

Psychedelics and Cognition: A New Look

March 29 2023



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The synthesis of LSD and psilocybin in the early to mid-20th century sparked not only a new counterculture in the United States but also a new interest in brain science, specifically the role of neurotransmitters. Despite these discoveries, research on psychedelics went dormant for decades due to anti-drug sentiment. A recent renaissance in psychedelic research seeks to understand how these drugs might be leveraged as tools in treating mental illness. While this work has focused largely on mathematical modeling and resting-state neuroimaging, that is now

shifting: Cognitive neuroscientists are bringing new rigor to the field, using behavioral and clinical studies to investigate the cognitive effects of psychedelic drugs.

"Despite [psychedelics](#) having some of the most interesting subjective effects of any psychoactive drug, they're generally being shown to impair cognition like most psychoactive drugs," says Manoj Doss of Johns Hopkins University, who is chairing a symposium on psychedelics and cognition at the Cognitive Neuroscience Society (CNS) annual meeting today in San Francisco. "One reason for this is that cognitive neuroscientists have been less involved with this work, so when the impact of psychedelics on cognition is measured, the tasks tend to be relatively simple and outdated."

The landscape for these studies is rapidly changing, however, with a wealth of new research, looking at everything from how psychedelics can aid in understanding the malleability of [memory](#) to exactly how psilocybin can increase the spontaneous creative process.

"There are massive over-arching gaps in our knowledge regarding psychedelics and cognition," says Natasha Mason of Maastricht University who is presenting work at the CNS symposium. "There is a huge surge of interest in these substances therapeutically, but until now, there has been no neurocognitive account that ties acute and persisting psychedelic-induced changes in cognition with long-term therapeutic response."

Creating Creative Cognition

Natasha's Mason interest in psychedelics research began the way many do in neuroscience, with a deep desire to better treat brain diseases. While initially pursuing a career in pharmacy, she remembers searching the literature for alternative treatments for mental health disorders, and

finding a paper on the promise of psychedelics in treating depression and anxiety.

"The literature seemed exciting: a one-time ingestion of a psychedelic resulted in long-term symptom reduction. This was unheard of in my pharmacy classes, she says. "Unfortunately, the science was young, the substances illegal, and only a handful of universities could conduct this research." Mason then decided to move to Maastricht University in the Netherlands to pursue this line of investigation.

In new work she is presenting in the CNS symposium, Mason's team investigated whether a moderate dose of psilocybin affects creative cognition, looking both at the acute and persisting effects. "I find it quite an exciting study, as despite this historical association between psychedelic use and creativity, it is the first modern trial to assess this in a scientifically rigorous way," she says.

Indeed, many individuals have anecdotally reported enhanced creative capacity after psychedelic drug use, and psychedelic-assisted clinical trials have been used to treat a range of disorders characterized by extremely inflexible thought patterns. The premise is that the psychedelic experience can provide therapeutic relief by breaking patients out of their rigid, maladaptive thought patterns.

In [their double-blind, placebo-controlled study](#), Mason's team found that psilocybin increased ratings of spontaneous creative insights while also decreasing deliberate, task-specific creativity. They also found that novel ideas increased 7 days after the psilocybin exposure. Brain imaging supported the behavioral changes in creativity.

Mason hopes that their work will lead to a better understanding of whether psychedelics induce a "window of opportunity" for enhanced therapy. "If there is a persistent, subacute change in creative cognition,

maybe we can use this period to help people integrate their acute insights with a therapist, and come up with new, more effective strategies that facilitate adaptive interpretation and coping abilities," she says.

Making Memories More Malleable

Manoj Doss' interest in psychedelics stems from his interest in [human memory](#), and in particular reconsolidation—reactivating memories to make them more fluid in order to help patients suffering from disorders like depression and posttraumatic stress disorder (PTSD).

"Unfortunately, reconsolidation paradigms in humans have not exactly led to clinical breakthroughs, but one reason may be that complex memories maintained over several years are not easily rendered labile," Doss says. That's where psychedelics could come into play, by potentially inducing plasticity in the cortex.

But before scientists can test psychedelics' role in reconsolidation, they first need to better understand how the drugs affect various aspects of memory. In [a preprint analysis](#), Doss will be presenting at the CNS meeting, he and colleagues looked at 10 datasets from studies investigating how psychedelics influence episodic memory. They found that while psychedelics such as psilocybin and MDMA impair the encoding of memories that rely on recalling specific details, they can enhance the encoding of memories that rely on familiarity. This differs from hallucinogens like ketamine, which appear to impair both types of memory encoding.

"Interestingly, non-drug studies have found that when recollection fails and familiarity is high, peculiar phenomena emerge, reminiscent of someone on psychedelics, such as déjà vu and premonition," Doss explains. "Although psychedelics may actually help some come to tangible insights, much of the psychedelic experience might be turning up the gain of such feelings of familiarity or insight, and like non-drug

studies that can induce such feelings through cognitive manipulations, these feelings can potentially be misattributed to unrelated stimuli or ideas, giving rise to false memories and illusory insights."

The new work suggests that psychedelics may enable the brain to bypass or minimize the need for the hippocampus. The hippocampus is thought to help mediate how the cortex learns with more "permanent" memories arising from regular representations across episodic memories.

"Having a negative sense of self or a defining traumatic moment may thus come to be coded in the cortex, especially after years of suffering," Doss says, "and maladaptive representations may be particularly difficult to disrupt when new information coming in is biased by a negative sense of self and recent negative experiences." Psychedelics thus could provide an opportunity to "rapidly overwrite maladaptive memories and perhaps even provide a fresh set of contextual influences that aid new encoding even once one is sober."

Doss cautions that there is still much to be developed not only in terms of understanding these drugs' impact on memory and cognition but also at the intersection of psychotherapy and drugs. Current studies administer to subjects high doses of psychedelic drugs—2 to 3 times that which someone may use for a "substantially intoxicated walk through the woods"—while they lay on a couch with eyeshades on. "Although there are therapists in the room that may provide support during difficult moments, there's no formal therapy during the acute effects, and participants are encouraged to 'direct their attention inward,'" he says.

Doss sees the future in testing how certain types of therapy or stimuli could assist in [psychedelic](#)-induced therapy sessions. He also points toward developments with the drugs themselves becoming more targeted toward specific desired effects or time courses. Doss and Mason hope the CNS session will help spur new collaborations and directions for

psychedelics and cognition research.

More information: The symposium "[Altered States of Cognition: The Acute and Persisting Consequences of Psychedelic Drugs on Cognition](#)" is taking place at 1:30pmPT on Tuesday, March 28, as part of the CNS 2023 annual meeting from March 25-28, 2023 in San Francisco.

Provided by Cognitive Neuroscience Society

Citation: Psychedelics and Cognition: A New Look (2023, March 29) retrieved 19 April 2024 from <https://medicalxpress.com/news/2023-03-psychedelics-cognition.html>

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