Uncovering the neurobiological mechanisms of altered states of consciousness

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Overview

Understanding the neural mechanisms of altered states of consciousness is of huge importance in the current climate: at the same time that altered states of consciousness are experiencing a breakthrough status in psychiatry, an increase in mental health problems due to the long-term consequence of COVID-19 is predicted. Methods of altering consciousness, including psilocybin, LSD, DMT, hypnosis, and meditation offer a promising transdiagnostic treatment strategy for a range of psychiatric disorders. However, we still do not fully understand the underlying neural mechanisms of altered states of consciousness. Such an understanding is vital if we are to leverage altered states clinically. This symposia will bridge diverse research methods to provide a comprehensive state-of-the-art overview of altered states of consciousness and integrate these results to aid in the rational development of novel treatments and for the design and success of future clinical trials.

Lecture 1: *Neurochemical underpinnings of psychedelic-induced altered states of consciousness*

Natasha Mason Presenter

The unique ability of psychedelic drugs to induce transient alterations in normal-waking consciousness, as well as their reported therapeutic efficacy in treating psychiatric disorders like depression, has many people wondering how these drugs act in the brain to produce such effects. Whereas assessment of psychedelic-induced disruptions of global brain activity has led to intriguing theories of the neural correlates of these altered states, consideration of the underlying neurochemical substrates which mediate such disruptions can prove insightful. Here, multimodal study designs utilizing human pharmacological fMRI and magnetic resonance spectroscopy offer a way to quantify both large-scale network activity and in-vivo concentrations of neurotransmitters such as glutamate and GABA. Using such designs, we have begun to uncover the role of these neurotransmitters in unique aspects of the psychedelic experience, such as reductions in self-referential awareness (ego dissolution) and inductions of visual (pseudo)hallucinations. I will give an overview of the research to date, and present novel, unpublished data demonstrating that psychedelics acutely induce region-dependent alterations in glutamate that correlate with key facets of the psychedelic experience, including changes in network connectivity and subjective state. I will further discuss the (clinical) relevance of this work. Can these findings provide a neurochemical basis for the therapeutic effects witnessed in psychedelic-assisted clinical trials? What do they tell us about (normal) brain function?

Lecture 2: *Neural mechanisms of psychedelic-induced altered states of consciousness*

Adeel Razi Presenter

Interest in psychedelic compounds is growing due to their remarkable potential for understanding altered neural states and their breakthrough status to treat various psychiatric disorders. However, there are major knowledge gaps regarding how psychedelics affect the brain. In this talk, I will discuss hypotheses of brain's functional reorganization under psychedelics, which are informed by the accounts

of hierarchical predictive processing and tested by using dynamic causal modelling (DCM). DCM is a generative modelling technique which allows to infer the directed connectivity among brain regions using functional brain imaging measurements. Using resting-state functional MRI and DCM, I will showcase new findings of how changes to synaptic mechanisms, under the control of serotonin receptors, across the brain hierarchy influence integration of sensory and associative brain connectivity. Understanding these neural mechanisms of subjective and therapeutic effects of psychedelics is critical for rational development of novel treatments and for the design and success of future clinical trials.

Lecture 3: *Comparing different methods of inducing altered states of consciousness: from psychedelics to hypnosis and meditation*
Flora Moujaes Presenter

In recent years, a wide range of methods of inducing altered states of consciousness (ASCs) have shown clinical efficacy in the treatment of psychiatric disorders including depression, anxiety, PTSD, and addiction. However, the neurobiological correlates of ASCs are still not well understood. ASCs can be induced both pharmacologically and non-pharmacologically. There is evidence of significant overlap in the phenomenology of pharmacologically and non-pharmacologically induced ASCs: both involve a shift in the subjective experience of one's self that defines normal waking consciousness and alterations in sensory perception. However, prior work has not tested whether there is also an overlap between pharmacologically and non-pharmacologically induced ASCs at the neural level. I will present novel, unpublished data directly comparing two pharmacological methods (psilocybin, LSD) and two non-pharmacological methods (hypnosis, meditation) using resting state fMRI, and assess the predictive value of the data using a machine learning approach. I will discuss the implications of these findings for both consciousness research and clinical use, as these results may aid in the search for common clinical mechanisms of action, biomarkers for treatment efficacy, and a better targeting of treatments in line with a precision medicine approach.

Lecture 4: *Neural correlates of the DMT experience*
Christopher Timmermann Slater Presenter

DMT is a psychedelic that induces immersive experiences associated with experiencing 'alternate realms' and communication with sensed presences or 'entities', in a state of partial disconnection from the external environment. We have performed a simultaneous EEG-fMRI involving healthy volunteers in order to capture the neural correlates of the DMT state. Our results show that immersive psychedelic states are associated with increased global brain connectivity in high-level networks and a flattening of the principal gradient of brain organization

Results were particularly strong in the transmodal association pole (TOP) comprising default, frontoparietal and salience networks, implied in abstract information processing, decision making and integration of sensory information. Finally we found that these effects were linked with density of 5-HT2A receptors and higher-order cognitive functions related to language, semantics and theory of mind, among others. Our findings suggest that psychedelics enhance information processing capacity in the developmentally and evolutionary recent cortex and dysregulate the high-level, species-specific TOP properties of consciousness.