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Psychedelics – Medicines of the Future

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2 October 2016

I think we have reached a very exciting tipping point in the study of psychedelics.

After decades, in which research was stifled by repressive drug laws and stigma, we are finally seeing the doors reopen, and a new interest in the possibilities of what psychedelics can offer, both science and society, emerge.

Psychedelics are a key to unlock a deeper level of the psyche. They can transform the individual in ways that modern science is only just beginning to understand. Their latent potential lies in their ability to profoundly alter consciousness and evoke a rich subjective experience. It is the special quality of this alteration that underlies their wide-ranging utility, including as a set of tools with which to better understand consciousness itself. Most significantly, as demonstrated by an increasing number of scientific studies, psychedelics are on track to create a *new psychiatry* – not only in how we treat, but also in how we understand, psychological disorders, and help cope with terrible existential problems, like being told one is terminally ill.

Importantly, it is not merely a small subset of illnesses that psychedelics have the potential to treat effectively. But rather, psychedelics may be conceived as *non-specific medicines* for a wide range of mental disorders.

It is now 50 years ago that I first realized what amazing tools psychedelics can be. In 1965 I was introduced to LSD, and most importantly, in 1966 I met, and became deeply involved with a Dutch scientist, Bart Huges, from whom I learnt the hypotheses about the mechanism underlying altered states of consciousness, and the description of the ego as a conditioned reflex mechanism that controls the distribution of the blood in the brain.

That is when I decided that I had found my 'mission' in life– to scientifically research these changing states of consciousness, and their potential value for humanity, and to integrate this knowledge into modern society.

It has been a long, slow process – rather like Sisyphus pushing his rock up the wretched mountain – but now, finally, I think we have reached a plateau, where there is a freshly-kindled renaissance of interest in the possible advantages brought about by informed use of the psychedelics, and their cousin, cannabis.

Of course, our ancestors have made use of this knowledge since the beginning of human culture. Look at the cave paintings of Chauvet (roughly 40,000 years old); of Tassili (12,000 years ago); and all the other high points of cultural history, from Chatal Huyuk (8,000 years ago) to Egypt and India, from Crete and Eleusis to the Amazon and Mesoamerica.

However, in modern times, thanks to the UN's drug conventions, promoted particularly by the US, for over four decades, society, and most importantly suffering patients, have been denied access to these medications of the mind - and the scientific community has been blocked from researching their potential usefulness.

Over the last 18 years, since setting up the Beckley Foundation in 1998, I have helped reform global drug policies, and undertaken many collaborations with scientists and institutions around the world.

This year our research has borne some particularly delicious fruit. I would like to mention just three studies in particular:

The first, which is part of the *Beckley/Imperial Programme*, is the *first-ever brain-imaging study with LSD* and human subjects. This study was a major breakthrough- demonstrating important characteristics of the mechanisms underlying the effects of LSD, including the amazing *increase* in *connectivity* between regions throughout the whole brain. We launched this study at the Royal Society in London.

The second *Beckley/Imperial* study results launched this year, also from a pilot study led by Robin Carhart-Harris, investigated the use of psilocybin in overcoming treatment-resistant depression. This study had the remarkable success rate of 67% of subjects attaining *remission* after the first week of treatment with psilocybin, and 43% remaining depression-free after 3 months. These are exceptionally positive results.

The success of this study reinforces the success of the Beckley-sponsored *Johns Hopkins* study which investigated the efficacy of overcoming treatment-resistant nicotine-addiction with psilocybin-aided psychotherapy. This pilot study had an amazing 80% success-rate at 6 months, and has now led to an expanded study.

The third recent study of special interest, which shows great promise for the future, is part of the Beckley/Sant Pau collaboration, led by Jordi Riba. Although these results are currently only from a Petrie dish, they show how two components of ayahuasca - harmine and tetra-hydra-harmine, promoted neurogenesis – i.e. the birth of new neurons in cells of the hippocampus. The hippocampus plays a key role in learning and memory, and if we can replicate these findings in 'vivo', this would open up a totally new avenue of research in the treatment of neuro-degenerative disorders such as Parkinson's and Alzheimer's.

These and other studies show the great promise of psychedelics in both healing illness, increasing well-being, and evoking transformational experiences for the individual. The mechanisms behind their therapeutic and transformational potential are beginning to being uncovered by our research.

There are many aspects of the effects of psychedelics that we are researching within the *Beckley Scientific Programme*, such as the interaction with music, the enhancements of mindfulness abilities, the importance of mystical experiences, or understanding the mechanisms behind visual hallucination. However, due to the time constrains tonight I will focus mainly on the effect of the psychedelics on the *Default Mode Network*. The better understanding of this particular neural network holds great promise, and is of special interest to me, as it is the neural correlate of what I worked on with Bart Hughes in the 1960's when we called it the 'mechanism of the ego'.

Higher-order cognitive processes result from the human brain's ability to function as an assemblage of neural networks, which work together to *constrain* consciousness, so that we may navigate the world using predictions from our past experience. These networks integrate information from multiple, anatomically-distinct regions in the brain, to construct a cohesive, unified conscious experience.

The Default Mode Network is particularly important in regulating our conscious experience – it censors what enters consciousness, and what does not - like the conductor in an orchestra. It is the integrity of this network that enables us to think about ourselves – to self-reflect, to remember the past and to plan the future. Importantly, the DMN underlies our ability to

maintain a sense of ego, or self, that is familiar to us, based on our accumulated memories and behavior patterns, that seem fundamental to who we are.

But just as the normal functioning of the *Default Mode Network* affords a relative stability to this sense of self, an *over-active* DMN can result in maladaptive thought patterns, and behaviours, that become over-dominant and entrenched, and seemingly inescapable. These can manifest as a sense of hopelessness for personal change, contributing to the development of psychological ailments, such as depression and addiction.

A common underlying mechanism of many mental illnesses, is *abnormal hyperactivity* and *rigidity* in the *Default Mode Network*.

In the past decade, we at the *Beckley/Imperial Research Programme* have undertaken pioneering neuroscientific studies that show that psychedelics reduce the integrity, or connectivity, between the different regions *within* the Default Mode Network.

We found that psilocybin both decreased the blood supply to the posterior cingulate cortex – a key integrative hub of the DMN - and also significantly *decreased* the *functional connectivity* between the *medial pre-frontal cortex and the posterior cingulate cortex*, thereby diminishing the integrity of the network, and the feed-back of *negative* chatter between these two hubs, that forms the basis of the neurotic problem, whether it be "I'm so depressed", or "I want another drink."

Importantly, further Beckley/Imperial studies with both psilocybin and LSD, showed that *decreased* connectivity between the key regions of the DMN correlated with the phenomenon known as "ego-dissolution", or the loss of ego identity. Since the default-mode network can be regarded as the neural correlate of the ego or self, *decreasing the integrity of this network* allows us to view ourselves from outside the normal confines of our everyday waking consciousness, and enables us to reset the rigid thought patterns that form the basis of many mental health problems.

In addition to the disruption of connectivity in the DMN, our research shows that the acute psychedelic state is characterized, neurologically, by a great *increase* in communication between the different networks of the brain. Connections appear, or are strengthened, between regions that don't normally communicate with each other. This leads to a looser style of cognition, more prone to making new associations, which can facilitate spontaneous self-insight, fresh perspectives and creativity.

This cognitive flexibility has also been demonstrated to persist following the psychedelic experience, and personality traits such as an increase in openness, or an ability and willingness to change one's mind are witnessed. The effects therefore are not limited to the acute psychedelic experience, but can lead to lasting changes that can transform patterns of thought and behaviour in the long term.

These findings present a breakthrough in our understanding of mental illness and how we might be able to improve the treatment of a variety of disorders, such as addiction, depression, obsessive compulsive disorder, and post-traumatic stress disorder, that blight the lives of millions of people worldwide. We need to open clinics which make available psychedelic-assisted psychotherapy.

At the Beckley Foundation we are preparing many more exciting studies that will expand and strengthen the knowledge-base of the therapeutic potential and neural effects of psychedelics. We have many studies in the pipeline from basic neuroscience to clinical trials.

Clinical trials that are currently ongoing or are in preparation, include:

- A randomized, controlled, trial using *psilocybin-assisted psychotherapy* for treatment-resistant *depression*
- Investigating the efficacy of *LSD-assisted psycho-therapy* to treat *alcohol addiction*
- A larger, follow-up study to further evaluate the effectiveness of *psilocybin assisted psychotherapy* for overcoming *nicotine-addiction*
- A brain-imaging study into the effectiveness of *MDMA* for the treatment of *Post-Traumatic Stress Disorder*

Studies in healthy volunteers, include:

- A brain imaging study investigating the effects of DMT, in comparison with the changes brought about by LSD, psilocybin and placebo
- A study investigating the potential of LSD to enhance creativity, using the game of 'Go' as a measure of intuitive pattern recognition, and problem solving
- Reconstruction of the visual hallucinations experienced on LSD
- A study investigating the effect of psilocybin on creativity
- A brain-imaging study comparing the effects of DMT and 5-MeO-DMT (toad venom)

Basic neuroscientific studies in animals, include:

- Investigating the effects of LSD on pyramidal cells and blood vessels using opto-genetics.
- Investigating the neurovascular and neuroimaging effects of 1p-LSD
- Further investigating the effects of ayahuasca components on neurogenesis
- Investigating the effects of regular rat-dose LSD in an ideal Rat-Park, compared with placebo on behavior, including problem solving, sociability, life-span and well-being.

As this new era of psychedelic research progresses, it will be essential to understand the minutiae of the brain network dynamics underlying the psychedelic state. It is also imperative that we create the political environment where psychedelic-assisted psychotherapy can be made available to those in need. I have long wished to gain greater understanding of the flexibility of consciousness gifted by psychedelics, and how less integrated, more interconnected networks subserve this fluid, more chaotic conscious state that has the potential to alleviate psychological distress, enhance human creativity and innovation, and ultimately lead to an evolution of our species.

October 2016