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Psychological and psychiatric aspects of psychogenic non-epileptic seizures (PNES): A systematic review

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ABSTRACT

Psychogenic non-epileptic seizures (PNES) are common in neurological settings and associated with considerable distress and disability. The psychological mechanisms underlying PNES are poorly understood and there is a lack of well-established, evidence-based treatments. This paper advances our understanding of PNES by providing a comprehensive, systematic review of the evidence pertaining to the main theoretical models of this phenomenon. Methodological quality appraisal and effect size calculation were conducted on one hundred forty-one empirical studies on the following aspects of PNES: life adversity, dissociation, anxiety, suggestibility, attentional dysfunction, family/relationship problems, insecure attachment, defence mechanisms, somatization/conversion, coping, emotion regulation, alexithymia, emotional processing, symptom modelling, learning and expectancy. Although most of the studies were only of low to moderate quality, some findings are sufficiently consistent to warrant tentative conclusions: (i) physical symptom reporting is elevated in patients with PNES; (ii) trait dissociation and exposure to traumatic events are common but not inevitable correlates of PNES; (iii) there is a mismatch between subjective reports of anxiety and physical arousal during PNES; and (iv) inconsistent findings in this area are likely to be attributable to the heterogeneity of patients with PNES. Empirical, theoretical and clinical implications are discussed.

KEY WORDS

Psychogenic; seizure; dissociation; somatization; trauma; psychopathology

HIGHLIGHTS

- The quality of evidence on the psychology/psychiatry of PNES is low to moderate
- The evidence for most theories of PNES is limited and often inconsistent
- Increased physical symptom reporting is a consistent correlate of PNES
- There is a mismatch between subjective anxiety and physical arousal during PNES
- Future research needs to accommodate the heterogeneity of patients with PNES

INTRODUCTION

Psychogenic nonepileptic seizures (PNES[1]) are periods of abnormal behaviour and experience typically involving impairment of consciousness, flaccid or rigid collapse and/or tremulous limb movements (Hubsch et al., 2011). Their subjective and objective manifestations superficially resemble epileptic seizures, but PNES are not associated with the abnormal electrical activity in the brain which characterises all forms of epilepsy. In view of the paroxysmal nature of both epilepsy and PNES, tests carried out between seizures (such as structural brain scanning or electroencephalography, EEG) usually fail to provide clear diagnostic pointers, and most patients with PNES are initially misdiagnosed as having epilepsy. In those with sufficiently persistent and frequent seizures a definite distinction from epilepsy is ultimately possible by the simultaneous recording of seizure manifestations using video and electrocardiography and EEG demonstrating the absence of ictal electrical changes during PNES (LaFrance, Baker, Duncan, Goldstein, & Reuber, 2013).

The overwhelming majority of PNES are reported by patients as being beyond their voluntary control, and most fulfil the diagnostic criteria of dissociative (conversion) disorder (ICD-10) or conversion (functional neurological symptom) disorder (DSM-5). Controversy exists over the most appropriate name for these events and the disorders they characterise. The term PNES is most commonly used in the recent scientific literature, as it is more specific than other terms that also encompass non-epileptic episodes with recognised physiological causes. The term is potentially problematic, however, as it makes (arguably unsubstantiated) presumptions about the etiology of these events, whilst maintaining an unhelpful narrative about the distinction between mental and physiological processes. The term "functional seizures" has been suggested as an alternative, but has not entered popular usage amongst epileptologists for whom "functional" has quite different implications to those intended within psychiatry. For that reason, we have elected to follow common practice in the field by adopting the term PNES here. We regard the term as synonymous with "dissociative seizures", "conversion seizures", "nonepileptic attack disorder" and (historically) "pseudoseizures" and "hysterical seizures".

[1] ABBREVIATIONS USED: DERS = Difficulties in Emotion Regulation Scale; DID = dissociative identity disorder; EEG = electroencephalogram; FND = Functional Neurological Disorder; ICM = Integrative Cognitive Model; MUS = Medically unexplained symptoms; PNES = psychogenic non-epileptic seizures; PTSD = post-traumatic stress disorder

Approximately 20% of patients presenting to physicians with seizures-like events receive this diagnosis (Kotsopoulos et al., 2003). PNES are one of the three commonest diagnoses in patients presenting with transient loss of consciousness. PNES are also the commonest functional (i.e., 'medically unexplained') symptom presenting to neurologists (Stone, Carson, Duincan et al., 2010). The incidence of PNES has recently been observed to be 4.9/100.000/year (Duncan, Razvi, & Mulhern, 2011). The prevalence is more uncertain, with estimates ranging from 2 to 33/100.000 of the general population (Benbadis & Hauser, 2000). PNES most commonly manifest from ages 15-30; three quarters of the patients in most series are female (Reuber, 2008), although the gender distribution of patients with PNES is more equal in certain populations (e.g., children, people with intellectual disability, older adults). A number of therapeutic interventions have been described, such as psychoeducation, relaxation, symptom control methods (such as focussing attention on fixation points outside the body), eye movement desensitization and reprocessing, identifying and managing seizure triggers, improving emotion recognition and tolerance, reducing avoidance, addressing maladaptive interpersonal patterns and narrative reconstruction of trauma memories (LaFrance, Reuber, & Goldstein, 2013). Some treatment packages have shown promise, such as those based on Cognitive Behaviour Therapy (Goldstein, Chalder, Chigwedere et al., 2010; LaFrance, Baird, Barry et al., 2014) and Psychodynamic Interpersonal Therapy (Mayor et al., 2010), but there is a lack of adequately powered, controlled studies (LaFrance et al., 2013).

Although PNES are considered a mental health condition, there is little agreement on the psychological mechanisms underlying these events. Various theories exist, with theorists citing findings that seemingly support their positions but often failing to report contradictory studies or the limitations of the studies that they do cite. There have been selective narrative reviews of the aetiology literature in this area (e.g., Baslet, 2011; Reuber, 2009) that can also be criticised on these grounds. Narrative reviews have also focused on specific aspects of the psychology/psychiatry of PNES, such as the relationship with childhood sexual abuse (Fiszman, Alves-Leon, Nunes, D'Andrea & Figuera, 2004; Sharpe & Faye, 2006), posttraumatic stress disorder (PTSD; Fiszman et al., 2004), personality disorder (Lacey, Cook, & Salzberg, 2007) and neuropsychological dysfunction (Cragar, Berry, Fakhoury et al., 2002). In each case, however, the main focus has been on reviewing the general association with PNES rather than what this might mean for theories of the phenomenon. There has also been one attempt at a systematic review (Bodde et al., 2009), which took a very broad approach covering issues such as diagnosis, semiology, treatment

and prognosis as well as aetiology. Despite this breadth, Bodde et al., (2009) identified only 93 possible articles for inclusion in their review, of which only 65 were empirical studies. As we shall see, this represents a small fraction of the literature in this area. What is more, Bodde et al., (2009) made no attempt systematically to appraise methodological quality or to calculate effect sizes. Clearly, a more rigorous evaluation of the research in this area is needed.

In the following sections, we describe the main theories of PNES and provide a comprehensive review of the psychiatric and psychological evidence pertaining to them. A systematic approach to both literature searching and quality appraisal is used, and effect sizes are provided where possible. Our goal was to evaluate what is known about the aetiology and mechanisms of PNES, to inform future theoretical, empirical and clinical work in this area.

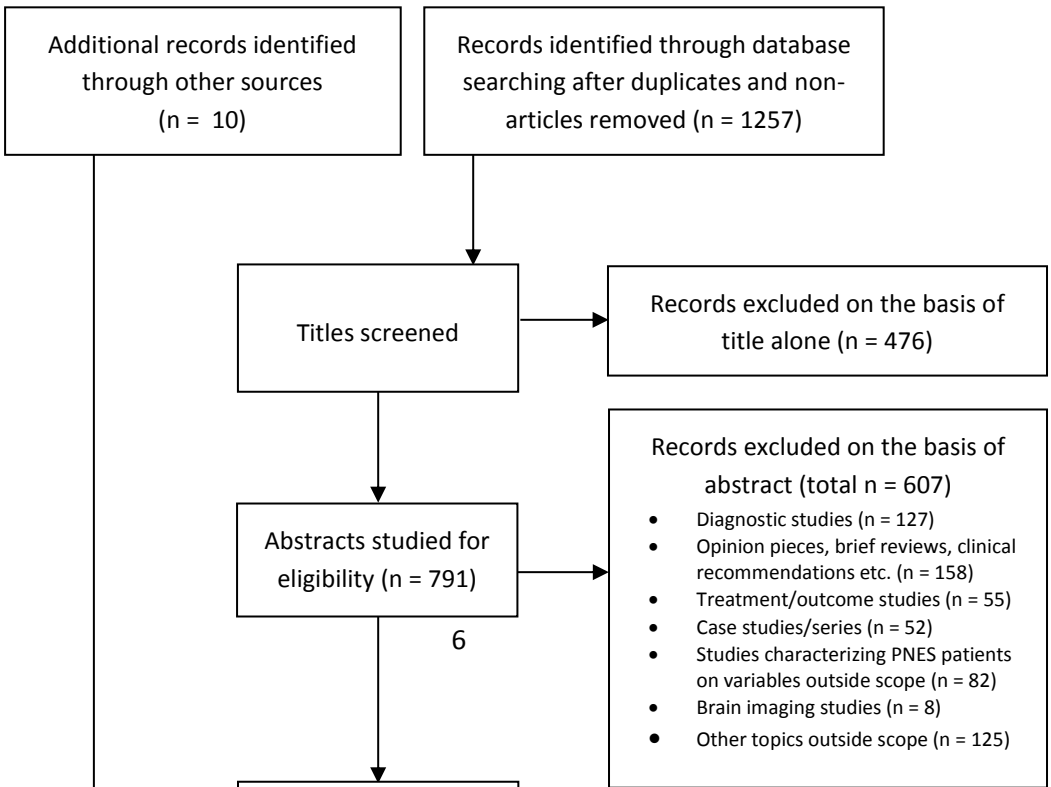
SCOPE AND METHODS OF REVIEW

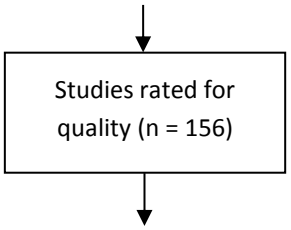
The review methods were informed by the PRISMA standards for reporting systematic reviews (Moher et al, 2009), although the PRISMA checklist and a formal review protocol were not used due to the breadth of our aims and the wide-ranging nature of the material under consideration. To capture all the relevant studies, we searched the abstract, title and keyword fields in the three most relevant databases (Ovid MEDLINE 1952 to June week 4 2015; Embase 1980 to week 27, 2015; PsycINFO 1952 to June week 5 2013), using the following terms: ((nonepileptic adj attack$) OR (non-epileptic adj attack$) OR (nonepileptic adj seizure$) OR (non-epileptic adj seizure$) OR (pseudoseizure$) OR (dissociative adj seizure$) OR (dissociative adj convulsion$) OR (pseudoepilep$) OR (hysterical adj seizure$) OR (hysterical adj convulsion$) OR (hysteroepilepsy$) OR (conversion adj seizure$) OR (psychogenic adj seizure$) OR (functional adj seizure$) OR (nonepileptic adj event$) OR (non-epileptic adj event$)) AND ((psych$) OR (aetiolog$) OR (etiolog$)).

Any papers describing research on PNES that was deemed relevant to one or more of the theories in this area were included. Only English language journal articles describing quantitative empirical studies were included in the formal review, although relevant theoretical papers, review articles and books were consulted to supplement our knowledge of the area, ensuring that all of the main theoretical approaches to PNES were covered. We excluded studies focusing on clinical features, the diagnostic process, management and prognosis, except where these were directly relevant to at least one of the theories under scrutiny. We also excluded epidemiological studies, single case studies and small N (< 15)

case series, studies on the comorbidity between epilepsy and PNES, studies on conversion disorder in general, studies on PNES in children and people with intellectual disabilities, conference abstracts, book reviews, journal notes, and journal letters. Electrophysiological and brain imaging studies were considered outside the scope of the article and also excluded.

Figure 1: PRISMA flow diagram detailing search process





Following removal of duplicates and citations from non-English language journals, paper titles were scrutinised by RB; those evidently outside the scope of the review were rejected (Figure 1). The majority of citations excluded at this stage had titles referring to case studies, research on children or intellectual disabilities, or epilepsy alone. The abstracts of the remaining articles were then checked by RB for relevance, with any paper judged as potentially relevant to the psychological mechanisms of PNES being retained for full text scrutiny, along with a small number of additional papers that were identified by checking reference lists. To ensure reliability, abstracts of excluded articles were then checked by MR and any discrepancies were discussed until agreement was reached. As the literature on childhood abuse, PTSD and neuropsychological functioning in PNES has been reviewed elsewhere, we elected not to systematically review all of the literature on those topics. Whilst retaining more recent papers on these topics, several articles predating these reviews were removed. A small number of other articles that were not considered directly relevant after closer scrutiny were also discarded.

QUALITY APPRAISAL

Papers deemed relevant for inclusion in the review after full text reading were then subjected to formal quality appraisal. In the absence of an established system for rating study quality in the field, a bespoke quality rating method was developed based on the authors' knowledge of the area and the Centre for Reviews and Dissemination guidance for

conducting systematic reviews (CRD, 2009). To establish a reliable rating system, ten articles were independently rated by the authors using the initial set of criteria, with areas of significant discrepancy being identified and the system modified accordingly. This process was repeated for two further sets of ten randomly selected papers, before a fourth set of ten was rated to determine interrater reliability using Cohen's kappa. A value of $\kappa = 0.73$ indicated substantial inter-rater agreement (Landis & Koch, 1977). The remaining empirical papers were then evaluated by RB, who highlighted uncertain ratings for subsequent discussion and agreement with MR.

The final rating system placed particular emphasis on the steps taken by researchers to identify appropriate and representative participants with PNES, based on whether (i) all diagnoses had been confirmed using video-EEG (yes/no); (ii) there was explicit reference to epilepsy having been ruled out (yes/no); (iii) there was explicit reference to a procedure that would enable the events in question to be distinguished from anxiety attacks (defined as the use of either diagnostic criteria for conversion disorder, psychiatric assessment more generally, or the presence of ictal loss of/alteration in consciousness; rated yes/no); and (iv) recruitment was consecutive (yes/no or unclear). As most studies adopted a case-control design, we also recorded the type and number of controls used and whether (a) each control group was comparable to the PNES group in terms of age and gender (defined as $\leq 10\%$ difference in the number of females and an age difference of ≤ 5 years; yes/no); and (b) explicit reference was made to PNES having been excluded in the controls (yes/no). We also recorded whether all of the dependent variables (DVs) were standardised (yes/no). As very few studies presented a formal power calculation or justification of their sample size, we opted to rate sample size adequacy with reference to the commonly-used power and effect size conventions suggested by Cohen (1988). Sample sizes for case-control studies were rated as being very poor (< 15 participants in each group; i.e., < 80% power to detect a very large effect size, Cohen's $d = 1.1$), poor (< 26 participants in each group; i.e., < 80% power to detect a large effect size, $d = 0.8$), moderate (26-63 participants in each group; i.e., $\geq 80\%$ power to detect a large effect size, $d = 0.8$) or good (≥ 64 participants in each group; i.e., $\geq$ 80% power to detect a medium effect size, $d = 0.5$), assuming a two-tailed independent t test with alpha = .05.

Ratings were then used to calculate the overall quality of the study methods, which was defined by the proportion of items given a 'yes' rating. Studies were rated as high quality if they received $\geq 80\%$ yes ratings (equating to no more than one of the methodological standards receiving a 'no' rating) and had a good sample size. Studies with 50-79% 'yes'

ratings (i.e., at least half of the methodological standards were met) with at least a moderate sample size were rated as medium quality, as were studies with ≥ 80% 'yes' ratings and a moderate sample; studies with 20-49% 'yes' ratings or a poor sample size were rated as low quality; studies with <20% 'yes' ratings or a very poor sample size were rated as unacceptable. Any unacceptable studies were disregarded in the review; all other studies were potentially eligible for inclusion but quality ratings were taken into account when drawing conclusions, with low quality studies often being disregarded when evidence from superior studies was available. Quality ratings are provided in Appendix A.

Of the 156 papers rated, 53% (n = 83) were judged to be of low quality, 35% (n=54) as medium quality, and four (3%) as high quality (see appendix B); 10% of studies (n=15) were deemed unacceptable. Nearly half of the studies rated as low quality (i.e., a quarter of the overall sample) would have achieved a medium quality rating with a better sample size. Across all studies, the median sample size was 33. The sample size was very poor in 10 (8%) of the 130 case control or experimental studies included, poor in 51 (39%), moderate in 46 (35%) and good in 23 (18%). Table 1 summarises the proportion of studies meeting individual quality criteria. The mean quality rating was 0.52, at the border of low and medium quality. A failure to explicitly mention how or whether PNES were distinguished from anxiety disorders, non-consecutive sampling and potential incomparability of PNES and control groups were particularly common problems.

Table 1: Proportion of rated studies meeting individual quality criteria (most commonly omitted first; N = 156 studies unless otherwise stated)

	No (%)	Yes (%)
Explicit reference to procedures that could allow PNES to be distinguished from an anxiety disorder	73.1	26.9
Comparability of PNES and epilepsy control groups in terms of age and gender (104 studies only)	69.2	30.8
Consecutive recruitment of PNES group	66.0	34.0
Comparability of PNES and other control groups in terms of age and gender (54 studies only**)	55.6	44.4
Explicit reference to exclusion of PNES in other control groups (54 studies only**)	50	50

Adequately powered* (130 studies)	47.7	52.3
Explicit reference to all PNES and epilepsy patients having video-EEG confirmed diagnoses	39.7	60.3
Explicit reference to exclusion of concurrent epilepsy in PNES group	33.3	66.7
Explicit reference to exclusion of PNES in epilepsy control group (104 studies)	26.9	73.1
All DVs standardised	19.9	80.1

* For the purposes of the table, adequate power is defined as at least a moderate sample size. See main text for proportions of articles meeting more specific sample size criteria. ** Some studies included more than one non-epilepsy control group, which are double counted in this figure.

We present effect sizes at the relevant point in the text. Where possible, we provide values for Cohen's d for group differences and r for correlations, either as provided or calculated using Ellis (2009). Where it was necessary to calculate Chi-squared values prior to conversion to d, we used the calculator provided by Wilson (2002). In cases where no effect size is presented this is due to a lack of relevant information in the paper in question. Following Cohen (1988), we regard d values of 0.2, 0.5 and 0.8 and r values of 0.1, 0.3 and 0.5 as representing small, medium and large effect sizes respectively. Non-significant findings with medium or larger effect sizes are highlighted to indicate issues with power.

THEORETICAL APPROACHES TO PNES

The main theoretical approaches to PNES are summarised in Table 2, along with the areas of research that are most relevant to each. We consider them in turn.

Table 2: Overview of main theoretical models and associated areas of research. N.B. The models are not mutually exclusive and evidence presented here as pertaining to one model may also apply to other models (see text for further details)

Model	Central tenets	Relevant areas of research
PNES are dissociative phenomena	PNES result from the activation of memory fragments dissociated from awareness as a result of trauma	• Trauma and PTSD • Stressful life events • Dissociation during PNES • Co-morbidity between PNES and other dissociative symptoms • Suggestibility • Attentional dysfunction
PNES serve a psychological function	PNES reflect the operation of a defensive process that prevents the individual from becoming overwhelmed by the emotional consequences of adversity	• Family/relationship problems • Insecure attachment styles • Anxiety and arousal • Defence mechanisms • Somatization/conversion • Coping styles • Emotion regulation • Alexithymia and emotional processing
PNES as a hard-wired reflex	PNES reflect the operation of hard-wired behavioural tendencies akin to the defensive reflexes seen in other animals	• Symptom stereotyping
PNES as learned behaviour	PNES are like normal behaviours that are maintained by positive and negative reinforcement	• Exposure to seizure models • Reinforcement • Effort on neuropsychological testing
PNES as disturbances of cognitive control	PNES result from the automatic activation of learnt seizure programmes, maintained by factors that increase the activation of seizure programmes or undermine inhibition of them	• Expectancy models

PNES AS DISSOCIATIVE PHENOMENA

The first detailed psychological account of the condition now called PNES was Janet's (1889) dissociation theory of hysteria, and many aspects of Janet's model are still incorporated in contemporary accounts of the phenomenon (e.g. Bowman, 2006; Kuyk, Van Dyck, & Spinhoven, 1996).The central tenet of this approach is that symptoms arise when the individual's ability to synthesise mental contents breaks down in the face of stress or intense emotion, resulting in disturbances of voluntary control, heightened suggestibility and the fragmentation (i.e., dissociation) of psychological systems. According to this account, PNES reflect the activation of memory fragments pertaining to the precipitating event. As such, they can be thought of as a kind of somatic flashback in which the individual has limited awareness that they are re-living a previous experience. Following the initial breakdown in integration, these memory fragments remain separated from awareness because of the anxiety associated with recalling them, but can be triggered automatically by internal or external cues. In this account, the likelihood of fragmentation is thought to be partly dependent on individual differences in the ability to integrate mental states more generally.

Adversity

Research concerning the prevalence of early trauma and other forms of adversity is often cited as evidence in support of the dissociation concept, reflecting the widespread belief that adversity is a necessary pre-requisite for fragmentation in Janet's model.

Potentially traumatising events and PTSD

Dozens of studies have investigated whether patients with PNES are disproportionately likely to report exposure to potentially traumatising events (including, but not exclusively, childhood neglect/abuse) and/or symptoms of PTSD. As much of this literature has been reviewed elsewhere (Fiszman et al., 2004; Sharpe & Faye, 2006), we concentrate on the main points, and only provide effect sizes and quality ratings for relevant studies published since those reviews. Most of the available studies suggest that exposure to potentially traumatic events is comparatively common in patients with PNES, although prevalence rates vary considerably. Across 32 studies reviewed by Sharpe and Faye (2006), childhood sexual abuse was reported by 33.2% of PNES patients (range 5.9-84.6%), compared to 16.6% in non-PNES comparison groups (calculated from 15 controlled studies); the combined odds ratio indicated that PNES patients were almost three times more likely to report sexual abuse than controls. Estimates of physical abuse in PNES patients ranged from

0% to 52.5% across 16 studies reviewed by Sharpe and Faye (2006), with the mean physical abuse rate (29.9%) closely mirroring the sexual abuse rate in the same studies (31.0%); no statistical comparison with physical abuse in non-PNES control groups is provided by Sharpe and Faye, however. Fiszman et al. (2004) found that 82.6% of PNES patients across seven studies reported "general traumatic events" other than abuse, compared to 62% in epilepsy patients across three studies.

Several studies have considered whether childhood emotional/psychological abuse is more common in people with PNES than other groups, with the frequency of abuse reports varying considerably according to definitions used. In all studies, emotional abuse and neglect were significantly more common in patients with PNES than both patients with epilepsy (Myers, Perrine, Lancman et al., 2013; Reilly, Baker, Rhodes & Salmon 1999; Salmon, Al-Marzooqi, Baker & Reilly, 2003; Kaplan et al. 2013) and healthy controls (Ozcetin et al. 2009; Proença, Castro, Jorge & Marchetti (2011). Effect sizes vary considerably, regardless of study quality (d range: 0.43-2.38; median = 0.63). Salmon et al. (2003) found that childhood psychological abuse was a unique predictor of diagnosis, unlike childhood physical and sexual abuse; psychological abuse no longer predicted group membership when family characteristics were controlled for, however.

In terms of PTSD, the mean percentage of PNES patients currently meeting criteria for the disorder was 38.9% (range 9-100%) across ten studies reviewed by Fiszman et al. (2004), compared to a control mean of 21.3% across the four studies that included a comparison group; only two of these found a significant difference in PTSD rates between PNES and epilepsy patients, however. Since then, Dworetzky et al. (2005) found higher rates of PTSD in veterans with PNES (n = 22) than those with epilepsy (n = 34; d = 1.32).

Although the literature seems to provide consistent support for a relationship between PNES and exposure to traumatic events, several problems with research in this area have been identified, including the use of retrospective correlational designs that do not allow causality to be inferred; the inclusion of disproportionate numbers of women in PNES samples; the use of non-standardised clinical interviews that are subject to interviewer bias (particularly when interviewers are not blind to participant group); inadequate sample matching in terms of age, social or educational background; the use of epilepsy rather than psychiatric controls groups; the use of clinical samples that are potentially unrepresentative; varying definitions of trauma; and inadequate specification and evaluation of possible mediating variables, such as family dysfunction (Sharpe & Faye, 2006). The frequent co-occurrence of different forms of abuse/trauma also obscure which, if any, aspects of trauma

are particularly relevant to PNES.

For these reasons, it is premature to draw firm conclusions about the relative prevalence of trauma exposure or its aetiological importance in the development of PNES. Indeed, it is clear that exposure to potentially traumatising events is not present in everyone with PNES, suggesting that this is neither a necessary nor sufficient condition for symptom development. It is nevertheless apparent that exposure to traumatic events is reported by many patients with PNES. Moreover, there appear to be clinical differences between patients with PNES who have and have not been exposed to traumatic events such as sexual abuse. Selkirk, Duncan, Oto and Pelosi (2008), for example, found that patients with PNES who reported antecedent sexual abuse (n = 64) had more severe attacks than those who did not (n = 112; d = 0.52), and were more likely to report histories of depression (d = 0.65), deliberate self-harm (d = 0.98), medically unexplained symptoms (MUS; d = 0.35), personality disorder (d = 0.49) and referral to secondary mental health services (d = 0.85). Similarly, Bakvis, Spinhoven, Giltay et al. (2010) found higher serum cortisol levels in sexually abused than non-abused PNES patients. As such, trauma exposure, seems to confer vulnerability to PNES to at least the same extent as to other mental health problems.

Stressful life events prior to symptom onset

A small number of studies have investigated whether PNES are triggered by stressful life events, which might be considered a necessary antecedent for dissociation in Janet's theory, even if outright trauma is not. Bowman and Markand (1999) conducted psychiatric interviews with 58 patients with PNES and identified possible precipitants in 91%. Numerous methodological problems are apparent, however, particularly the lack of a control group and the use of an unstructured, non-standardised measure more than seven years following the onset of PNES on average. The precise timing of the events in question is also unclear, and may have occurred at any time in the year prior to symptom onset.

A more systematic assessment was adopted by Binzer, Stone and Sharpe (2004), who recorded the frequency of life events in patients with PNES or epilepsy (both n = 20) shortly after initial seizure manifestation. The PNES group had significantly more life events in the 12 months prior to symptom onset, but not in the three months immediately beforehand; although we could not calculate effect sizes due to the information provided, the large relative difference in the latter suggested that this was a product of low power. The PNES group also rated their life events as significantly more negative, unexpected and difficult to adjust to. The same group of PNES patients were also found to have significantly more life

events in the year (but not the three months) prior to symptom onset than a group with motor conversion disorders (Stone, Binzer, & Sharpe, 2004), although the latter reported significantly more negative events. Taken together, these findings suggest that repeated adverse experience in the longer term may be just as relevant as acute life events.

Other studies have considered recent or lifetime stressful life events (e.g., Frances, Baker, & Appleton, 1999; Testa, Krauss, Lesser, & Brandt, 2012; Tojek, Lumley, Barkley, Mahr, & Thomas, 2000) in PNES patients, without evaluating whether they had any temporal relationship with seizure onset; as such, they say little about the development of PNES. Testa et al. (2012) found no difference between individuals with PNES (n = 40), epilepsy (n = 20) and healthy controls (n = 40) in terms of the frequency or severity of "recent" (past 12 months) or "remote" (1-5 years ago) stressful life events; there was also no difference between the PNES and epilepsy groups in terms of the distress associated with these events. In contrast, Tojek et al. (2000) found a significant difference between patients with epilepsy (n = 33) and those with PNES (n = 25) in terms of exposure to stressful life events across the lifespan (d = 0.82), although this study was rated as lower quality and may be subject to bias.

Dissociation during PNES

Surprisingly few studies have assessed whether patients with PNES experience dissociative phenomena immediately before or during their attacks. A postal survey of 100 patients with PNES found that very few were regularly aware of symptoms typically associated with dissociation at this point (Reuber et al., 2011): in response to questions about the 8 symptoms thought to be specific for pathological dissociation, the proportion of people who reported these were "always" or "frequently" present ranged from 1% to 26%, with the mean item response being 11%; in contrast, the number of people who reported that these were "never" or "rarely" present ranged from 43% to 77% (mean item response = 66.6%).

Goldstein and Mellers (2006) found that symptoms related to the individual's mental state (primarily depersonalization-derealization) during the attack were widely variable and equally frequent in their patients with PNES (n = 25) and epilepsy (n = 19), although this study was rated as low quality due to the small sample size. These authors argue that a better illustration of dissociation in their patients with PNES was the occurrence of more frequent physical symptoms of arousal during their attacks than in controls with epilepsy, coupled with comparable levels of self-reported anxiety in the preceding week. According to these authors, this pattern suggests that PNES are "a paroxysmal dissociative response to heightened arousal" (p. 616), with the lack of accompanying fear reflecting the dissociation

of distress during the attack (so-called "panic without panic"). It is unclear from Goldstein and Mellers' findings whether their participants' attacks were actually characterised by a lack of subjective fear, however, as this was not measured directly in their study. Nevertheless, Hendrickson et al. (2014) found that 82.6% of 224 patients with PNES reported four or more panic symptoms before, during or after their attacks, but comparatively few reported a fear of dying (28.1%) or losing control/going crazy (17.9%). Similarly, Galimberti et al. (2003) found that substantially more (51.6%) of their 31 patients with pure PNES exhibited autonomic signs and symptoms during their attacks than reported affective phenomena like fear (16.1%). Other fears or concerns were not specifically enquired about in these studies, however, and both studies used apparently unstandardized methods to assess panic symptoms. The large sample studied by Hendrickson et al. (2014) is nevertheless noteworthy.

Others have suggested that amnesia for ictal events is evidence of dissociation during PNES. Evidence for this comes from Kuyk, Spinhoven and van Dyck (1999), who hypnotised patients with amnesia for events occurring during epileptic or non-epileptic seizures and gave them suggestions to recall ictal material. Recall was measured before and after the hypnotic induction and compared by blind raters to videotapes or witness reports of seizures. Using this procedure, none of the 17 epilepsy patients recalled new material under hypnosis, suggesting permanent memory loss related to an ictal encoding deficit. In contrast, 17 of 20 (85%; d = 1.04) PNES patients recovered accurate seizure memories, indicating that their initial amnesia resulted from a retrieval deficit due to dissociation within the cognitive system. This study received a low quality rating, however, and alternative explanations of this finding are clearly possible (e.g., PNES participants might have deliberately withheld memories during the first retrieval attempt); should this phenomenon prove reliable and valid in replication studies, it would represent compelling evidence for dissociation during PNES.

Co-morbidity between PNES and other dissociative symptoms

One of the most commonly cited reasons for regarding PNES as dissociative phenomena has been evidence suggesting that many PNES patients describe co-morbid dissociative symptoms (e.g. Kuyk et al., 1996). Numerous studies have used the Dissociative Experiences Scale (DES; Bernstein & Putnam, 1987) to measure the occurrence of dissociative symptoms in patients with PNES and those with epilepsy (Appendix C), with both significant and non-significant group differences being reported. On average, participants with PNES score in the moderate range on the DES, broadly comparable to patients with depression (which is commonly co-morbid with PNES), and somewhat lower

than the cut-off of 30 thought to indicate a possible dissociative disorder (Van Ijzendoorn & Schuengel, 1996). Although the median between-group difference (d = 0.66) across thirteen studies suggests that some of the non-significant differences are attributable to low power, it is also possible that this effect size is inflated in studies with relatively low quality ratings. Indeed, the largest and most rigorous study in this area (Alper et al., 1997) failed to find a significant difference between 132 patients with PNES and 169 patients with complex partial epilepsy on the DES. PNES patients did score more highly than controls with epilepsy on a DES factor interpreted as measuring depersonalization-derealization, although this was attributed to a higher prevalence of childhood abuse in the PNES group.

Inconsistencies in the data aside, there are several other issues that must be considered when interpreting these findings. None of the studies in this area used psychiatric control groups, making it impossible to determine whether dissociation is unusually common in PNES patients or a feature of psychiatric illness more generally. Indeed, general psychopathology is rarely controlled for when comparing patients with PNES and controls, despite correlating highly with dissociation. In one notable exception, an association between DES scores and PNES severity/outcome became non-significant when controlling for psychopathology and other factors (Reuber, House, et al., 2003). Moreover, where elevated group means have been found on dissociation measures, there are still many patients with PNES who do not score highly.

It has also been suggested that scales such as the DES include items pertaining to at least two qualitatively different phenomena (‘detachment’ and ‘compartmentalization’), with only the latter being characterized by mental fragmentation per se (e.g. Brown, 2006; Holmes et al., 2005). As such, a low score on the DES could simply indicate a paucity of items pertaining to compartmentalization. Lawton, Baker and Brown (2008) tested this by measuring detachment and compartmentalization separately, finding a significant difference between PNES and epilepsy patients on the compartmentalization measure only (d = 0.70; detachment: d = 0.24; Total DES: d = 0.39); this was no longer significant when anxiety and depression were controlled for (d = 0.25).

Ability to integrate mental states

According to the dissociation model, patients with PNES should display a deficit in the ability to integrate mental states that contributes to both symptom development and maintenance. Although measures like the DES are often presented as indices of integrative capacity, such scales measure symptoms rather than mental functioning per se. Janet

described various manifestations of this integrative deficit, including high suggestibility and a reduction in the number of stimuli that can be attended to simultaneously; only a handful of small studies have tried to investigate these in PNES patients specifically, however.

Suggestibility: Kuyk, Spinhoven and van Dyck (1999) found significantly higher hypnotic suggestibility in their patients with PNES (n = 20) than those with epilepsy (n = 17; d = 0.85), with 55% and 11.8% of the samples (d = 1.01) scoring as highly hypnotizable respectively. Barry, Atzman and Morrell (2000) also found significantly higher scores on the Hypnotic Induction Profile (Spiegel & Spiegel, 1978) for patients with PNES (n = 47) versus those with pure epilepsy (n = 22; d = 0.50). However, Kuyk et al. found that 20% of their PNES sample fell in the low suggestible range, contradicting Janet's claim that suggestibility is a universal feature of patients with PNES. Moreover, Goldstein et al. (2000) also failed to find a significant difference between epilepsy and PNES patients (both n = 20) on a measure of imaginative suggestibility (d = -0.36). All three of these studies were rated as low quality, meaning that these findings should be interpreted with caution.

One possibility is that some PNES patients do not engage fully with suggestibility testing for fear of 'losing control' or attracting a psychiatric diagnosis; identifying and tackling such fears may allow for a more meaningful test of the proposed relationship between suggestibility and PNES in future studies. Even if such a relationship is confirmed, however, there are numerous theories of hypnosis and suggestibility that do not cite dissociation as an explanatory mechanism (see e.g. Heap, Brown & Oakley, 2004); it is therefore unclear whether elevated suggestibility would constitute strong evidence for a dissociative interpretation of PNES.

Attentional dysfunction: Following Janet, most researchers and theorists identify integration as an attentional function, but tend to be less specific about which aspects of the multi-faceted construct of attention are most relevant. Previous reviews suggest that a substantial proportion (40-50%) of PNES patients score outside the normal range on neuropsychological test batteries (Cragar et al., 2002; Reuber, Fernández, Helmstaedter, Qurishi, & Elger, 2002), with particular weaknesses in attention, working memory and executive functioning being reported by Strutt, Hill, Scott, et al., (2011). In contrast, Bakvis et al. (2009) found no difference between healthy controls (n = 20) and patients with PNES (n = 19) on the non-emotional Stroop paradigm at baseline or following a stress induction, suggesting their basic inhibitory processing was comparable. Almis, Cumurcu, Unal, Ozcan and Aytas (2013) found that patients with PNES were slower overall on a non-emotional Stroop task than healthy controls (both n = 22), but comparable cognitive interference scores

suggested no differences in inhibitory processing as such.

Using an N-back test with emotional distractors, Bakvis, Spinhoven, Putman, Zitman and Roelofs (2010) found that patients with PNES (n = 19) exhibited significantly greater interference from distracting face stimuli (both neutral and emotional faces) at baseline than healthy controls (n = 20), even when controlling for differences in self-reported anxiety and depression. Under stressful conditions, this interference effect also occurred in the absence of distracting stimuli, with the stress-related increase in interference correlating significantly with cortisol levels in the PNES but not the control group. These findings are more consistent with a general attentional deficit than emotion-specific difficulties, although the precise nature of this deficit remains unclear. One possibility is that patients with PNES fail to filter out irrelevant stimuli, consistent with reduced pre-pulse inhibition (PPI) in this group (n =17) compared to healthy controls (n = 20; Pouretemad, Thompson, & Fenwick, 1998). A problem with sensorimotor gating of non-threatening stimuli in patients with PNES compared to healthy controls (both n = 22; d = -0.89) was also found by Almis et al. (2013). It is noteworthy that all of these studies on attentional dysfunction received low quality ratings, however, suggesting that better-designed replication studies with larger samples are urgently required to verify this hypothesis.

PNES SERVE A PSYCHOLOGICAL FUNCTION

In Janet's original account of hysteria, symptoms such as PNES reflected an intrinsic propensity for psychological fragmentation (i.e., a lack of 'mental glue') that is exposed by stressful events. Since Breuer and Freud (1893-1895/1955), however, the tendency to fragment or dissociate has been described not as a deficit but as a defensive ("conversion") process that enables people to cope with overwhelming feelings, traumatic experiences and stress more generally (e.g., Bowman, 2006; Goldstein & Mellers, 2006; Kuyk et al., 1996). Since then, the idea that PNES can serve the individual in some way has been broadened to encompass a wide range of intra-psychic, interpersonal or systemic functions (e.g., Bowman & Markand, 1996; Rusch, Morris, Allen, & Lathrop, 2001; Kalogjera-Sackellares, 2004).

Psychodynamic/interpersonal correlates of PNES

If PNES serve a psychological function then we might expect individuals with PNES to have been exposed to situations where such a function would be necessary or might be expected. Evidence concerning the relationship between PNES and adversity, summarised in the previous section, provides only limited support for this hypothesis. It is possible, however, that the adversity encountered by patients with PNES is more subtle, or that patients

with PNES have an abnormally low capacity for coping with "normal" adversity.

Family/relationship problems

Several studies present data concerning potential stressors in the interpersonal environment of patients with PNES. The two studies with higher quality ratings both found evidence for family problems with managing emotions. Krawetz et al. (2001), for example, found that patients with PNES rated their families as having had greater problems with affective involvement, communication, conflict and overall functioning than patients with epilepsy (both n = 31). Similarly, Salmon et al (2003) also found evidence for lower emotional expressiveness in the childhood families of adult patients with PNES compared to those with epilepsy (n = 81) as well as greater parental over-protection and perceived control over their behaviour. No differences were found in terms of cohesion, conflict or independence, however. Further complicating the picture, a medium quality study by LaFrance et al. (2011) found no differences between patients with epilepsy (n = 32) and PNES (n = 45) in terms of perceived family problem-solving (d = 0.13), communication (-0.12), roles (-0.07), affective responsiveness (-0.09), affective involvement (0.03), behaviour control (-0.36) or general functioning (-0.19); both groups had mean ratings in the unhealthy range for the general family functioning sub-scale only.

We identified a single study (Stanhope, Goldstein, & Kuipers, 2003), albeit with a low quality rating, in which a behavioural measure was used to study relationship quality and family affective climate. A significantly greater proportion of PNES relatives were classified as exhibiting high- than low- expressed emotion (EE; 71% vs. 29%; d = 0.95), a difference that was not significant for the epilepsy relatives (53% vs. 47%; d = 0.12). Positive relationship ratings were significantly more common than negative ratings in the high-EE relatives of PNES patients, consistent with a greater frequency of emotional overinvolvement (e.g., excessive concern; pitying) for these individuals.

Insecure attachment styles

Insecure attachment with early caregivers can give rise to both interpersonal and emotional difficulties (Bowlby, 1979) and could therefore be an important psychodynamic and/or interpersonal antecedent for PNES. Holman, Kirkby, Duncan and Brown (2008) found that patients with PNES (n = 17) had significantly lower secure attachment scores than controls with epilepsy (n = 26; d = -0.67), and significantly higher fearful attachment scores (1.18); other insecure attachment styles (dismissing; preoccupied) were not elevated in the PNES group (0.38, 0.25 respectively). Fearful attachment predicted group membership in this

study even after controlling for anxiety, dysthymia and total trauma exposure. Reuber, Pukrop, Bauer, Derfuss and Elger (2004) found evidence of elevated attachment insecurity in patients with PNES (n = 85) compared to those with epilepsy (n = 64; d = 0.47) and healthy controls (n = 100; d = 0.96), but this difference was attributable to a sub-group (n = 43; d = 1.99) with high levels of psychopathology and emotional dysregulation. A similar pattern was observed by Brown et al. (2013), with a non-significant difference in attachment between their emotionally dysregulated sub-group (n = 11) and patients with epilepsy (n = 24; d = 0.63) arguably being due to low power.

Anxiety

It may be that PNES are an avoidant/defensive response to acute anxiety whatever its source, rather than to adversity per se. Some studies have found relatively high rates of comorbid anxiety disorders in PNES patients (e.g., Bowman & Markand, 1996; Direk, Kulaksizoglu, Alpay, & Gurses, 2012; Driver-Dunckley, Stonnington, Locke, & Noe, 2011; 16/22: Dworetzky et al., 2005; Scevola et al., 2013), whereas others have not (Galimberti et al., 2003; Jawad et al., 1995; Turner, Piazzini, Chiesa et al., 2011; Salinsky, Evrard, Storzbach, & Pugh, 2012); the latter includes the one study on this topic to be rated as high quality (Bailles et al., 2004). Comparisons of anxiety symptoms in epilepsy and PNES patients have also revealed a mixed picture, with only nine of 28 studies finding comparatively high levels of explicit anxiety in PNES (Appendix D). Just over three quarters of the studies that found a significant difference were of low quality, compared with just over half of the studies where a difference was not found. Across studies, the average effect size indicates that anxiety is only slightly elevated in patients with PNES compared to those will epilepsy, with scores suggesting that anxiety is often in the moderate range in both groups. It is therefore unclear whether anxiety is associated with PNES per se, or simply having a seizure disorder. It may be that the mixed findings in this area reflect the heterogeneity of patients with PNES. Indeed, Reuber et al. (2004) identified a cluster of patients with PNES who had high levels of anxiety (d = 1.50) compared to controls with epilepsy and a separate cluster who did not (d = -0.32). Another possibility is that patients with PNES are less aware of, and/or prefer not to report, their anxiety (see below).

Fewer studies have considered the presence of anxiety symptoms immediately before or during PNES themselves. In a retrospective postal survey of 100 patients with PNES, Reuber et al. (2011) found that only a minority of patients reported being regularly aware of physical or other symptoms of anxiety during their attacks: across the 14 symptoms included

in the anxiety summary score, the number of people who reported that these were "always" or "frequently" present ranged from 11% to 58% (mean item response: 25.7%); in contrast, the number of people who reported that these were "never" or "rarely" present ranged from 17 to 60% (mean item response: 40%). We saw previously that estimates tend to be much higher when data concerning the presence of ictal anxiety symptoms are collected systematically as part of the clinical assessment, although subjective fear itself is comparatively infrequent (e.g., Galimberti et al., 2003; Hendrickson et al., 2014).

With regards objective measures of arousal, Reinsberger, Perez, Murphy and Dworetzky (2012) provided some evidence for an ictal increase in heart rate during PNES (n = 41; d = 1.23) that then drops in the post-ictal phase (d = -1.31), although the authors did not indicate whether these changes were statistically significant. A similar pattern was found by Opherk and Hirsch (2002) but only for patients with convulsive attacks, where the sample size was too small to draw meaningful conclusions. The same criticism applies to the one other study (e.g., Ponnusamy, Marques & Reuber, 2012) that considered changes in objective measures of arousal in patients with PNES.

In relation to experiences immediately prior to attacks, Reuber et al. (2011) found that attacks were "always" or "frequently" associated with emotional stress in only 17% of patients in their postal-survey sample, whereas 26% said this was "rarely" or "never" the case. In this study, 26% said they always/frequently felt irritable or upset immediately before their attacks (compared to 36% who said this was rarely/never the case) and 26% indicated that they always/frequently felt anxiety or nervousness (39% said this rarely/never happened). Reuber et al. (2011) also found that seizure witnesses were more likely than patients to identify a link between seizures and emotional distress, however, suggesting that their patients' self-report might be an underestimate. The discrepancy may also reflect the different methods used in these studies, or the characteristics of the sample; Selkirk et al. (2008), for example, found that emotional triggers were more likely to be reported by patients with a history of sexual abuse (70.3% vs. 48.2%).

Taken together, these findings suggest that autonomic arousal is present before, during and/or after many PNES, resulting in a range of physiological symptoms that may be (but often are not) accompanied by subjective fear and/or distress. We have already considered the idea that PNES might be a dissociative response to intense anxiety or panic. Another possibility is that some PNES are panic attacks that are misinterpreted as seizures by inexperienced physicians. It is known that 30% of panic attacks are characterised by physical symptoms of arousal but not subjective fear (Chen, Tsuchiya, Kawakami, & Furukawa,

2009), and it is possible that some participants in studies on PNES fall into this category. In one consecutive series, Alper, Devinsky, Perrine, Vazquez and Luciano (1995), for example, found that nearly a quarter of 92 patients with a diagnosis of PNES had a psychiatric condition other than conversion disorder, of whom many met criteria for anxiety disorders that could account for their attacks. The characteristics of these patients appear to be quite different from others with PNES (Alper et al., 1995), who can be distinguished by the presence of features that are inconsistent with an anxiety disorder diagnosis (such as impairment of consciousness). It is relatively uncommon for researchers to take steps to exclude patients whose attacks might be diagnosed as anxiety disorders (Table 1), however, which is a clear problem with research in this area.

Defence mechanisms

Various characteristics of PNES patients have been posited as evidence that their symptoms serve a function, although few studies in this area have explicitly included participants with recent-onset PNES, making interpretation difficult. A handful of studies have assessed the defence mechanisms of PNES directly. Jawad et al. (1995), for example, compared 46 consecutive women with convulsive PNES and 50 female general psychiatric outpatients on an objective test of defence with generally good psychometric properties. Compared to controls, patients in the PNES group had significantly higher scores on the aspect said to indicate a repressive style characterised by denial/avoidance of threat and an unwillingness to confront problems directly ($d = 1.41$). This is probably the best direct evidence for a particular defensive style in patients with PNES, although it is unclear what proportion of the PNES patients exhibited this pattern.

Consistent with Jawad et al. (1995), Stone, Binzer and Sharpe (2004) found that patients with new-onset PNES were more likely than patients with epilepsy (both $n = 20$) to attribute their problems to somatic rather than psychological causes, and were more likely to deny life stresses, despite reporting more adverse life events prior to seizure manifestation. These findings could be seen as evidence that patients with PNES focus on their physical symptoms as a way of avoiding emotional difficulties, and are therefore invested in seeing their problems as caused by physical factors. Alternatively, they may reflect understandable concerns about their symptoms being dismissed as ‘all in the mind’ by doctors (Stone,

Binzer, et al., 2004). Indeed, Testa and Brandt (2010) found no evidence of elevated denial in their comparison of patients with PNES (n = 40), epilepsy (n = 20) and healthy controls (n = 40). Kaplan et al. (2013) also found no differences in the defensive styles of patients with epilepsy (n = 66) and PNES (n = 67; mean d = -.05). Our ratings suggest that these discrepancies are unlikely to be related to variations in study quality.

Numerous studies have compared patients with PNES and epilepsy on the MMPI, which includes a number of 'validity' scales designed to identify people who are exaggerating their symptoms, presenting themselves in an unusually positive light or responding in a defensive manner. None of the MMPI studies comparing epilepsy and PNES patients on these scales found evidence of increased defensiveness or socially desirable responding in the PNES group (Binder et al., 2000; Cragar et al., 2003; Derry & McLachlan, 1996; Hixson et al., 2006; Johnson et al., 2010; Shaw, 1966; Purdom, Kirlin, Hoerth et al., 2012; Lie scale median d = 0.04, range -0.81-0.44; denial/evasiveness scale median d = -0.06, range = -1.75-0.49). Two studies found elevated F scores in PNES patients (Locke et al., 2010; Shaw, 1966; d = 0.26 and 1.15 respectively) suggesting a tendency to exaggerate (rather than deny) psychopathology, although the remaining studies found no evidence for such a difference (median d = 0.24, range -0.07-0.27). Owczarek (2003) found that PNES patients had elevated scores on the MMPI expressive-repressive index (ERI) compared to epilepsy controls, which was cited as evidence for "inadequate defence mechanisms" in the former. However, this difference could simply reflect higher scores on the hysteria sub-scale (which contributes to the ERI) in the PNES group, rather than repression or other defences. One possibility is that these validity scales, which are indirect measures of defensiveness in general, are not a good way of assessing the use of actual defence mechanisms.

Historically, it has been suggested that the operation of defensive processes in patients with conversion disorders is indicated by an apparent lack of concern about the symptoms in question, so-called la belle indifférence. We were unable to locate any studies addressing this directly in a meaningful sample of PNES patients.

Somatization/conversion

It is often suggested that the predominant defences used by patients with PNES are somatization and conversion, both of which are characterised by a tendency to express distress in the form of physical symptoms. Numerous studies have been described as studying somatization in PNES, although almost all have measured the relative frequency of physical symptoms (besides the seizures themselves) without addressing whether these symptoms are

an expression of distress or serve some other psychological function. Moreover, in most cases, studies have used generic measures of symptom reporting without formally establishing whether the symptoms in question can be attributed to a medical disorder or are "medically unexplained". Significantly higher symptom reports in patients with PNES have been found in all sixteen studies comparing them to controls with epilepsy (Appendix E), with a medium to large effect size on average. Similar conclusions may be drawn from eight studies demonstrating between-group differences on the hysteria and hypochondriasis subscales of the MMPI (Appendix F), which largely consist of items pertaining to perceived physical health and symptoms; on this measure the differences are even more marked. These findings are remarkably consistent, despite variable study quality.

Some of these positive findings may be attributable to between-group differences in general psychopathology, although physical symptom reporting was still elevated in PNES patients in the one study where these were statistically controlled (Reuber, House, et al., 2003). Roberts et al. (2012) also found a significant difference in somatization scores between their patients with PNES and a matched group of trauma-exposed individuals with PTSD symptoms (both n = 18; d = 1.33), despite similar levels of psychopathology in all other domains. Similarly, Brown et al. (2013) found elevated somatization scores in two distinct clusters of PNES patients (n = 11 and 32) compared to epilepsy controls (n= 24; d = 1.54, 1.15 respectively), with only the former reporting more psychopathology.

The few studies that have reported the proportion of patients who exhibit MUS other than PNES suggest that these are extremely common. Bowman and Markand (1996) found that 82% of their 45 PNES patients had lifetime histories of a non-seizure conversion disorder, whereas McKenzie et al (2011) found that 70.1% of 187 patients with PNES had a history of at least one MUS, increasing to 76.5% at 6-12 month follow-up. Duncan et al. (2011) found that 57.4% of 54 new onset PNES patients had a history of other MUS, with 18.5% having "multiple" symptoms. Dixit, Popescu, Bagić, Ghearing and Hendrickson (2013; d = 0.83) and Elliott and Charyton (2014) found that diagnoses of other functional syndromes (e.g., chronic pain or fatigue, fibromyalgia, irritable bowel syndrome) and health conditions more generally were more common in PNES than epilepsy. Al Marzooqi et al (2004) found that patients with PNES rated their general health and physical functioning, as well as their pain and fatigue, as worse than patients with epilepsy (both n = 97) and a reference sample with long-standing illness. Dworetzky et al. (2005) found that 19 of 22 (86.4%) veterans with PNES had a history of chronic pain, which was more common than PTSD, anxiety, depression and substance misuse in that sample. Driver-Dunckley et al.

(2011) found reference to chronic pain in the notes of 78 of 116 (67.2%) patients with PNES. Chronic pain symptoms were also found in 77% of PNES patients studied by Ettinger, Devinsky, Weisbrot, Goyal and Shashikumar (1999), of whom 79% reported headaches; in this study, patients with persistent PNES were significantly more likely to report chronic pain than people whose PNES had resolved (96.3% vs. 58.6%). In contrast, Gazzola et al. (2012) found that headaches were mentioned relatively infrequently (7/85) in the notes of patients with PNES, whereas non-headache pain was much more common (45/85).

The presence of MUS or high symptom reports more generally are often interpreted as evidence for a defensive process in patients with PNES, particularly in the apparent absence of significant emotional symptoms. For example, the sub-group of PNES patients who exhibit a "conversion V" profile on the MMPI (i.e., elevations on the hypochondriasis and hysteria sub-scales, coupled with a smaller elevation on the depression sub-scale; see Appendix F) have been described as "somatic defenders", with "a primary difficulty with somatization tendencies in the face of significant psychological stress" (Cragar et al., 2005; p. 597). Whilst it is possible that these physical symptoms result from a defensive process, their mere presence does not constitute adequate evidence for defence. The same applies to other studies measuring "somatization" using physical symptom counts, medically unexplained or otherwise. Similarly, comparatively lower depression scores on the MMPI could simply indicate that patients with PNES have fewer problems with their mood than with their physical symptoms; it is an explanatory leap to suggest that this reflects the operation of a defensive process. In any case, significant depression is still a feature of the conversion V.

We were only able to identify a single study that explored the possible function of physical symptoms in patients with PNES more directly. Testa and Brandt (2010) used the Implicit Association Test (IAT) to investigate whether PNES patients exhibit positive covert attitudes towards sickness, which might be regarded as evidence for an unconscious motivation to adopt a "sick role". Contrary to prediction, there were no differences between PNES ($n = 48$), epilepsy ($n = 59$) and healthy ($n = 33$) groups ($d = 0.19$). Moreover, there were negative correlations between somatic complaints and health concerns on the PAI ($r = -0.36$ and -0.37 respectively) and IAT difference scores in the PNES group, indicating that patients with more physical symptoms had less positive attitudes to illness. This seems more consistent with a common sense model of illness than a psychodynamic account of PNES.

Coping styles

There is a small literature on how patients with PNES cope with stress and other

aversive experiences; this also speaks to the question of defence and the possible function of physical symptoms, although coping is generally seen as a conscious process and defence as unconscious. Myers, Fleming, Perrine, and Lancman (2013) found that 30.5% of 82 consecutive patients with PNES had elevated emotion-focused (indicating a greater tendency to cope with stressful events through emotional expression) and 25.6% had low task-oriented coping (indicating a diminished tendency to cope by confronting and solving problems). Although otherwise of high methodological quality, control data from patients with epilepsy are not provided in this study, meaning it is unclear whether it speaks to the aetiology of PNES or what it is like to live with a seizure disorder in general. Indeed, Testa et al. (2012) found no difference between patients with PNES (n = 40) and epilepsy (n =20) on 14 domains of coping (positive growth, mental disengagement, emotional venting, social support, active coping, denial, religion, behavioural disengagement, restraint, emotional suppression, substance abuse, acceptance, suppression, planning). The PNES group did score significantly lower than healthy controls (n = 40) on the planning and active coping scales, however, mirrored by patients with PNES scoring significantly lower than healthy controls (both n = 20) on planful problem solving in a separate study (Goldstein et al., 2000). Frances et al. (1999) also found that patients with PNES had significantly lower planful problem solving (d = -0.96) than healthy controls; although seemingly comparable to patients with epilepsy on this measure, the effect size (0.56) suggests that this was due to low power (all n = 30). Similarly, there was non-significant evidence for less confrontive coping (d = -0.55) and social support seeking (-0.53) in the PNES group, but little evidence for differences in self-controlling (-0.26), accepting responsibility (-0.06), reappraisal (-0.28) and distancing (-0.03). The only study that did not find a group difference on planful coping (Cronje & Pretorius, 2013) had a low quality rating and should perhaps be disregarded.

Frances et al. (1999), Goldstein et al. (2000) and Cronje and Pretorius (2013) all found significantly higher escape-avoidance in patients with PNES compared to healthy controls (d = 1.02, 0.76, 1.15 respectively). In contrast, only 15.9% of the PNES sample in Myers, Fleming et al (2013) had a heightened tendency to cope using avoidance, and people with high scores on this scale were less likely to have low positive emotions. This may reflect their measure of avoidance, which encompassed strategies that are typically seen as positive ways of coping (e.g., distraction, social activity) compared to the more maladaptive approaches captured in other avoidance measures (e.g., avoiding being with people, wishful thinking, using food, alcohol or drugs). Frances et al. (1999) found no difference (d = 0.41)

between patients with PNES and epilepsy on escape-avoidance, however, suggesting that these strategies may be shared by patients with seizure disorders regardless of aetiology. In contrast, Goldstein and Mellers (2006) found that patients with PNES (n = 25) reported significantly more agoraphobic avoidance (e.g., avoidance of travelling or being far from home alone) than patients with epilepsy (n = 19; d = 0.91), and there was a non-significant trend for increased avoidance of stimuli associated with blood injury phobia (0.60). Similarly, Dimaro, Dawson, Roberts, Brown et al. (2014) found significantly higher scores on a measure of distress avoidance in patients with PNES (n = 30) compared to controls with epilepsy (n = 25; d = 0.88). The heterogeneity of patients with PNES may help explain these inconsistencies.

Emotion regulation

Other studies have considered whether patients with PNES have difficulties regulating their emotional states, which may be a driver for maladaptive defensive or coping responses. Gul and Ahmad (2014) found that patients with PNES reported significantly more emotional suppression (d = 1.20) and less cognitive reappraisal (-1.17) than healthy controls (both n = 72), and took longer to switch from an emotional to a non-emotional face categorization task; this 'switch-cost' was correlated positively with suppression (r = 0.47) and negatively with reappraisal (-0.31) in the PNES group. The authors suggest that suppressing affect rather than engaging in reappraisal leads to a problem in disengaging attention from emotional stimuli in patients with PNES. The between-group difference in switch-cost may also be attributable to faster engagement with emotional stimuli (i.e., faster switching from non-emotional to emotional stimuli), however. Moreover, the direction of causality is unclear: problems suppressing and reappraising stimuli may be the product of quicker attentional engagement with, or slower disengagement from, emotional material. In addition, most patients with comorbid mental health problems (including somatization) were excluded from this study, raising questions about generalizability.

Reuber et al. (2004) compared patients with PNES (n = 85) or epilepsy (n = 63) and healthy controls (n = 100) on various personality traits thought to be associated with emotional dysregulation. Using cluster analysis, Reuber et al. (2004) identified two main groups of patients with PNES, the first (n = 43) characterised by high scores on all aspects of emotion dysregulation and the second (n = 37) with very similar total scores to the healthy controls but significantly lower scores in a number of domains (anxiousness, self-harm, suspiciousness, narcissism) and significantly higher compulsivity. Reuber et al. (2004)

interpreted these findings as evidence for two distinct personality profiles in patients with PNES, one characterised by emotional dysregulation and the other characterised by conforming, overly controlled behaviour; in this study, the former had significantly poorer prognoses than the latter (d = 0.56) and were more likely to have been a psychiatric in-patient (0.59). Although not compared statistically by Reuber et al. (2004), the second cluster of PNES patients scored lower than the patients with epilepsy across all aspects of emotion regulation, with particular differences in identity problems (d = -0.66), social avoidance (-0.82), suspiciousness (-0.53) and narcissism (-0.49; other scales: median d = -0.36).

Several studies have investigated emotional regulation using the Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004), which focuses on how people respond to their emotions. Roberts et al. (2012) found significantly higher total DERS scores in patients with PNES compared to trauma-exposed controls with relatively few PTSD symptoms (d = 0.97) but not controls with higher levels of PTS (-0.22; all n = 18). Uliaszek, Prensky and Baslet (2012) cluster analysed DERS scores from 55 patients with PNES and identified two sub-groups, one (n = 14) with significantly higher scores across all sub-scales. This group also had poorer quality of life and higher levels of depression (d = 1.52), anxiety (1.31), stress (1.53), dissociation (1.01) and physical symptoms (1.23). Compared to the DERS normative sample, the larger sub-group (n = 41) reported significantly fewer problems with emotional awareness or engaging in goal-directed activity, but the two groups were otherwise broadly comparable. Brown et al. (2013) also identified a group (n = 11) who scored higher than a second cluster (n = 32) of PNES patients and controls with epilepsy (n = 24) across all DERS domains apart from difficulties with emotional awareness. Both clusters had significantly higher depression (cluster 1: d = 1.58; cluster 2: d = 0.80) and somatoform dissociation (cluster 1: 1.54; cluster 2: 1.15) scores than the patients with epilepsy, although this was more marked for the first cluster, which also had higher levels of anxiety than the epilepsy group (cluster 1: 1.06; cluster 2: 0.45). There were no differences between the clusters in terms of depression, anxiety or somatoform dissociation, although the effect sizes (0.72, 0.70 and 0.41 respectively) suggest that this was a product of low power.

Alexithymia and emotional processing

The relatively low levels of psychopathology seen in some patients with PNES might be attributed to problems recognising or acknowledging affect, so-called alexithymia. Alexithymia may reflect a motivation not to recognise emotional states (e.g., because anxiety is seen as unacceptable), coupled with a tendency to suppress affect and focus on the physical

aspects of emotion. Alternatively, it may reflect an intrinsic deficit in recognising, thinking about and describing feelings. From this perspective, PNES are either symptoms of emotional arousal that the individual incorrectly attributes to a physical disorder (as in non-fearful panic attacks; see above) or a 'pressure-valve' for releasing unrecognised emotional tension.

Some studies have found no difference between epilepsy and PNES groups on measures of affective inhibition (Stone, Binzer, et al., 2004; Testa et al., 2012) or alexithymia (Tojek et al. 2000; Myers, Matzner, Lancman, Perrine & Lancman, 2013; see appendix G) on the Toronto Alexithymia Scale (TAS-20; Bagby, Parker, & Taylor, 1994). In contrast, Urbanek, Harvey, McGowan and Agrawal (2014) found that patients with PNES (n = 56) were significantly more likely than healthy controls (n = 88) to describe a tendency to control anxious (d = 0.37) and unhappy (0.43) emotional reactions but not anger (0.22). The PNES group in this study also described their emotions as significantly more overwhelming, shameful, useless, damaging and contagious (d = 1.09, 1.01, 0.52, 1.19, 0.90 respectively), but no more intense (0.30) or invalid (0.12). In addition, Novakova, Howlett, Baker and Reuber (2015) found significantly higher scores on several aspects of emotional processing in their sample of patients with PNES (n = 49) compared to healthy controls (n = 244). Furthermore, Kaplan et al. (2013) found a significant difference between patients with epilepsy (n = 66) and PNES (n = 67) on the Difficulty Identifying Feelings (DIF; d = 0.34) sub-scale of the TAS-20. With the exception of Urbanek et al. (2014), who used a healthy control group, none of the studies in this area have found between-group differences on the Externally Oriented Thinking sub-scale of the TAS-20, although the validity of this sub-scale has been questioned (e.g., Kooiman, Spinhoven, & Trijsburg, 2002).

Roughly a third of patients with PNES in the studies by Tojek et al. (2000), Myers, Matzner et al. (2013) and Wolf et al (2015) fell in the definitely alexithymic range on the TAS-20, rising to 40% in Kaplan et al. (2013; Dwivedi, personal communication, 2014); although this is higher than in the normal population, it is broadly comparable to patients with epilepsy and other medical outpatients (Taylor, Bagby, & Parker, 1997). In contrast, Urbanek et al. (2014) identified an unusually high proportion of patients with PNES (63%) in the alexithymic range, while Bewley et al. (2005) found this in both their PNES (90.5%) and epilepsy groups (76.2%). It seems likely that sampling differences are responsible for this.

One possibility is that these studies under-estimate the true importance of alexithymia in patients with PNES due to the use of controls with temporal lobe epilepsy, which has a well-documented association with emotional processing deficits (Hixson & Kirsch, 2009). Alternatively, the negative findings may be related to the heterogeneity of patients with

PNES. Brown et al. (2013), for example, found a cluster of patients (n = 11) with high levels of emotion dysregulation and psychopathology, all of whom fell in the alexithymic range on the TAS-20, and a second cluster with alexithymia scores that were comparable to patients with epilepsy, where only a third of participants were identified as definitely alexithymic. Another possibility is that patients with emotional processing deficits are unable to provide reliable self-reports of their emotional skills on self-report measures such as the TAS-20, and that other measures would yield clearer differences in PNES patients. Consistent with this, a high quality study by Reuber et al. (2011) found that caregivers of patients with PNES were more likely to perceive a link between the attacks and emotional stress than the patients themselves. Similarly, Prigatano and Kirlin (2009) found that patients with PNES (n = 23) performed significantly worse than patients with epilepsy (n = 22) on a battery of affect perception/expression tasks; individual sub-tests scores were not provided, however, and the overall study quality rating in this case was low.

Two other studies have used behavioural paradigms to investigate the affective reactions of patients with PNES to emotional stimuli. Roberts et al. (2012) presented participants with pleasant, unpleasant and neutral pictures alongside startling bursts of white noise and asked them to rate the valence and intensity of the pictures, whilst their cardiovascular activity and emotional behaviour (external expressions of emotion) were monitored. Performance was compared between the PNES group and two groups of trauma-exposed individuals with either few or many PTSD symptoms (all n = 18). There were no differences between the groups in their emotional valence ratings for the three picture types but the PNES group described the neutral pictures as more intense than both controls; they also rated the positive pictures as more intense than the PTS-low group, although there were no between-group differences for the negative pictures. Similar proportions of participants in each group exhibited negative emotional behaviour in response to the negative pictures, but positive behaviour in response to the positive pictures was less common in the PNES than the PTS-high group; a similar difference between the PNES and PTS-low groups failed to reach significance, possibly due to low power. No between-group differences were found in cardiovascular responses to the emotional pictures.

These findings suggest that the patients with PNES were able to experience and differentiate between positive and negative emotions, but that they were more aware of their physiological reactions to neutral stimuli, possibly due to enhanced body-focused attention or a deficit in sensory gating. This is consistent with the elevated physical symptom reporting seen in other studies. The lower rate of positive emotional behaviour in the PNES group was

interpreted as evidence of emotional blunting and possible emotional suppression, although it is unclear why this did not extend to negative emotional behaviour.

Bakvis, Roelofs, et al. (2009) also found that patients with PNES (n = 19) showed greater interference for angry faces on a masked emotional Stroop task with negative words than healthy controls (n = 20), which correlated with sexual trauma scores. This could indicate preconscious hypervigilance for social threat in patients with PNES or difficulties inhibiting responses to it.

PNES as a hard-wired reflex

Picking up earlier ideas by Kretschmer (1923), Baslet (2011) suggested that PNES reflect the activation of hard-wired, cognitively impenetrable behavioural tendencies, perhaps akin to the defensive reflexes (e.g., freezing) seen in other animals. This idea is supported by the relatively stereotypic nature of PNES (Seneviratne, Reutens, & D'Souza, 2010), and the fact that a moderate number of semiological subtypes can be distinguished by automated cluster analysis of observable motor features (Hubsch et al., 2011). There are also several different culture-specific syndromes that resemble PNES, and have similar semiologies, phenomenologies and psychosocial precipitants (Brown & Lewis-Fernández, 2011). Whilst these findings suggest a universal, potentially hard-wired, phenomenon, there are also important differences in the presentation and correlates of culture-specific syndromes resembling PNES (ibid). This suggests a degree of cognitive penetrability in these phenomena, as does evidence suggesting that verbal or motor responsiveness is very common in this group; Hubsch et al. (2011), for example, found responsivity to the doctor or nurse in 58.5% of 145 attacks observed in their study of 52 patients with PNES, although the low quality rating suggests this finding should be interpreted with caution. Other findings raise questions about the stereotypic nature of PNES. About a fifth of patients have attacks conforming to more than one semiological category (Hubsch et al., 2011), for example, and most patients describe their PNES as variable, with only a small minority reporting that their seizures are always associated with particular symptoms (Reuber et al., 2011). Nevertheless, taken together, these findings raise the possibility of a reflex component to PNES, which may be more than a manifestation of simple reflex action.

PNES as learned behaviour

In psychodynamic theories, the function thought to be served by PNES is one of reducing anxiety (so-called “primary gain”), although extrinsic motivations (such as being relieved of duties, obtaining benefits or care from others etc.; so-called “secondary gains”)

are also considered important. Similar ideas are embodied in the behavioural approach to PNES, which identifies them as learned behaviours that are maintained by positive (i.e., reward) and negative reinforcement (i.e., removal of punishment; e.g., Ramani et al., 1981). According to this approach, patients' PNES-associated behaviours and experiences are 'modelled' on experiences of seizures in themselves and others, representations of seizures in the media, questions about their symptoms from health professionals etc.

Lancman et al., (1993) present data indicating that over a third of patients with PNES have a family history of epilepsy, suggesting a source of possible seizure models. Moreover, the prevalence of comorbid epilepsy in patients with PNES (3.6-58%; Reuber, Qurishi, et al., 2003) is higher than the population prevalence (~0.8%). Almost invariably, PNES start after epileptic seizures in these cases (Rabe, 1970). The only systematic study investigating seizure modelling in PNES was by Bautista, Gonzales-Salazar and Ochoa (2008), who interviewed 27 patients with PNES and 35 patients with epileptic seizures and asked about possible seizure models. A significantly larger proportion of their patients with PNES (66% vs. 11% patients with epilepsy) reported witnessing a seizure before the onset of their own seizure disorder. These figures may be underestimates, since learning about seizures may be incidental/implicit, and not available for later recollection.

In contrast, there is very little direct evidence for the role of reinforcement in maintaining PNES. Two studies found that patients with PNES are more likely to be receiving health-related public benefits than patients with similarly severe epileptic seizure disorders (Binder et al., 1994; Kristensen & Alving, 1992); there is, however, no evidence that patients with PNES produce their seizures to obtain benefits, and other explanations for this association (e.g., psychiatric comorbidity) are more plausible. With regards intrinsic gain, a recent case series by Stone and Carson (2013) describes patients with PNES who report 'submitting' to attacks to relieve emotional tension, although Reuber et al. (2011) found that only a third of patients (n = 100) reported "always" or "frequently" feeling relieved afterwards and 42% "rarely" or "never" felt like this.

One problem with the 'learned-behaviour' model is that it leaves unanswered why patients produce seizure-like behaviour in the first place (i.e., pre- reinforcement), although the implication seems to be that the behaviours are voluntary to begin with. Research considering whether patients with PNES show poor effort on neuropsychological tests is seemingly premised on a similar idea. Such studies have yielded variable findings, with Drane et al., (2006) finding that patients with PNES were more likely to fail a simple memory test (thought to indicate poor effort) than patients with epilepsy (n = 41; 49% of 43 PNES vs.

8% of 41 epilepsy), whereas Dodrill (2008; 28% of 27 PNES vs. 25% of 19 epilepsy) and Cragar, Berry, Fakhoury et al., (2006; 24% of 21 PNES vs. 22% of 41 epilepsy) did not. Poor effort was slightly more common in a study by Williamson, Holsman, Chaytor et al. (2012; 35% of 91 patients with PNES), but this was better explained by psychopathology and a history of reported sexual abuse than by financial incentives, seemingly inconsistent with malingering. Benge, Wisdom, Collins et al., (2012) found that patients with PNES (n = 91) scored significantly higher than patients with epilepsy (n = 29) on a measure of atypical or "implausible" symptoms in different domains (median d = 0.91). Whether this indicates feigning or simply a tendency to experience functional symptoms is unclear, however.

PNES AS DISTURBANCES OF COGNITIVE CONTROL

Like the learnt behaviour account, the Integrative Cognitive Model (ICM) of MUS (e.g., Brown, 2004, 2006, 2013) assumes that PNES are underpinned by mental representations of seizures derived from past experience. Rather than being voluntary, however, the ICM asserts that PNES reflect the activation of automatic, ego-dystonic processing routines (or "rogue representations"), resulting in a transient disturbance in cognitive control. Broadly speaking, the ICM claims that PNES are a kind of "self-fulfilling prophecy", in which the expectation that a seizure will occur automatically gives rise (under certain triggering conditions) to behaviour resembling a seizure, which the individual then struggles to control for various cognitive and emotional reasons. The ICM integrates key concepts from the dissociation and psychodynamic models, arguing that many of the factors that contribute to PNES in those accounts do so by increasing the activation of rogue representations (e.g., suggestibility, emotional avoidance, reinforcement), or undermining the individual's capacity to inhibit them (e.g., attentional dysfunction, trauma, stress, negative affect). The evidence reviewed above pertaining to those factors potentially applies to the ICM as well; whether these factors operate via their effect on the activation of rogue representations is yet to be assessed, however.

Expectancy models

There is evidence that many patients have been exposed to events that might result in them expecting to experience subsequent seizures. Evidence that PNES may arise in the context of pre-existing epileptic seizures (Reuber et al., 2003) falls in this category. Similarly, numerous casenote reviews have found that a substantial proportion of patients with PNES (range 20.3-82.6% depending on definition; median 43.2%; Appendix H) have a history of head injury, with the injury being regarded as the precipitant for PNES in many cases. In

most cases, the injury is mild (median proportion: 82.6%; range 73.2-91%) but often associated with brief loss of consciousness (Mokleby et al., 2002). Elliott and Charyton (2014) found that patients with PNES were almost twice as likely as patients with epilepsy to have a history of head injury recorded in their notes. How PNES might develop in the absence of these or other events that create an expectation of seizures is less clear, however.

GENERAL DISCUSSION

SUMMARY AND THEORETICAL IMPLICATIONS

Despite the relatively low quality of research in this area, the consistency of certain findings suggests that some tentative conclusions about PNES may be drawn. To begin with, patients with PNES reliably report more physical symptoms than controls with epilepsy. This lends credence to the idea that PNES reflect a broader tendency to experience and report physical complaints, and that related processes are operating across all symptom types. However, there are some differences between patients with PNES and other functional symptoms that could have a bearing on mechanism (e.g., Guz, Doganay, Ozcan et al. 2003; Stone, Sharpe, & Binzer, 2004; Driver-Dunckley et al., 2011; Ludwig, Whitehead, Sharpe, Reuber & Stone, 2015), which should be considered in future research. Almost none of the studies in this area have evaluated whether physical symptoms serve a psychological function for patients. Whilst such a function remains possible, alternative (or complementary) explanations might be that patients with PNES are hyper-vigilant for changes in their body, are less able to ignore such changes when they occur, and/or are more likely to interpret such changes as threatening and therefore describe them as symptoms (Goldstein et al., 2010; Rief & Barsky, 2005). Studies using more objective, experimental paradigms are needed to tease these possibilities apart.

Second, there is a tendency for groups of patients with PNES to report more dissociative experiences than patients with epilepsy. The effect is inconsistent, however, with the most robust study in this area finding only a small and non-significant difference between patients with PNES and those with epilepsy. Furthermore, overall group means tend to be somewhat lower than those seen in dissociative conditions such as PTSD and DID and potentially driven by a small subset of individuals with particularly high scores. Taken together, these findings are consistent with the idea that a general capacity for dissociation is a common correlate of PNES, but is neither necessary nor sufficient to explain the phenomenon. This would explain the inconsistent findings in relation to suggestibility and attentional dysfunction, although our quality ratings suggest that these aspects of the model

require more rigorous evaluation. The same is true of exposure to potentially traumatising events. Whilst that particular literature is beset with methodological problems, addressing these is only likely to strengthen the case that trauma is not a universal antecedent of PNES, even though it may be common and etiologically significant to a subgroup of patients in this group. Importantly, dissociative mechanisms can still operate in the absence of trauma and "trait" dissociation (Brown, 2013), indicating that other methods are required to test the dissociation model of PNES. The reversibility of amnesia in patients with PNES potentially provides a more direct demonstration of dissociation, but the extent and quality of research on this particular topic preclude even tentative conclusions. More studies on "state" dissociation, such as those evaluating whether patients experience phenomena such as depersonalization and derealization before, during and after PNES, are also needed.

A more tentative conclusion concerns the apparent mismatch between the subjective anxiety reports of patients with PNES in general and their experience of physiological arousal during the events themselves. There is consistent evidence that the difference between patients with PNES and those with epilepsy on measure of subjective anxiety symptoms is relatively small, with both group averages in the moderate range. Moreover, there is some evidence that this difference is attributable to a sub-group of PNES patients with high levels of psychopathology. Subjective fear around the time of the ictus also seems to be relatively uncommon in PNES. In contrast, there is both self-report and physiological evidence for a substantial increase in autonomic arousal for patients with PNES at the time of their attacks. This is consistent with one interpretation of the dissociation model, which posits that PNES are akin to panic attacks in which the distress component has been dissociated. As the relevant studies all present group averages, however, it is unclear how many patients experience both physiological arousal and a lack of subjective fear during their attacks. Moreover, such an account is difficult to reconcile with other features of PNES (e.g., loss of consciousness, abnormal motor activity) without additional theoretical assumptions.

The apparent mismatch between subjective anxiety and physiological arousal might be interpreted as evidence for a defensive process, an emotional processing deficit or both. Although a number of studies have found evidence for more avoidant and less planful coping in patients with PNES, other research on defence, alexithymia, emotional processing and emotion regulation in this group is highly inconsistent. Cluster analyses suggest that these discrepancies are probably attributable to the heterogeneity of patients with PNES, with several studies pointing to two distinct sub-groups, with only one characterised by emotion dysregulation, attachment insecurity and significant psychopathology. A key question for

future research is whether the low levels of psychopathology seen in the other sub-group reflect emotional suppression and the indirect expression of distress through physical symptoms.

Although it is commonly assumed that PNES develop in response to stressful life events, the evidence for a temporal relationship between such events and PNES onset is limited to a single, very small study. Whilst it is clearly premature to draw firm conclusions from this, the available data suggest that circumstances in the year before seizure onset may be as important as more proximal life events, suggesting that both should be considered in future studies. There is consistent evidence that events resulting in a head injury and/or loss of consciousness may be particularly important to capture in this regard. It is essential that we move beyond retrospective casenote review methods if we are to estimate the true significance of these factors.

Most recent accounts of PNES assume that a range of different factors contribute to the onset and maintenance of PNES (e.g., Baslet, 2011; Bodde et al., 2009; Reuber, 2009). Although not always explicit, it is apparent in these accounts that concepts like dissociation, somatization, modelling and so on are not mutually exclusive. In some cases, theorists simply describe the factors involved in the creation and maintenance of PNES, without making specific assumptions about underlying mechanisms (e.g., Bodde et al., 2009; Reuber, 2009). Others are more specific, but the mechanisms vary widely. Thus, the cognitive-behavioural model (Goldstein et al., 2004) proposes that PNES are dissociative responses to heightened arousal, Baslet (2011) assumes they that are a hard-wired reflex and the ICM claims that they are automatic action slips. The state of the current evidence base simply does not allow firm conclusions to be drawn about the relative merit of these accounts. It is even unclear how different these accounts really are; a central task for theorists is to either reconcile the apparent differences or to articulate key predictions that would enable them to be teased apart empirically.

One limitation of this review is that we excluded studies where the only comparison was individuals with a different functional neurological disorder (FND), such as functional motor symptoms. Several studies have identified similarities between PNES and motor FND (Driver-Dunckley et al., 2011; Hopp, Anderson, Krumholz et al., 2012; Stone, Sharpe et al., 2004) and it is often suggested that the two share common mechanisms (e.g., Mula, 2014; Paola, Marchetti, Teive & LaFrance, 2014). Although we are sympathetic to this view, there are also important differences between these groups that need to be accounted for in any comprehensive account of PNES. For example, patients with PNES tend to be younger, more

likely to experience alterations in consciousness and more likely to report childhood abuse and stressful life events prior to the onset of their symptoms than patients with motor FND (Driver-Dunckley et al., 2011; Hopp et al., 2012; Stone, Sharpe et al., 2004). More detailed consideration of these studies, as well as the literature on FND more generally, may shed further light on the nature of PNES.

EMPIRICAL IMPLICATIONS

This review is the first to use a systematic method for rating the quality of research on the psychology and psychiatry of PNES. The results of this process clearly demonstrate that, despite the considerable quantity of publications, most research on these aspects of PNES has been of limited quality. Whilst we identified a small number of high quality studies, most were only powered to detect large effect sizes and used non-experimental designs with self-report measures and control groups of questionable relevance. Many studies (or the reports that describe them) are beset by methodological shortcomings, particularly a failure to report how PNES were distinguished from anxiety disorders, the use of highly selected populations in specialist settings, and the use of control participants from different demographic groups. Even apparently basic methods for ensuring internal validity, such as the use of standardised measures, are neglected by some researchers.

One possibility is that some of our quality benchmarks have been set too high. For example, some researchers take bilateral motor activity as a criterion for ruling out anxiety disorders, which we rejected on the grounds of being too likely to result in false positive diagnoses. Similarly, our judgements of sample size adequacy had to be made in the absence of any information about anticipated effect sizes, and could be overly strict in the case of studies where particularly large effects might be expected. Moreover, it is likely that some of the limitations we identified were due to poor reporting rather than poor design; indeed, many of the studies reviewed here were published before the introduction of publication guidelines such as CONSORT and STROBE. Equally, however, our ratings may represent a generous estimate of the quality of research in this area. The criteria we used to rate quality evolved over a series of iterations, with the required level of methodological sophistication reducing over time as the quality of the evidence-base became apparent. Perhaps inevitably, this resulted in lower quality thresholds than in other areas of research where appraisal tools have been in use for some time. Rather than dismissing most of the literature as uninterpretable, however, we believe that many of the findings are sufficiently consistent to draw meaningful conclusions about certain aspects of PNES and the people who experience them.

Nevertheless, it is clear that the field has a long way to go.

An urgent priority for future work is to draw on established publication guidelines (e.g., STROBE) to develop a set of standards for reporting research on PNES that can be adopted by journals to drive up the quality of empirical work in this area. Although this is beyond the scope of the current article, we suggest that particular attention is paid to: ensuring adequate power; detailed description of the procedures and criteria used to diagnose PNES, and to rule out epilepsy and other causes (e.g., anxiety); prospective and ideally consecutive recruitment, with information being presented about participants who refuse to take part or are excluded for other reasons; standardised measurement with clear information about psychometric properties; and the use of control participants who are matched in terms of age, gender, trauma exposure and other relevant psychiatric features.

Also problematic is the tendency for researchers to conduct studies that simply repeat what has been done previously (consider, for example, the large number of studies on dissociation, anxiety, somatization and the MMPI), leaving fundamental questions about the aetiology and mechanisms of PNES unanswered. Ultimately, much larger, better-designed studies are needed, preferably using a combination of subjective and objective methods such as cognitive, psychophysiological and neuroimaging paradigms to study under-developed areas. The exclusion of the latter is clearly a limitation of our review, but was deemed necessary given the large literature already under consideration and the relatively limited contribution neuroimaging studies have been able to make to our understanding of PNES so far. Researchers should also move beyond correlational studies to embrace the methods of experimental psychology, manipulating key variables such as expectancies, affect/stress, attention, inhibition, context and so on. There is also growing evidence that patients with PNES are heterogeneous, which may account for the often inconsistent findings in this area. It is essential that we characterise relevant sub-groups in more detail, so that they can be considered separately in research and so that treatments can be targeted to address the differing needs of these individuals.

CLINICAL IMPLICATIONS

Given the state of the evidence, perhaps the most important clinical implication of our review is that theories of PNES are not as well established empirically as often thought. How we approach this with patients is of paramount concern. On the one hand, it is necessary to be able to convey a degree of confidence that we understand our patients' difficulties and can offer meaningful ways of conceptualising these that enable them to move forward. On the

other, we must be careful not to create the false impression that PNES are better understood than they really are, and to maintain an open mind about the best way of formulating a particular presentation. Ultimately, it may be more therapeutic to present patients with a range of different ways of thinking about their difficulties and let them judge which is the most useful for them, than to assume that we always "know best". To that end, we must resist the temptation to assert that PNES are always the product of early trauma, life adversity or emotional stress, and that the patient's claims to the contrary must be a sign of resistance or defensiveness. Whilst this may prove to be the case, we must remain open to the possibility that it is not. Similarly, a degree of humility is essential in the inevitable turf wars that spring up between clinicians of different theoretical persuasions.

Clearly, much still needs to be done to elucidate the nature of PNES. Although much of the evidence on the psychology and psychiatry of PNES is deficient in one way or another, we believe this review will provide a basis for higher-quality, hypothesis-driven research in future.

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