

The Psychedelic Experience: The Importance of ‘Set’ and ‘Setting’

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We welcome the renewed interest in the therapeutic potential of psychedelic compounds. In their recent editorial, Sessa and Johnson¹ echo the fervent research climate surrounding psychedelics spanning the 1950s and 60s. They suggest that psychedelics may cause prolonged changes in subjects’ personalities and attitudes following mystical-spiritual experiences. This unique and exciting potential mechanism of action certainly warrants the current renaissance in psychedelic research, and has important implications for study design and subject selection. As we move towards re-exploring the clinical applications of psychedelics, however, we must appreciate that the phenomenology of the psychedelic experience is likely to depend not only on a drug’s pharmacodynamic properties, but also on the makeup of the subject (‘set’) and the environmental context (‘setting’) in which the drug is administered.

Recent work suggests that the potential importance of ‘set’ in the psychedelic experience should not be overlooked. Hallucinogenic compounds act via the serotonergic 5-HT_{2A} receptor to effect experience and behaviour. Genetic and neuroimaging evidence suggests that inter-subject differences in serotonergic neurotransmission relate to personality differences and vulnerability to psychiatric illness.² Relatedly, research with hallucinogenic compounds has reported sustained changes in personality traits and behaviour.³ Moreover, anecdotal reports suggest that the quality of the psychedelic experience (whether the ‘trip’ is ‘good’ or ‘bad’) has some connection to the attitude and particular psychological landscape of the person taking the drug.⁴ Finally, a closer look at the psychological profile of subjects who volunteer for psychedelic research studies reveals that they may not be representative of the general population, and in particular may be more ‘open’ to new experiences, limiting the generalisability of study findings to clinical samples.³ The effect of a hallucinogenic compound on an individual’s experience, therefore, may be influenced by the individual’s neurobiological and psychological composition.

The quality of the psychedelic experience is also inextricably linked to the environmental and social ‘setting’. In the late 1960s several studies strove to isolate the hallucinogenic effect of a drug from external influences, such as the use of concomitant therapy.⁵ Their efforts generated less promising results than studies that, by design, emphasised the importance of the ‘setting’.⁵ As an illustrative example, one study found sensory deprivation to be antagonistic to the ‘LSD experience’.⁶ Consequently, the relationship between the psychedelic experience and the ‘setting’ must be considered in experimental design. Even a structured test or interview can radically alter the resulting phenomenology.⁶

We propose that a fruitful research programme investigating the therapeutic potential of psychedelic compounds must take the complex interaction between ‘set’ and ‘setting’ into account in its subject recruitment and study design. By acknowledging this association future research will be in a position to understand the full breadth of the psychedelic experience and its potential clinical applications. Although practically challenging, such a comprehensive approach will allow us to re-examine the perhaps premature assertion of the mid 1970s that psychedelics had no therapeutic applications.⁵

Conflicts of interest

Nil

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