Psychedelics and the science of self-experience

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Brief biography of authors

Dr Matthew Nour is an Academic Clinical Fellow in Psychiatry at King's College London and South London and Maudsley NHS Foundation Trust. Dr Robin Carhart-Harris is head of Psychedelic Research at the Centre for Neuropsychopharmacology, Imperial College London, where he studies the neuroscience and therapeutic potential of psychedelic drugs.

Summary

Altered self-experiences arise in certain psychiatric conditions, and may be induced by psychoactive drugs and spiritual/religious practices. Recently, a neuroscience of self-experience has begun to crystallize, drawing upon findings from functional neuroimaging and altered states of consciousness occasioned by psychedelic drugs. This advance may be of great importance for psychiatry.

Defining the self

The experience of a coherent and well-circumscribed 'self' is a cardinal feature of human waking consciousness [1]. Despite our ready use of personal pronouns such as 'me' and 'I', the nature of self remains one of the central questions confronting philosophy, psychology and cognitive science, and continues to defy simple definition.

Philosophers distinguish between two notions of self. At one level, self-experience comprises the experience of a unified personal identity, associated with our own individual life narrative, enduring character traits, life goals and a hierarchy of personal values. This 'narrative self' may be understood as a cognitive theoretical construct - an *object* of knowledge, emerging from the stories that we tell, and are told, about ourselves. At a more fundamental level, first person experience is saturated by immediate aspects of self, which include the unity and familiarity of experience, a sense of embodiment and a sense of agency. This 'minimal self' forms the *subject* of experience, and is independent of the contingent facts that give substance to the narrative self [2].

Self in neuroscience

The heterogeneous and multi-layered nature of self-experience presents a challenge for an emerging neuroscience of self-consciousness, which ultimately seeks to identify underlying neuronal correlates and mechanisms.

The neural correlates of self have been investigated using tasks that seek to identify brain regions that display increased activity (typically measured using functional magnetic resonance imaging, fMRI) during processing of self-specific stimuli (e.g. images, voices, trait adjectives), compared with stimuli related to others. A recent quantitative meta-analysis, pooling data from nearly 1500 participants, implicated activity in cortical midline brain regions as a neural correlate of self-experience. Specifically, activity in the perigenual anterior cingulate cortex was associated with processing of self-specific stimuli, compared with non-self stimuli [3].

Interestingly, the brain regions implicated in self-processing show anatomical overlap with important nodes of the default mode network (DMN) [3]. The DMN is a network of mostly cortical brain regions that appears to be involved in high-level psychological functions including introspection and autobiographical memory [1,3]. The brain regions comprising the DMN act as 'connector hubs' within the brain, displaying high metabolic demands and inter-region functional connectivity at rest.

The studies discussed above may shed light on the neuronal mechanisms underlying self-attribution to physical and mental features (approaching the self as an *object* of attribution), but are not well suited to identify neuronal correlates of minimal self-experience (self as knowing *subject*) [2]. Phenomenological features of minimal self-

experience, such as self-ownership and self-agency, are present in the structure of first-person subjective experience itself [4], suggesting that their neuronal correlates may be found in the very building blocks of neuronal computation.

Theoretical considerations suggest that the brain is perpetually engaged in generating predictions about the 'state of the world', and testing these predictions against incoming sensory signals [1,4]. Perception and action depend on neuronal mechanisms that minimize the mismatch between predicted and actual incoming signals. This process of mismatch-minimization would theoretically imbue perception and action with a pre-reflective feeling of familiarity, self-ownership and self-agency, making it a good candidate for the neuronal correlate of minimal self-experience [2,5]. It is conceivable that the development of more 'cognitive' facets of self, such as personal narrative, may be predicated on minimal self-experiences.

Self-disturbance

Distortions of self-experience are a central feature of a number of altered states of consciousness, such as the psychedelic state and the mystical experience [1,6–9]. In these contexts the experience of a reduction in the normally well-circumscribed experience of self has been termed 'ego-dissolution', and is related to a feeling of increased unity with others and one's surroundings [1,6–8].

Abnormalities of self-consciousness have also been recognized in a number of mental health conditions [10]. A disrupted sense of self was considered to be a core phenomenological feature of early and acute psychosis [4]. Kraepelin, for example, wrote of a 'disunity of consciousness' in schizophrenia, whilst Bleuler wrote of a

slackening of the associative links that tie together thoughts, perceptions, and affects [4]. More recently, it has been proposed that a central phenomenological alteration in schizophrenia is an instability of 'pre-reflective self-awareness', which has close parallels to conceptions of minimal self-experience, and is related to a feeling of immersion in a social world [4,11]. Recent efforts to operationalize self-disturbance in schizophrenia, using the Examination of Anomalous Self-Experience (EASE) questionnaire, suggest that this feature may predict clinical trajectory of first episode psychosis [11].

By contrast, the depressed state is characterized by an increase in self-focus, and an inability to disengage from self-referential ruminative thought. Intriguingly, depressed individuals show abnormal activity in the perigenual anterior cingulate cortex, a region that has been shown to exhibit increased activity for self-specific stimuli [3,10]. More generally, it is noteworthy that both schizophrenia and depression are characterized by abnormal DMN resting-state activity [10].

Psychedelics as a window into the self

Given the prominence of self-experience in normal waking consciousness, and the prevalence of self-disturbance in certain psychiatric conditions, a greater understanding of the neuronal correlates of self-experience is highly desirable.

Psychedelic drugs (5-HT_{2A} receptor agonists) reliably perturb self-consciousness and occasion ego-dissolution experiences in a reversible, transient and dose-dependent manner [8]. These substances therefore provide a fruitful avenue for research into the neuronal correlates of normal and abnormal self-consciousness [1,7,12].

In recent years, several studies have examined the neuronal correlates of ego-dissolution experiences occasioned by the classical psychedelic drugs psilocybin (the active agent in 'magic mushrooms') and lysergic acid diethylamide (LSD) using fMRI and magnetoencephalography (MEG).

These studies reveal that psychedelics decrease the integrity of important resting-state brain networks associated with the sense of self (such as the DMN) as well as the degree of segregation between these and other brain networks. As a result, psychedelics occasion a more globally unified mode of brain function [1]. Importantly, these changes (i.e. DMN disintegration and whole-brain integration) correlate with participants' ratings of ego-dissolution [6,7]. A similar pattern of decreased segregation between functional networks has also been observed in meditators during maintenance of non-dual awareness (where equal attention is given to events 'inside and outside' the body) compared with maintenance of focussed attention on a single object [13].

A recent MEG study demonstrated that ego-dissolution experiences occasioned by psilocybin correlate highly with decreased alpha power (a marker of locally synchronous activity) in the posterior cingulate cortex, arguably the core DMN 'hub' region [12]. Moreover, two recent studies found that the degree of ego-dissolution occasioned by LSD was correlated with increased whole-brain integration [7], and inversely correlated with DMN network integrity, functional connectivity between the parahippocampus and retrosplenial cortex, and decreased delta and alpha power (e.g.

in posterior cingulate cortex) [6], nicely corroborating the earlier findings with psilocybin.

Together, these studies suggest that abnormalities in self-experience may arise when the normal modular organization of the brain's resting-state functional networks is disrupted. One limitation of these studies, however, is that they did not use independently validated measures of ego-dissolution. To rectify this limitation we recently validated a new 8-item self-report assessment of ego-dissolution, the Ego-Dissolution Inventory [8], with the aim of demonstrating the construct validity of ego-dissolution, and increasing the reliability of its measurement in future studies.

Therapeutic implications

An understanding of the neuronal correlates of abnormal self-experience is of great relevance for our understanding and treatment of certain psychiatric conditions.

In recent years the therapeutic utility of psychedelic drugs in anxiety, addiction and mood disorders has received increased attention [14]. Several small studies suggest that psychedelic substances can produce improvements in these conditions when given in controlled therapeutic environments. Recently, a small open-label pilot study of psilocybin in treatment-resistant depression demonstrated improvements in self-reported depressive symptoms at three month follow-up [15]. The precise mechanism by which psychedelics can occasion positive and lasting changes in mood, attitudes and behaviours is deserving of further investigation. It is worth noting, however, that one influential model of psychedelic therapy places great therapeutic importance on the

experience of ego-dissolution, and 'loss of boundaries between the subject and the objective world, with ensuing feelings of unity' [8].

In non-clinical populations, previous work has established that mystical experiences occasioned by psilocybin (which are closely related to ego-dissolution experiences [8]) correlate positively with well-being, increases in the personality trait of openness, and the meaningfulness / spiritual significance of the experience [8,14].

It should be noted, however, that these clinical and nonclinical studies have strict exclusion criteria, small sample sizes, and relatively short follow-up periods. Consequently, further research is required to adequately test the proposed link between ego-dissolution / mystical experiences and positive changes in mood, attitudes and behaviour.

Conclusions

In conclusion, a neuroscience of self-experience is of great importance for neuroscience in general, and for our understanding and treatment of certain psychiatric conditions in particular. Classical psychedelic drugs occasion transient and dose-dependent reductions in the normally well-circumscribed experience of self (termed ego-dissolution), providing a valuable tool with which to investigate the neuronal correlates of normal and abnormal self-experience. More speculatively, the ability of psychedelics to occasion ego-dissolution experiences may be of clinical utility when used in controlled therapeutic environments.

Declaration of Interest

The authors declare that this work was completed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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