



Paradox of Psychedelics: From Mind-Bending to Mind-Mending

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Once a symbol of 1960s counterculture, psychedelic substances are now at the forefront of modern scientific research with a focus on their therapeutic potential for mental health conditions such as, major depressive disorder, posttraumatic stress disorder and substance use disorder. Notable studies have highlighted the efficacy of psychedelics in treating these conditions. For example, in one study, 75% of people with major depressive disorder showed improvement after taking psilocybin, and 58% were symptom-free after a year (Gukasyan et al., 2022). For reference, typical response and remission rates for conventional treatments are 58% and 46%, respectively (DeRubeis et al., 2005). However, direct comparisons with standard antidepressants remain debated. In a recent head-to-head clinical trial, psilocybin was found to be comparable, though not superior, to the SSRI escitalopram (Carhart-Harris et al., 2021). Recognizing its potential, the Food and Drug Administration (FDA), a federal agency of the United States Department of Health and Human Services, has recognized psilocybin as a promising treatment for major depressive disorder by giving it a 'Breakthrough Therapy' status. Despite these breakthroughs, the underlying mechanisms of psychedelics' therapeutic effects remain largely unknown.

Perceptual and Emotional Effects

One of the most pronounced immediate effects of these substances is changes in how one sees or experiences the world (Swanson, 2018). These include intensifications, illusions, geometric and complex hallucinations, and altered sense of meaning. Reports of walls appearing to talk or dance, warped edges, and distorted space are common. The nature and intensity of these hallucinations vary with the type and dosage of the psychedelic substance, with complex hallucinations like perceiving entities being more common with drugs like Dimethyltryptamine (DMT), especially when users have their eyes closed.

Another crucial aspect of the acute psychedelic experience is the mystical experience, characterized by feelings of sacredness, ineffability, and transcendence of space and time (Griffiths et al., 2006). As such, people may feel a deeply personal and profound moment of being connected to something greater than themselves. The historical use of psychedelics in indigenous ceremonies (Fotiou, 2019), such as the use of ayahuasca by South American natives, reflects their long-standing cultural significance. In an effort to quantify the effects of psychedelics on mystical experience, in the 60s, Walter Pahnke (1969), conducted an experiment called the Good Friday experiment on students in a private chapel during the broadcast of the traditional Christian Good Friday religious service. In this study, 30–40% of

participants in participants who received psilocybin reported significant mystical experiences compared to none who received a placebo. Alongside changes in perception and deeply moving experiences, psychedelics profoundly affect emotional states (Bernasconi et al., 2014; Nichols, 2016). They tend to amplify emotions and bias them towards positivity. For instance, under the influence of LSD, individuals show reduced sensitivity to experiences that are typically considered negative such as social exclusion, a shift accompanied by reduced activity in brain regions typically associated with negative emotions (Preller et al., 2016). This bias towards positivity can be particularly therapeutic for individuals with depressive disorders. However, higher doses of psychedelics can also induce negative and challenging emotions (Griffiths et al., 2011), often due to a diminished sense of self-control, which paradoxically may also lead to therapeutic outcomes (Agin-Liebes et al., 2020).

Cognitive Effects

Cognition is another domain acutely impacted by psychedelics. These cognitive effects parallel the subjective experience of 'ineffability,' where volunteers struggle to accurately articulate their experiences. This difficulty in describing their experiences often comes with increased distractibility, making it harder to perform usual thinking tasks (Carter et al., 2005). Consequently, these substances notably impact cognitive functions essential for adaptable and goal-directed behavior (the ability to plan, make decisions, and pursue objectives in a flexible way), functions also commonly disrupted in mental health conditions.

Important mental abilities, such as controlling impulsive reactions, holding information in mind, and adapting to new situations, are significantly affected by psychedelics. People tend to respond more slowly and make more mistakes on tasks that require focusing, remembering,

or switching between rules (Barrett et al., 2018; Pokorny et al., 2020; Quednow et al., 2012). These effects are short-lived but illustrate how psychedelics temporarily loosen the mind's usual control systems. These changes underscore the significant, albeit temporary, impact of psychedelics on cognitive processes.

Interestingly, while psychedelics can briefly interrupt normal thinking, they may also help people become more mentally flexible over time, meaning better able to adjust their thoughts and behaviors to new situations. For example, Doss and colleagues (2021) found that people with depression made fewer mistakes on a computer task that measures how well someone can notice changing rules and adjust their choices accordingly — a kind of mental flexibility test — one month after psilocybin therapy. This suggested their thinking had become more adaptable. Similarly, Close et al. (2020) showed that being able to adjust one's perspective and accept experiences, known as psychological flexibility, helps explain how psychedelics can reduce anxiety and depression.

A lingering question in psychedelic research is then understanding how a single use can have such lasting impacts on cognition and mood. In contrast to substances like alcohol, which may also offer a temporary spike in creative task performance that requires flexible thinking (Benedek et al., 2017) but lack enduring cognitive benefits, psychedelics seem to facilitate long-lasting positive changes in cognitive processes tied to mental health. This paradoxical nature of the treatment, involving transient (short-term) cognitive impairment followed by sustained (long-lasting) cognitive improvement, highlights a complex yet potentially valuable connection that could open new paths for therapeutic interventions.

One explanation for the effects of psychedelics is their ability to help balance different ways of thinking depending on the situation (Sayali & Barrett, 2023). Imagine your brain like a well-trodden path in a

forest, where negative thoughts and worry are like deep ruts that make it hard to stray onto new paths. In conditions like depression, this path becomes so entrenched that it's difficult to think any other way, leading to constant worrying or fixating on certain thoughts. This is where psychedelics come into the picture, acting like a surprising guide through the mental wilderness. They offer a chance to switch between being stuck in our ways (mental rigidity) and being open to change (flexibility). This flexibility is crucial for treating conditions like depression.

A New Path for Mental Health Treatment

When psychedelics disrupt our usual focus, it's like they're shaking up the snow globe of our thoughts. This disruption can guide those stuck in negative thinking towards a more adaptable mindset, initiating a much-needed shift in thought patterns. What's more fascinating is that these effects are not just fleeting. With their rapid and lasting impact, psychedelics can enhance the brain's ability to learn and adapt. This is shown by an increase in substances in the brain that help it grow and adapt after taking psychedelics (Holze et al., 2021; Hutten et al., 2020) - a process known as neuroplasticity. Research has shown that after taking psilocybin, there is a change in how certain brain networks communicate (Barrett et al., 2020; Devon Stoliker et al., 2022; McCulloch et al., 2021). These networks are involved in how we manage our thoughts, focus our attention, and make decisions. Along with these changes, there's also a decrease in behaviors and brain activity linked to bad moods. So, what does all this mean? Psychedelics might be opening a window for therapeutic change. They make it easier to manage thoughts, regulate mood, and enhance the brain's ability to adapt and learn from new experiences. In the context of psychotherapy, this improved capacity for change and learning could be particularly valuable for

individuals struggling with mental health issues. Think of it as being equipped with a map and tools to explore new, healthier paths in the forest of your mind. In conclusion, the therapeutic promise of psychedelics lies in their extraordinary capacity to initially disrupt normal perception, emotion, and cognition, while paradoxically leading to long-term improvements in cognitive flexibility. This contrast, where initial disorientation evolves into therapeutic insight and resilience, reflects the path many traverse in overcoming mental health challenges. Psychedelics, by reshaping entrenched thought patterns and promoting beneficial changes in brain plasticity, emerge not merely as remnants of a past cultural epoch but as vital instruments of hope in contemporary mental health care. As research continues to peel back the layers of their complex mechanisms, we move closer to a potential paradigm shift in treating mental health disorders, pushing the boundaries of our understanding of the mind's remarkable ability to heal and evolve.

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