0.2;p=0.01), a higher frequency of sleep disorders (1.4±0.6vs.1.0±0.4;p=0.001) and a higher daytime dysfunction over the last month (1,7±1,1vs.0,8±0,6;p=0.001) compared to controls. Finally, BN patients were found to be more "morning-type" than controls (34.3±8.9vs.30.3±4.5;p=0.003).
Conclusion: Dream content appear to be altered in BN. Dream characteristics in patients with BN, as well as poor sleep quality and morningness circadian typology, may be related to peculiar psychopathological aspects or to overeating-induced biological changes. Future longitudinal studies will assess the changes in dream contents brought by therapeutic interventions and/or weight gain.

1111

REM PRESSURE MAY BE DISTURBED IN IDIOPATHIC NIGHTMARE SUFFERERS

Paquette T,[1] Nielsen T,[2] Stenstrom P,[2] Lara-Carrasco J,[2] Solomonova E,[3] Bourdeau G[4]
(1) Hopital du Sacre-Coeur de Montreal, Montreal, Quebec, Canada, (2) Universite de Montreal, Montreal, Quebec, Canada, (3) McGill University, Quebec, Canada, (4) Universite du Quebec à Montreal, Quebec, Canada

Introduction: The pathophysiology of idiopathic nightmare disorder remains unknown. Non-traumatized nightmare sufferers were subjected to a partial REM deprivation protocol and attributes of their REM sleep compared with that of non-nightmare controls.
Methods: Nightmare sufferers (NM: n=13; 10W; M=26.5±9.5yrs) and controls without nightmare complaints (CTL: n=12; 8W; M=25.6±7.0yrs) slept in the laboratory for 3 consecutive nights. Only results for night 1 are reported here. REM sleep variables were assessed with standard criteria by a trained polysomnographer. REM latency, average REM/NREM cycle duration, REM fragmentation, REM efficiency, total time in REM, sleep onset latency, sleep efficiency, time to persistent sleep (10 min uninterrupted sleep) and # `skipped´ REM periods were compared for NM and CTL groups using chi-squares and one-way ANOVA.
Results: The NM group showed longer REM latency (M=129.3±66.7min) than the CTL group (M=78.2±28.6; F(1,23)=6.010, p=0.022) and longer REM/NREM cycle duration (M=117.1±30.7 min) than the CTL group (M=88.2±14.5min; F(1.23)=8.806, p=0.0069) but no differences on other assessed variables. However, these differences were potentially explained by the fact that more NM sufferers skipped first (6/13), second (3/13) and third (1/13) cycle REM periods (total: 6/13) than did CTL subjects (2/12; 0/12; 0/12; 2/12 total; chi-sq=2.49, p<.11). Therefore, analyses were repeated excluding all REM period `skippers´. NM `non-skippers´ (n=7; 4W; 27.0±10.0yrs) nevertheless still scored higher on REM latency (NM: M=83.5±17.5min, CTL: M=67.8±8.1min; F(1,15)=6.258, p=0.024) and REM/NREM cycle duration (NM: M=99.95±12.98min, CTL: M=84.25±9.09min; F(1,15)=8.679, p=0.0100) than did CTL non-skippers (n=10; 7W; 24.4±5.6yrs).
Conclusion: REM sleep pressure, especially early in the night, is reduced in non-traumatized nightmare sufferers compared to controls. While such a reduction may enable skipping early-night REM periods, it may also—and independently—lengthen REM latency and cycle length. Such REM pressure dysregulation may also underlie occasional bouts of high REM pressure later in the night and contribute to nightmare formation at this time.
Support (optional): Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council of Canada

1112

COGNITIVE PERFORMANCE AND SLEEP IN AIR FORCE ACADEMY CADETS AND OFFICERS

Pinchak A,[1] Kajdasz J,[1] Dyche J[2]
(1) US Air Force Academy, CO, USA, (2) United States Air Force Academy, USAFA, CO, USA

Introduction: Sleep deprivation causes a decline in cognitive functioning, impairment in vigilance, and increases in both depression and anxiety. Previous studies have illustrated that sleep deprived adolescents, similar in age to cadets at the United States Air Force Academy, have lower cognitive functioning compared to the well-rested (Carskadon, 2002). The need for vigilance, decision making, and other cognitive functions is crucial to the military. As a training ground for future officers in the Armed Services, the objective of this study is to measure sleep and cognitive performance of senior cadets compared to 2nd Lieutenants in the United States Air Force.
Methods: Fifteen Cadets and thirteen 2nd Lieutenants wore an actigraph for one week and recorded their sleep habits in a journal for the duration of the week. Participants also completed three cognitive performance tests daily throughout the course of the study on a hand held palm pilot using the ANAM performance battery. Cadets and officers were closely age-matched.
Results: No significant differences were found between officers and cadets. All were sleeping far less than the recommended amount for this age group.
Conclusion: Our officers did receive, on average, more sleep than cadets but was not significant due to much greater variance compared to cadets. None slept for an appropriate amount of time for this age category. We are concerned about the potential climate of sleep deprivation at our military college that may extend into an operational theater. We suggest replicating with larger N or using older officers (older than 26) who have adult patterns of sleep verses the adolescent pattern which persists through the early 20s.
Support (optional): Defense Advanced Research Projects Agency (DARPA).

1113

SCHOOL SLEEP/WAKE HABITS AND SCHOOL ENGAGEMENT AMONG ETHNICALLY DIVERSE ADOLESCENTS

Daly B,[1] Sloane T,[2] Collins B,[1] Postolache T,[3] Weist M[2]
(1) Temple University, Philadelphia, PA, USA, (2) MD, USA, (3) National Institutes of Health (NIH), MD, USA

Introduction: Shortened total sleep time, and late bed and rise times during the school week have a significant negative impact on adolescent´s academic performance (e.g., grades). Little research, however, has investigated the relationship between these sleep/wake variables and school engagement among ethnically diverse adolescents. Examining school engagement is important as it may be one of the most important factors for student success in school, particularly among economically disadvantaged adolescents living in an urban environment.
Methods: The present study examined the sleep patterns and school engagement among 96 racially diverse inner-city adolescents (male 57%, female 43%) enrolled in ninth grade and between the age of 14 and 17 years old. The ethnic diversity of the sample includes African-American (66%), Caucasian (20%), Multi-racial (7%), Hispanic (3%), Asian-American (1%), and `Other´ (3%). All participants completed the School Sleep Habits Survey as part of this study. Linear regression analysis was performed between school night bedtime, school day rise time, total school night sleep time, and school engagement.
Results: Hierarchical linear regression analyses indicated that self-reported total sleep time significantly predicted school engagement (β = 1.16; t = 3.05; p = .003). None of the other school week sleep variables (school night bedtime or school day rise time) were predictive of school engagement. The analysis yielded an R2 = .10 of explained variance in school engagement, indicating that 10% of the unique variance is accounted for by total sleep time, above and beyond demographics (gender and ethnicity).
Conclusion: Adolescents reporting more total sleep time on a school nights indicated higher school engagement scores. Overall, these results are consistent with previous research demonstrating an association between school sleep/wake variables and academic grades among adolescents. These findings suggest a need to address total sleep times in ethnically diverse populations in order to help these adolescents achieve optimal school engagement.

1114

NIGHTMARE AND BAD DREAM FREQUENCY: DIFFERENTIAL IMPACT OF TWO PROSPECTIVE LOG MEASURES.

Robert G, Zadra A
Universite de Montreal, Montreal, Quebec, Canada

Introduction: Prospective dream logs are now considered the gold standard for assessing the nightmare frequency. These daily logs have one of two formats: questionnaire (e.g., subjects indicate if there was dream recall and if so, the number and type of dreams recalled) and narrative (e.g., a complete written transcript is provided for each dream recalled). Our goal was to compare the frequency of nightmares and bad dreams obtained with these two types of logs.
Methods: Participants were 260 undergraduates (228 women, 32 men, 22.8±5.2 years) who completed a dream log for 2-5 consecutive weeks. 203 participants completed a questionnaire log and 57 a narrative log. All participants had to indicate if a recalled dream was a bad dream or a nightmare. Bad dreams were defined as very disturbing dreams that do not awaken the dreamer and nightmares as very disturbing dreams that awaken the sleeper. Given varying log durations, log frequencies were prorated to one year for comparative purposes. Total dream recall per week was also calculated.
Results: T-tests revealed that a significantly greater frequency of nightmares was reported in the prospective narrative logs (17.1±20.2) than in the prospective questionnaire logs (8.9±15.6). Similarly, a significantly greater frequency of bad dreams was reported in the narrative logs (45.1±44.6) than in the questionnaire logs (29.2±38.4). The mean number of dreams recalled per week was also significantly greater in the narrative logs (7.9 ± 2.8) as compared to the questionnaire logs (6.1±3.5). All ps < .05.
Conclusion: This was the first study to compare dream recall frequency data between two types of prospective logs. When compared to questionnaire logs, narrative logs consistently yield higher frequencies of everyday dreams, nightmares and bad dreams. This difference may be due to an attentional bias related to the greater time involvement required to complete narrative logs.
Support (optional): Research supported by the Social Sciences and Humanities Research Council of Canada.

1115

EVIDENCE THAT REM SLEEP THETA TROUGH ACTIVITY DEPOTENTIATES SYNAPSES: HIPPOCAMPAL PLACE FIELD BACKWARD SKEWNESS DURING SUBSEQUENT WAKING

Booth V,[1] Riley B,[2] Poe G[1]
(1) University of Michigan, Ann Arbor, MI, USA, (2) University of Michigan, MI, USA

Introduction: We tested the hypothesis that reactivation of hippocampal neurons during REM sleep strengthens synapses associated with novel memories and weakens synapses associated with consolidated memories. Place field backward skewness, when the hippocampal place field center of mass shifts to earlier track positions, is thought to be a result of long term potentiation (LTP) during exploration. Reset of place field skewness must occur between running sessions since the process is not incremental between sessions. Neural stimulation timed to theta troughs resets LTP (depotentiation). Dominant theta trough activity occurs exclusively during REM sleep and only for cells with place fields in familiar, well consolidated environments. Novel place cells fire at REM sleep theta peaks, consistent with maintenance or strengthening of LTP. We proposed that if REM theta trough and peak firing cause depotentiation and LTP of place field synapses, then novel place fields would not reset and would fail to show backward skewness the next day. However, familiar field cells that fire at theta troughs during REM sleep should reset the place field center of mass to enable skewing to occur the following day.
Methods: We recorded from multiple single unit hippocampal CA1 pyramidal cells while rats ran on an initially novel 8-box maze for 5 days and while they subsequently slept for 4 hours each day.
Results: Place cells fired at theta peaks during REM the first 2 days, then transitioned to theta troughs. Place field skewness did not occur after the population fired at theta peaks in REM, but did after REM trough firing.
Conclusion: REM sleep theta peak firing was associated with maintained backward skewness whereas REM trough firing preceded recovered place field backward expansion the next day. These data are consistent with the hypothesis that theta peak REM activity maintains LTP and trough activity depotentiates hippocampal synapses.
Support (optional): MIH-MH60670 and the Department of Anesthesiology. Special thanks to Jack C. Lyons, Ph.D. for suggesting this study.

1116

THE EFFECTS OF SLEEP INERTIA ON AUDITORY PSYCHOMOTOR VIGILANCE AND WORKING MEMORY

Jung C, Wright K
University of Colorado at Boulder, Boulder, CO, USA

Introduction: Sleep inertia has been reported to produce significant impairments in alertness, visual vigilance and cognitive function. In general, the time course of performance improvement after awakening is greatest in the first 10 minutes followed by smaller improvements to asymptote ~2h after awakening. It is unknown if auditory vigilance is impaired by sleep inertia and if so, how does the recovery of performance for auditory vigilance compare to that for other tasks. Thus, we compared the effects of sleep inertia on auditory vigilance, using an auditory version of the Psychomotor Vigilance Task (aPVT), and on working memory, using a mathematical addition task (ADD) known to be sensitive to sleep inertia.
Methods: Thirteen healthy participants (7 men, 6 women), aged 28.69±9.17 (Mean±SD), were scheduled to sleep 8h per night for three weeks at home, verified by diaries, time stamped call-ins, and by actigraphy for at least one week. After living in the laboratory for three days with sleep scheduled at habitual bedtime, subjects were awakened the fourth morning and performed a 2-min ADD followed by a 10-min aPVT at ~1, 20, 40, 60, 120 and 240 min after EEG verified awakening. Number correct for ADD and number of lapses and reciprocal median reaction time for aPVT were analyzed with repeated measures ANOVA.
Results: Eight subjects were awakened from stage 2 and five from REM sleep. ADD performance was worst immediately upon awakening and significantly improved with time awake ($p<0.05$); whereas aPVT performance did not significantly increase until after the first hour of wakefulness ($p<0.05$).
Conclusion: The influence of sleep inertia on performance appears to be task dependent as evident by a longer time course of recovery for auditory vigilance compared to working memory, however, it is possible that sleep inertia and fatigue due to sustained attention may also interact and contribute to the current findings.
Support (optional): Research Supported in part by NIH MH45130

1117

LATE-NIGHT REM SLEEP REBOUND IS REDUCED IN IDIOPATHIC NIGHTMARE SUFFERERS

Nielsen T,[1] Paquette T,[2] Lara-Carrasco J,[1] Solomonova E,[3] Stenstrom P[1]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) Hopital du Sacre-Coeur de Montreal, Montreal, Quebec, Canada, (3) McGill University, Quebec, Canada

Introduction: The pathophysiology of idiopathic nightmares (NM) remains unknown although a dysregulation of REM sleep pressure is likely. NM sufferers and controls were therefore subjected to partial REM deprivation (REMD) to assess the extent and distribution of their REM sleep rebound.
Methods: Non-traumatized NM sufferers (NMs: n=13; 10 W; M=26.5±9.5 yrs) and controls without nightmare complaints (CTL: n=12; 8 W; M=25.6±7.0 yrs) slept 3 consecutive nights (adaptation, REMD, recovery) in the laboratory. REMD by forced awakening began after 5 min of REM in all REMP after REM2; for CTLs, awakenings were only after 25 min of REM. Tracings were scored by trained polysomnographers using standard criteria. Total REM% was examined for nights 1 and 3 with a 2 (Groups) x 2 (Nights) ANOVA and contrasts. REM% distributed by thirds of the night was assessed with 3 identical analyses.
Results: For Total REM%, a Groups x Nights interaction ($F(1,23)=6.07$, $p=.021$) revealed that CTLs displayed a REM rebound (17.9% to 26.6%; $t(23)=6.44$, $p=.000007$) that was much greater than that for NMs (18.8% to 22.9%; $t(23)=3.15$, $p=.0045$), although the Groups contrasts were not significant. By thirds of the night, rebounds were indicated by Nights main effects for the 1st ($F(1,23)= 9.49$, $p=.005$) and 2nd ($F(1,23)=18.41$, $p=.0003$) thirds—which obtained for both Groups (all $p<.05$)—but no effect for the 3rd third. However, a Groups x Nights interaction ($F(1,23)=3.14$, $p=.089$) and significant contrast for CTLs ($t(23)=2.33$, $p=.029$) but not NMs ($t(23)=0.13$, $p=.895$) revealed a selective 3rd third REM rebound for the CTLs. Because more NMs than CTLs `skipped´ early-night REM periods (chi-sq=2.49, $p<.11$), analyses were repeated excluding all `skippers´. The pattern of results remained unchanged; NMs´ night 3 REM% even declined slightly in the 3rd third.
Conclusion: These results converge with results in accompanying abstracts to suggest that a dysregulation of REM sleep pressure exists in idiopathic NM disorder. NMs seem to fully rebound from partial REMD by the 2nd third of the night.
Support (optional): Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council of Canada

1118

OVERNIGHT SLEEP-DEPENDENT VISUAL DISCRIMINATION TASK IMPROVEMENT IS ASSOCIATED WITH WAKING AND LIGHT SLEEP

Breslin J, Fridel K, Bootzin R, Nadel L
University of Arizona, Tucson, AZ, USA

Introduction: Post-training sleep has previously been shown to be critical for improvement on the visual texture discrimination task, a type of perceptual skill learning. However, there are several discrepant findings in the literature concerning the sleep stages that are correlated with improvement.
Methods: Thirty-seven healthy 18-25 year olds were trained on a visual texture discrimination task and tested the following morning. They were randomly assigned to either a sleep group (n = 19), which had an 8-hour period of sleep during the retention interval, or a control group (n = 18), which remained awake during the retention interval.
Results: A mixed model repeated measures ANOVA revealed a significant group*time interaction ($F = 16.369$, $p < 0.0005$). The sleep group improved in performance while the wake control group got worse. Follow-up simple effects indicated that the sleep and wake groups did not differ at baseline, but the change in performance in both groups and differences between groups in the morning were significant. In addition, memory improvement in the sleep group was negatively correlated with sleep efficiency ($r = -0.592$, $p = 0.012$) and positively correlated with sleep-onset latency ($r = 0.719$, $p = 0.001$) as well as the percentage of time spent in stage 1 sleep ($r = 0.668$, $p = 0.003$).
Conclusion: Sleep is essential for improvement of visual texture discrimination skills. Interestingly, it is the time spent waking and the percentage of the night spent in stage 1 sleep that correlate with improvement in our sample, not the amount of slow-wave sleep or REM sleep.
Support (optional): Social and Behavioral Sciences Research Institute Predoctoral Graduate Research Grant, University of Arizona

1119

MODULATION OF REM SLEEP BY PLACEBO ANALGESIA MANIPULATIONS

Laverdure-Dupont D,[1] Rainville P,[2] Montplaisir J,[3] Lavigne G[1]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) AE (Canada), (3) Centre d'etude du sommeil, Hopital du Sacre-Coeur, Montreal, Quebec, Canada

Introduction: Pain perception can be modulated in some subjects (Placebo-responders, i.e. 20% or more pain intensity reduction) by heighten expectation of pain relief induced by suggestions of analgesia and sensory conditioning. The aim of this study was to evaluate the differences in sleep architecture between Placebo responders (PR) and Placebo non-responders (PNR), after evening Placebo analgesia manipulations.
Methods: 25 healthy young subjects were exposed to experimental heat pain after an inert cream was applied to the stimulation site on the left or right arm. Participants were told that the cream applied to one site was analgesic (placebo) while the other was a neutral cream (control). In the evening, all subjects were exposed to a conditioning procedure, in which the temperature of stimulation was surreptitiously lowered on the placebo site. The placebo analgesic effect was then evaluated by comparing pain ratings (visual analog scale) to the same stimulus temperatures across stimulation sites. Group 1 (n=12) was tested only in the next morning after reapplying the placebo and neutral cream while group 2 (n=13) was tested both 30 minutes after conditioning and in the next morning. Polysomnographic recording was performed in all subjects overnight.
Results: In group1, PR had reduced REM sleep compared with PNR (14.9% vs 21.47%; F(1,21)=4.69;p=0.042), whereas in group2, this difference was absent (22.54% vs 20.82%;ns). Additionally, group1 PR showed elevated stage 2 sleep (p=0.031) and reported more pain relief retrospectively (p=0.022), compared to group2 PR.
Conclusion: Results suggest that the induction of placebo effects may be associated with changes in sleep architecture. Specific changes observed in Group1 are consistent with previous studies suggesting that non-operant conditioning (here placebo conditioning) is associated with decrease in REM and increased non-REM sleep. Furthermore, increased stage 2 sleep in group1 PR might reflect better sensory learning and enhanced pain relief recall.
Support (optional): Supported by CIHR Placebo NET

1120

THE EFFECT OF SLEEP DURATION AND SUBJECT INTELLIGENCE ON DECLARATIVE AND MOTOR MEMORY PERFORMANCE

Tucker M,[1] Fishbein W[2]
(1) Beth Israel Deaconess Medical Center, Brookline, MA, USA, (2) The City College of The City University of New York, NY, USA

Introduction: The memory benefits following the first half of the nocturnal sleep period and the second half of the sleep period are fairly well understood in isolation. However, we still do not understand the nature of memory processing when early and late sleep are added together. The present study examined changes in memory following 3.5 and 7.5 hours of sleep using a declarative (paired associates-PA) and motor (number sequence learning-NSL) memory task. Additionally, subject intelligence was assessed as a potential modulator of the effect of sleep on memory.
Methods: Subjects (11 half night, 13 full night) arrived at the sleep lab at 12:30pm for a 1.5 hour intelligence testing session. After testing subjects were scheduled for one overnight in the lab. On the night of the study, subjects arrived at 9:30pm. Electrodes were applied to monitor sleep. At 10:45pm subjects performed a digit span task, followed by the PA and NSL tasks, which were counterbalanced across subjects. Subjects were either awakened after 3.5 or 7.5 hours of sleep for retest on the three memory tasks.
Results: Both groups learned all three tasks similarly (p>.2 for all tasks). At retest it was shown that both groups significantly improved (p<.01) on the PA and NSL tasks. However, the rate of improvement was similar for both groups across tasks (p>.7 or all interactions). Full scale intelligence correlated with acquisition and retrieval of all tasks, but did not correlate with improvement following sleep.
Conclusion: The results indicate that the amount of time spent asleep does not differentially affect performance improvement following sleep. Furthermore, the level of improvement on the PA and NSL tasks was very similar to recent studies assessing performance following a brief daytime nap. While intelligence predicted stronger information acquisition prior to sleep, it was not predictive of enhanced performance improvement following sleep.

1121

SLEEP PARALYSIS AND NIGHTMARES ARE BOTH RELATED TO AFFECT DISTRESS

Elizaveta S,[1] Nielsen T,[2] Stenstrom P,[3] Frantova E,[4] Lara-Carrasco J,[3] Donderi D,[1] Popova A[2]
(1) McGill University, Montreal, Quebec, Canada, (2) Université de Montréal, Montreal, Quebec, Canada, (3) Universite de Montreal, Montreal, Quebec, Canada, (4) Topological Media Laboratory Concordia University, Montreal, Quebec, Canada

Introduction: Sleep paralysis (SP) and nightmares (NM) are both REM-related parasomnias that have been linked to psychopathologies such as anxiety. Affect distress, a proposed personality trait characterized by strong emotional reactivity, reliably predicts the effects of NMs on well-being. Here we introduce a measure of SP distress and investigate its links to NMs and affect distress.
Methods: 193 participants aged 18 to 87 (mean=31.8 yrs; SD=12.85; 33.7% male; 59.1% female; 7.6% unspecified), responded to a battery of online questionnaires. All subjects reported having had at least 1 SP episode. SP distress was measured by 3 items modeled after the NM Distress Questionnaire, NM distress was assessed with a single general question and social anxiety was assessed by the 4 Liebowitz Social Anxiety Scale (LSAS) subscales, including “social interaction”, “public speaking”, “being observed” (OBS) and “eating and drinking in public”. The Other Experiences Questionnaire (OEQ), a new instrument for assessing a variety of social imagery and presence experiences, was also debuted.
Results: SP distress correlated positively with NM distress (r=.541; p<.001). Two multiple regression analyses with SP distress and NM distress as separate dependent measures and LSAS subscales and OEQ scores as predictor variables revealed similar factor solutions. SP distress had a 2-factor solution (p<.001, R=.359, 12% VAF), with the most sensitive predictor the OEQ score, followed by LSAS OBS score. NM distress also had a 2-factor solution (p<.001, R=.341, 11% VAF) with LSAS OBS score as the main predictor followed by OEQ score.
Conclusion: Distress following both SP and NM experiences is related to similar, social anxiety and social imagery, factors. More specifically, it is related to anxiety associated with being passively observed and a propensity to generate presence imagery in waking life. Thus, a common psychopathological factor may determine distress reactions central to two different REM sleep parasomnias.
Support (optional): Supported by the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council of Canada

1122

CRITICAL AND LOGICAL THOUGHT IN STAGE 2 AND REM SLEEP MENTATION

Stenstrom P,[1] Nielsen T,[1] Lara-Carrasco J,[1] Elizaveta S,[2] Osmani A[3]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) McGill University, Montreal, Quebec, Canada, (3) McGill University, Quebec, Canada

Introduction: While many dream theorists depict dreaming cognition as diminished and deficient, others maintain that higher order cognition is commonplace. The present study tests the hypothesis that while the ability to detect bizarreness within the dream environment is diminished, the ability to think logically is maintained.
Methods: Fourteen participants aged 21-32 years (M=23.4) slept an adaptation and 2 experimental nights in a sleep laboratory. For each experimental night participants were awakened four times after 10 minutes of REM or 2 sleep for mentation reports. Participants rated their sleep mentation on 9-point Likert scales for the presence and awareness of bizarreness and the logical rigor of thinking. For each participant, scores were averaged within stage to produce mean REM and mean Stage 2 scores.
Results: One-sample T-tests revealed that ratings of logical rigor (M=7.94, SD=0.87) were significantly higher than the middle value of its scale of measurement (5; t(8)=10.11, p=.001) while ratings of awareness of bizarreness (M=2.70 SD=2.27) were significantly lower (5; t(11)=.-3.64, p=.003). Thoughts were considered very logical (7, 8 or 9 out of 9) in 19 cases (91%). Of the 35 mentation reports containing bizarreness, no awareness of this bizarreness during dreaming was reported for 18 (51%); in only 2 cases (6%) was it fully appreciated. Paired T-tests found no stage differences for ratings of the degree of awareness of bizarreness (REM: M=2.46, SD=1.72; Stage2: M=3.46, SD=3.22; t(3)=-.471, p=.670) or the logical rigor of thoughts (REM: M=8.42, SD=1.20; Stage2: M=8.06, SD=0.94; t(5)=.55, p=.606).
Conclusion: The results suggest that the ability to detect bizarreness is either absent or diminished substantially in both stages of sleep, while logical rigor is preserved. Neither type of cognition seems to be differentially modulated by sleep stage.
Support (optional): Supported by Natural Sciences and Engineering Research Council of Canada

1123

SLEEP ONSET IMAGERY VIVIDNESS IS REDUCED IN REM SLEEP-DEPRIVED NIGHTMARE SUFFERERS

Stenstrom P,[1] Nielsen T,[1] Elizaveta S,[2] Lara-Carrasco J,[1] Paquette T,[3] Polotskaia A[2]
(1) Universite de Montreal, Montreal, Quebec, Canada, (2) McGill University, Montreal, Quebec, Canada, (3) Hopital du Sacre-Coeur de Montreal, Montreal, Quebec, Canada

Introduction: Little is known about the phenomenological characteristics of sleep onset (SO) imagery in subjects with nightmares (NM). However, our previous work has shown that the dreamlike quality (DLQ) of SO imagery is a sensitive indicator of prior REM sleep deprivation. In the present study, the SO imagery of NM sufferers was compared to that of non-nightmare controls (CTL) one night following a partial REM sleep deprivation procedure.
Methods: Subjects with (NM: n=11; 8 W; M=25.1±7.8 yrs) and without (CTL: n=11; 7 W; M=25.4±6.3 yrs) nightmare complaints slept in the laboratory for 3 consecutive nights. Following an adaptation night, they were partially REM-deprived (Night 2) by forced awakenings after 5 min of REM had elapsed in each REM episode after the 2nd. On Night 3, they were awakened multiple times after at least 5 sec of Hori SO stages 4 and 5 had elapsed. Subjects reported mentation and rated it for DLQ and visual intensity on 9 point scales. Scores were averaged for all trials and compared for NM and CTL groups using t-tests. Linear trends across trials were also examined.
Results: The NM group (M=3.79±1.60) reported less visually intense SO imagery than did the CTL group (M=6.26±1.42; t(10)=3.82 p=.001). They also tended to report lower DLQ (M=3.55±1.39) than did the CTL group (M=5.13±2.42; t(10)=1.88, p=.079). Across awakenings, DLQ scores increased linearly for the NM group (linear trend: F(1,8)=8.27, p =.005) but not for the CTL group (F(1,8)=.186, p =0.667).
Conclusion: This pattern of reduced SO imagery vividness after REM deprivation may be one of several indicators of dysregulated REM sleep pressure observed for these NM subjects. Accompanying abstracts report REM pressure anomalies for NM subjects (vs. CTLs) on the adaptation night (longer REM latency, longer REM/NREM cycle length, increased #skipped REM periods) as well as the post-deprivation night (lower REM rebound).
Support (optional): Supported by the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council of Canada

1124

SUBJECTIVE EXPERIENCES DURING SLEEP-ONSET PROCESS

Han H,[1] Huang Y,[1] Wu Y,[1] Tsai M,[1] Liao Y,[1] Yang M,[1] Yang C[2]
(1) National Chengchi University, Sleep Laboratory, Taipei City, Taiwan, (2) National Chengchi University, Department of Psychology, Taipei, Taiwan, Taipei, Taiwan

Introduction: The process of falling asleep consists of a continuous, interwoven series of changes that begins in relaxed drowsiness and continue through stage 1, and often into stage2. During the sleep-wake transition, we perceive the state of wake or sleep based on subjective experience, which may be inconsistent with the sleep stages determined by polysomnographic (PSG) features. Therefore, we investigated the subjective experiences at different points of sleep-onset process in order to further understand the process and to understand the subjective determinants of sleep onset.
Methods: Subjects consist of 13 college students, 7 male and 6 female. We awakened each subjects four times based on different PSG features that are associated with different points of sleep-onset process (emergence of slow eye movement [SEM], stage 1 sleep, stage 2 sleep, continuous 5 min of stage 2 sleep). A structured interview was then administered to assess their subjective experiences (e.g. sleep or not, thoughts, experience of external stimuli, emotion, orientation) prior to awakenings.
Results: Logistic regression showed that subjective perception of sleep or wake could be predicted by the ratings of the existence of thoughts and the level of control over their thoughts. These two items accounted for moderate to large portion of subjects´ judgments upon falling asleep or not (Cox & Snell R square: .55; Nagelkerke R square: .76). Furthermore, ANOVA results showed that the perception of external stimuli declined significantly from SEM to stage 1 sleep (F=3.91, P<.05), and the continuity of thinking process decreased significantly during the transition form stage 1 to stage 2 sleep (F=5.843, P= .005).
Conclusion: Our study showed that the absence of thought or the decreased control over thinking process are the primary determinants the perception of sleep during sleep-onset process. As we falling from awake into sleep, perception of external stimuli decline first while getting into stage1 sleep, and thinking process then becomes fragmented after falling into stage 2 sleep. These results consistent with the point of view that different aspects of subjective experiences changed at different

process of sleep onset. Also, thinking process is more important in determining the subjective perception of sleep than perceptual experiences.

Support (optional): N/A

Key Word Index

Term **Abstract Number**

4

5

A

B

C

D

E

F

G

H

I

N

O

P

Q

R

S

T

U

V

W

Y

Z