The Beckley Foundation's Program of Psychedelic Research

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What exciting times we live in! At last I feel we are on the cusp of great discoveries!

After decades in the wilderness, psychedelic science is experiencing a renaissance, as the taboo on scientific research is being broken down. The research being carried out, by the Beckley Foundation and others around the world, is starting to bear valuable fruit – not only in our understanding of brain function and consciousness, but, very importantly, also in terms of new clinical applications.

In this talk, I would like to briefly touch upon

Firstly, why neuroscientific research is so important, and why I set up the Beckley Foundation;

secondly, how our pilot studies cast new light on the mechanisms underlying the changes in consciousness brought about by psychedelics, and suggest new avenues of treatment for major scourges like depression;

thirdly, give a neuroscientific explanation of why psilocybin and MDMA can be such valuable aids for psychotherapy; and

lastly, I hope to briefly mention why reforming global drug policy, and rebasing it on scientific evidence rather than on ideology and panic, is so important for improving human well-being and promoting good science and therapy.

If it is well directed, a neuroscientific pilot study can provide invaluable information about changes in cerebral circulation and brain function, as well as showing how a psychoactive compound affects consciousness and how it may be harnessed to overcome trauma and enhance health, wellbeing and creativity.

Brain-imaging studies are an ideal complement to clinical trials. They provide new *discoveries* to drive medical advances, as well as new *explanations* that give medical research a powerful neuroscientific underpinning.

In 1966, I became passionately – one could say compulsively - interested in the physiological mechanisms underlying altered states of consciousness and the ego. I had

met a Dutch scientist of exceptional insight, Bart Huges, who had developed two new hypotheses: **one** concerning the *irrigation* of the brain, and the changes in blood supply to the brain underlying altered states of consciousness; and the **second,** describing the physiological basis of the ego, as a conditioned reflex mechanism, based on word recognition, which *directs* blood to those brain centres most essential for survival, while *repressing* blood flow to other brain centres. *This was the first time that a mechanistic explanation of the ego had been given.*

It also provided the first explanation of how brain functioning can be altered by such practices as meditation, yogic breathing and the ingestion of psychoactive substances, to name but a few. The underlying theory was that these practices brought about a change in blood supply to the brain, together with a loosening of the repressive control of the ego-mechanism over consciousness

This new explanation of the ego as a system superimposed over the rest of the brain could not in those days be tested.

However, with the development of more advanced brain-imaging technologies, and particularly fMRI in the early 1990s, it became possible to observe the changes in blood supply and brain function, correlated with subjective experience, during altered states of consciousness.

In 1998 I set up the Beckley Foundation with two main aims: firstly, to investigate consciousness and its changing states using these new technologies, and secondly, to reform global drug policy - ambitious tasks! I invited some of the world's leading scientists – including Albert Hofmann, Sasha Shulgin, Colin Blakemore, Dave Nutt, Les Iversen, and Dave Nichols among others – to form a Scientific Advisory Board.

In 2007, Dave Nutt and I agreed to embark on a collaborative programme of research. I was keen to start with psychedelics, but Dave advised caution, so we started with cannabis. In 2009, when Dave moved from Bristol to Imperial College, London, we set up the Beckley/Imperial Psychopharmacological Research Programme, and started a series of pilot studies, using psilocybin. The research was conducted by Robin Carhart-Harris, who together with Dave is here today and will tell you more about it.

So much for the background.

The programme has proved to be a dream come true. With very little funding, we have targeted our research to look at changes in blood-supply and brain function, underlying the changes in consciousness brought about by psychedelics. The findings have been both surprising and exciting.

Last year, we started publishing our results from a series of studies using fMRI and MEG, imaging the brains of volunteers, who had received an intravenous infusion of psilocybin or placebo.

The findings were confirmed with two different fMRI imaging techniques, ASL and BOLD, which both give information about the changes in blood flow that result from the brain's metabolic activity. The results were further confirmed and expanded using MEG imaging, which maps changes in brain activity by recording magnetic field changes produced by electrical currents, i.e. neural activity.

Contrary to our expectations - particularly mine - we found that, compared with placebo, psilocybin *decreases* blood flow and activity, *particularly* to the network of highly interconnected brain regions known as the *default mode network* or DMN. All the data showed reductions in blood flow and neural activity to this important network, and the degree of the reduction correlated with the subjective effects of psychedelic experience. That is, more intense subjective experiences correlated with larger decreases in blood flow to the Default Mode Network. We also found that the centres of the network became less *connected* with each other and with other brain regions.

The default mode network closely corresponds with Bart Huges' conception of the ego as a top-down controlling mechanism.

The brain is not a free-for-all among independent systems but a federation of *inter-dependent* components that is *hierarchically* organised. The DMN sits at the top of this hierarchy, exerting a top-down control on other brain regions, which feed their information into it, to be either repressed or routed onwards.

The censoring activity of this superimposed mechanism reflects Aldous Huxley's metaphor of the brain as a 'reducing valve', as well as Bart's description of the ego as a conditioned reflex mechanism, which censors what is allowed to enter consciousness by controlling the distribution of the blood in the brain. As in Bart's model of the ego, the development of the default mode network begins after infancy, during the time when *language* and *self-control* are being acquired through conditioning.

The Default Mode Network accounts for much of the brain's intrinsic activity, and is particularly active in the 'resting state', i.e. when we finish a task and are engaged in *inwardly*-directed thinking such as introspection, day-dreaming, and the recollection of autobiographical memories. Conversely, when we engage in *externally*-focused tasks, the activity of the DMN decreases, while activity in the so-called *task-positive networks* increases. In normal consciousness, the default mode and the task-positive networks are strongly *anti-correlated* – i.e. as one becomes more active, the other becomes less active. Taken together, these networks form the neurobiological basis of the ego/superego as described by Freud, and later elaborated by Bart.

[The default mode network comprises high-level cortical nodes that are highly connected to each other and to sub-cortical systems. These centres include the medial prefrontal cortex and the posterior cingulate cortex as well as parts of the thalamus and other areas.]

Psilocybin acts by constricting the flow of blood to the Default Mode Network, and thereby ***de***creasing its controlling and repressive activity. Thus, sensory and emotional impulses, which would normally be repressed, reach consciousness, and users experience a spontaneous, unconstrained mode of thinking – a more fluid and plastic state of consciousness. This state more readily allows access to areas of the brain normally kept repressed, e.g traumatic memories or spiritual awareness.

Also, under psilocybin, the anti-correlation between the *internally*-focused Default Mode Network and the *externally*-focused task-positive networks becomes weaker: the two networks become coupled, tending to act in synchrony. This also happens in meditation and psychosis. As a result of this coupling, there is a loosening of ego-boundaries, as the distinction between inner and outer worlds becomes blurred.

Most importantly, the subjective intensity of the psychedelic experience correlates with the extent to which the activity of the Default Mode Network is reduced.

It is worth noting that the centres of the Default Mode Network, whose blood flow and activity are particularly reduced by psilocybin, include the ***medial prefrontal cortex*** and the ***posterior cingulate cortex***.

Interestingly, it has been observed that, in people suffering from **depression**, the *medial prefrontal cortex* exhibits both chronically raised *activity,* and increased *connectivity* with the *posterior cingulate cortex*. This hyperactivity results in thinking becoming rigid and inflexible, leading to an endless cycle of self-obsessed negative rumination.

Our finding that psilocybin decreases both the *activity* of the medial prefrontal cortex and its *connectivity* with the posterior cingulate cortex, suggests that the drug may provide a valuable new avenue of treatment for depression, hopefully allowing the rigidly negative patterns of thought to be reset.

Recognising the value of this research, the UK's Medical Research Council has awarded over half a million pounds for a clinical trial to further investigate the use of psilocybin as a treatment for depression.

Our brain-imaging study into the effects of psilocybin is the first time that anyone has shown that the most basic effect of psychedelics is to reduce blood flow to the Default Mode Network, thereby lessening the grip of the control mechanism and permitting a looser style of awareness to surface into consciousness. This would explain why the psychedelics are conducive, not only to accessing repressed memories and alleviating depression, but also to experiencing mystical states, to enhanced creativity, and to seeing the unity and interconnectedness of all things and our place in the greater whole.

All of these characteristics can enhance the nobler aspects of the human personality.

THUS our research studies with both psilocybin and MDMA have gone a long way to giving a neuroscientific explanation as to why these compounds can be such valuable aids in psychotherapy… whether it is overcoming post-traumatic stress disorder, addiction, or anxiety associated with a terminal illness. By facilitating the access to repressed memories, even those which have, for much of a lifetime, been closed off from

conscious thought, the psychedelics facilitate the washing out of toxic memories, which can free the person from their unconscious grip.

Most of our studies imaged the brains of participants in the resting state. However, in some of the studies with both psilocybin and MDMA, we asked participants to perform a series of memory tasks, so we were able to correlate the brain-imaging findings with their subjective reports, and to compare both psilocybin and MDMA with placebo.

With psilocybin, subjects recalled a series of pre-arranged positive autobiographical memories. With MDMA, they were asked to recall both ***favourite*** and ***worst*** memories.

When we introduced the memory-recall task with psilocybin, we found an ***increase*** in blood flow and brain activity in visual and other sensory regions of the cortex during the period of recollection, as opposed to a *de*activation of these regions under placebo. Correlating with the brain-imaging findings, subjects reported their memories as significantly more ***vivid, 'real' and visual*** under psilocybin than under placebo. Furthermore, the *vividness* of the memories showed a positive correlation to the subjective wellbeing reported later by participants.

In the memory-recall study with MDMA, subjects rated their favourite memories as more vivid, emotional and positive than with placebo. Correspondingly, several brain regions were more strongly activated after MDMA than after placebo.

In contrast to *favourite* memories, which showed *increased* emotional intensity after MDMA, *worst* memories were rated as *less* negative after MDMA than after placebo. Corresponding with the subjective findings, the brain-imaging showed that areas involved in emotional response to negative memories were *less* activated after MDMA than after placebo.

This provides a neuroscientific explanation for the clinical observations that MDMA is helpful in the treatment of PTSD. By decreasing the brain's emotional response to painful memories, MDMA allows these memories to be recollected without the patient becoming overwhelmed, so that the traumatic memories can be worked through in the therapeutic setting.

I'm delighted to say that last month our protocol for an LSD-study gained ethical approvals. The study will investigate the physiological and neural mechanisms underlying the subjective effects of LSD, as well as its effects on perceptual and cognitive functions. This exciting research will be the first ever study to use modern brain-imaging technology during an LSD-experience. I am hopeful that it will provide equally significant advances as the psilocybin and MDMA research, both in our understanding of brain function and consciousness, and in the development of potential new clinical applications.

In this study, I am keen to introduce more task-related activities, in order to stimulate brain activity, and to investigate whether, with the addition of inspirational stimulation, the brain activity and corresponding blood supply shows a greater increase with LSD than with placebo, as I hypothesise it will. We plan to make a short video with inspiring music and wonderful images, to show to the participant, which may trigger a mystical experience, which can then be mapped using fMRI.

I am particularly excited about this study, as I have wanted to investigate the neurobiology underlying the LSD-experience for over 40 years. Also, I promised Albert Hofmann that, as a 100th birthday present, I would open the doors to scientific research into his beloved elixir.

In order to test the hypothesis that psychedelics potentiate creativity, we need to develop new creativity tests, as the ones currently on offer do not catch the kinds of creativity engendered by psychedelics and cannabis.

I'd now like to say a few words about another of the Beckley's collaborative scientific projects.

In 2008, in collaboration with **Roland Griffiths' wonderful group at Johns Hopkins**, we conducted the first study in modern times to harness the power of a psychedelic in treating addiction, in this case to nicotine. The protocol uses an intensive course of psychotherapy including three sessions with psilocybin.

Initial results have been absolutely remarkable, with every participant who has received psilocybin managing to quit smoking and to remain verifiably abstinent on follow-up. There has been no return to regular smoking. ***This success rate is far in advance of what we see with any other method for treating addiction***.

After the initial phase of the study, it received a valuable boost in funding from the Heffter Institute, enabling the pilot study to be expanded to the current eleven participants. On completion of the pilot study, it will be very important to follow it up with a full clinical study. Roland Griffith and Matt Johnson will tell you more about this study in a minute.

I believe our Beckley/Imperial studies demonstrate how well brain-imaging studies complement clinical studies. They show how psilocybin loosens the control of the

repressing and organising system of the brain, and temporarily grants the brain a greater degree of fluidity and plasticity, in which old restrictions are broken and there is a greater capacity to form new connections. Importantly, once formed, these new connections are enduring – so a change brought about by a relatively brief psilocybin experience can become consolidated and lasting. Many are the people who have told one that a psychedelic experience from long ago changed their life for the better.

I am very excited about the work the Beckley Foundation Scientific Programme can do over the next few years.

Over the past 15 years, I have built up a network of collaborative partnerships with leading scientists at some of the best institutions around the world.

Through my years of study of the subject of altered states of conscious, I feel I have a good idea of what are the most promising areas to investigate.

I am so fortunate to have the pleasure of working with some of the best and most dedicated scientists in the world, many of whom have access to the latest brain-imaging technology. I am also enormously grateful to the far-sighted and trusting funders who give the indispensible donations, without which we cannot do the work….

I feel the Beckley Foundation is now in a unique position to carry out cutting-edge research in this most important area of human development – consciousness research.

By great good luck, I find myself in a secret garden with an orchard of trees, heavy with low-hanging fruit.

I would just like to say that, if we can only increase our funding, we could enormously increase our output of great science into how these substances – and associated practices – work in the brain, and how we can harness them to benefit mankind.

Thankyou! And now I'd like to hand over to Roland and Matt, and then to Robin and Dave, who has this morning come all the way over from England.