

# Single-dose psychedelic boosts brain flexibility for weeks, peer-reviewed study finds

*A single dose of a psychedelic improves cognitive flexibility in mice for at least three weeks. This has implications for depression, PTSD, and Alzheimer's.*

ANN ARBOR, MI, UNITED STATES, April 22, 2025 /EINPresswire.com/ -- In a groundbreaking research study, University of Michigan researchers have discovered that a single dose of a psychedelic compound can enhance cognitive flexibility—the brain's ability to adapt to changing circumstances—for weeks after administration, potentially revolutionizing treatments for depression, PTSD, and neurodegenerative diseases.

The study, published today in the journal [Psychedelics](#), demonstrates that mice treated with a single dose of 25CN-NBOH, a selective serotonin 2A receptor agonist, showed markedly improved performance in reversal learning tasks compared to control groups when tested 2-3 weeks after treatment.

## Key Findings

"What makes this discovery particularly significant is the sustained duration of cognitive benefits following just one psychedelic dose," explains Professor Omar J. Ahmed, the study's senior, corresponding author from the University of Michigan's Department of Psychology. "We observed enhanced learning adaptability that persisted for weeks, suggesting these compounds may induce lasting and behaviorally meaningful neuroplasticity changes in the prefrontal



Illuminating Flexibility: Single-Dose Psychedelics and Cognitive Adaptation. The figure depicts a mouse with a lightbulb, symbolizing the remarkable cognitive enhancements discovered in psychedelic research. Against a vibrant, radiating background, this i

cortex."

Using an innovative automated sequential learning paradigm, researchers measured how effectively mice could adapt to rule reversals—a standard test for cognitive flexibility. The psychedelic-treated mice demonstrated superior adaptability compared to saline controls, with enhanced task efficiency, higher percentages of correct trials, and increased reward acquisition during the reversal phase.

### Implications for Brain Science

The results complement existing cellular research showing psychedelic-induced structural remodeling in the prefrontal cortex but uniquely demonstrate sustained cognitive benefits persisting long after the immediate effects of the drug have dissipated.

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*Elizabeth J. Brouns*

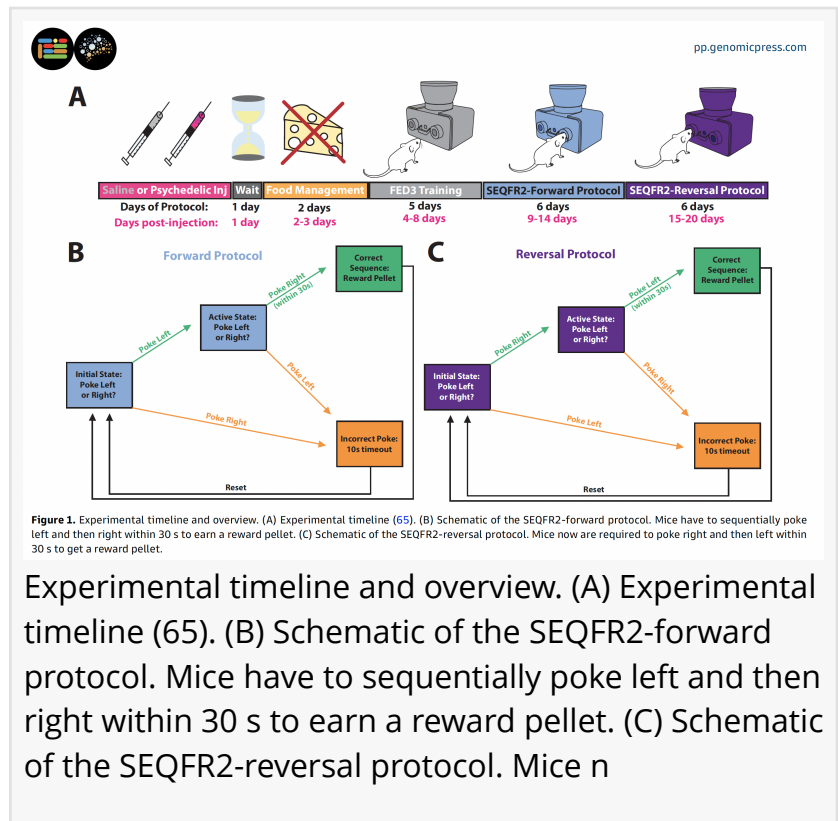
As interest in psychedelic medicine continues to grow, this research raises intriguing questions about how psychedelics might reshape neural pathways governing flexible thinking. Could these compounds potentially reopen critical periods of brain plasticity? What molecular mechanisms underlie these long-lasting cognitive improvements? How might the timing and frequency of administration affect long-term neuroplasticity?

“The current study focused on the long-term effects of a

single psychedelic dose. A key question is what happens with two, three, or even twenty doses taken over several months. Is every additional dose increasingly beneficial for flexible learning or is there a plateau effect or even a negative effect of too many doses? These are important questions to answer next in the quest to make psychedelic medicine more rational and mechanistic,” according to Dr. Ahmed.

### Sex Differences and Clinical Potential

Importantly, the study found that both male and female mice showed significant improvements in cognitive flexibility, suggesting the potential broad applicability of psychedelic therapy across



biological sexes.

"The most striking aspect of our findings is that these cognitive benefits were measured 15-20 days after a single psychedelic administration," notes Elizabeth J. Brouns, first author of the study. "This suggests that a single dose of a psychedelic isn't just temporarily altering perception, but potentially inducing lasting beneficial changes in brain function."

Methodological Advances

The study's automated behavioral task represents a significant methodological advance for evaluating flexible learning, enabling researchers to efficiently evaluate cognitive flexibility in future investigations of psychedelic compounds. This high-throughput approach could accelerate the development of targeted psychedelic therapies for specific cognitive deficits.

The full Psychedelics peer-reviewed research article, titled "Single-dose psychedelic enhances cognitive flexibility and reversal learning in mice weeks after administration" is available on 22 April 2025 in Psychedelics. The research includes Dr. Tyler Ekins as a co-author and was supported by the National Institutes of Health and the University of Michigan Eisenberg Family Depression Center. The article is freely available online at <https://doi.org/10.61373/pp025r.0002>.

About the Journal - Psychedelics: The Journal of Psychedelic and Psychoactive Drug Research (ISSN: 2997-2671) is a peer reviewed medical research journal published by [Genomic Press](#), New York. Psychedelics is dedicated to advancing knowledge across the full spectrum of consciousness altering substances, from classical psychedelics to stimulants, cannabinoids, entactogens, dissociatives, plant derived compounds, and novel compounds including drug discovery approaches. Our multidisciplinary approach encompasses molecular mechanisms, therapeutic applications, neuroscientific discoveries, and sociocultural analyses. We welcome diverse methodologies and perspectives from fundamental pharmacology and clinical studies to psychological investigations and societal-historical contexts that enhance our understanding of how these substances interact with human biology, psychology, and society.

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RESEARCH REPORT

Single-dose psychedelic enhances cognitive flexibility and reversal learning in mice weeks after administration

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Psychedelics; <https://doi.org/10.61373/pp025r.0002>

Genomic Press  
**Psychedelics**  
The Journal of psychedelic pharmacology

Psychedelic compounds have demonstrated remarkable therapeutic potential for treating neuropsychiatric disorders by promoting sustained neuroplasticity in the prefrontal cortex (PFC). Cognitive flexibility—the ability to adapt previously learned rules to novel situations—represents a critical PFC function that is frequently impaired in depression, PTSD, and neurodegenerative conditions. In this study, we demonstrate that a single administration of the selective serotonin 2A receptor agonist 25CN-NBOH produces significant, long-lasting improvements in cognitive flexibility in both male and female mice when measured 2–3 weeks posttreatment. Using a novel automated sequential learning paradigm, psychedelic-treated mice showed superior adaptability in rule reversal tasks compared to saline controls, as evidenced by enhanced poke efficiency, higher percentages of correct trials, and increased reward acquisition. These behavioral findings complement existing cellular research showing psychedelic-induced structural remodeling in the PFC and uniquely demonstrate sustained cognitive benefits persisting weeks after a single psychedelic dose. Our automated behavioral task provides a high-throughput method for evaluating cognitive flexibility effects of various psychedelic compounds, offering important implications for therapeutic applications in conditions characterized by cognitive rigidity, including depression, PTSD, and potentially Alzheimer's disease.

**Keywords:** Cognitive flexibility, neuroplasticity, psychedelic therapy, reversal learning, serotonin 2a receptor.

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