

# Predicting who may do best with psychedelic-assisted therapy

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Visual representation of the positive and negative effects of psychedelics as communicated by differences in color, saturation, rhythm, contrast and clarity.  
Credit: Leah Ryal

As psychedelics gain ground as a potential therapy for mental health disorders, there remains a pressing concern that patients in clinical trials may have adverse effects to the drugs.

New research identifies [personality traits](#) that have been associated with

positive and [negative experiences](#) on psychedelics in previous studies, information that could help predict how future clinical trial participants will respond to the drugs.

The findings suggest that people more open to [new experiences](#) and willing to surrender to the unknown may be best positioned to have a positive experience on psychedelics, and individuals who tend to be preoccupied or apprehensive could be more likely to have a negative, or challenging, experience.

These predictions could be used by scientists to help hesitant clinical trial patients feel more open to the potential therapy, possibly by offering lower doses as a starting point, researchers say—though such a concept remains speculative.

"The findings point to interesting testable things we can look at in future research," said Alan Davis, assistant professor of social work at The Ohio State University and senior author of the review. "It might be plausible to use threshold doses that are smaller than those used in a trial as a first exposure so people have less anxiety, experience the benefit and, from that, go into a higher dose later."

The study is published online in the journal *ACS Pharmacology & Translational Science*.

To arrive at these predictions, the researchers reviewed 14 published [clinical trials](#) and other types of studies conducted in recent years that documented participants' personality traits or states of mind and their associations with a positive or negative experience on psychedelics.

"It's been an open question so far in [psychedelic](#) science: How can we predict how people will react? We thought this review would be a good opportunity to develop a narrative of what the consensus is so far," said

study first author Jacob Aday, a Ph.D. candidate in psychology at Central Michigan University who collaborates with Davis.

Preliminary evidence has suggested that psychedelics may be effective in treating mood, anxiety, trauma-based and [substance use disorders](#).

"Psychedelics might broadly apply to a whole range of different psychiatric problems, and in part that might be because they're directly affecting neurotransmission and the brain's ability to communicate in new ways that involve different parts of the brain," Davis said. "But there is still a lot to unpack about exactly how this all works and why it may be effective."

Of the studies reviewed, 10 tested psilocybin (commonly known as magic mushrooms) as a therapy, two involved LSD, one used a hallucinogenic brew called ayahuasca and one examined psychedelic use in general.

Experiences on psychedelics vary in intensity and tend to comprise three categories: a mystical, insightful or challenging experience. A [mystical experience](#) can feel like a spiritual connection to the divine, an insightful experience increases people's awareness and understanding about themselves, and a challenging experience relates to emotional and physical reactions such as anxiety or increased arousal.

The review suggests that people who are high in the traits of openness, acceptance and absorption—the tendency to immerse oneself into imaginative experiences—and in a psychological state of surrendering to whatever may transpire are more likely to have positive psychedelic experiences.

A state of surrender, in particular, stood out for its association with a lower chance for acute dread and a higher likelihood of a mystical

experience and what is known as "ego dissolution," when one's sense of self gives way to a closer connection to other people and the broader world.

In contrast, people who are low in those traits or who are in preoccupied, apprehensive or confused states are considered more likely to experience adverse reactions.

"There was also tentative evidence that increased experience with psychedelics and increased age were associated with slightly less intense effects with the drugs," Aday said. "And there weren't any differences according to sex. Men and women responded similarly."

Three studies had identified potential neurological markers that could help predict research participant reactions to psychedelics, but the cost of collecting brain scans to screen trial candidates made them less practical predictors than psychological traits, Aday said.

Davis has already considered potential reactions to psychedelics for a psilocybin trial he is planning for veterans who have post-traumatic stress disorder.

"People who have experienced trauma are not very high in surrender, because they are anxious all the time about their past traumatic experiences," he said. "A possibility to explore is starting with a low or moderate dose prior to giving the full therapeutic dose, which might help them increase in surrender. We've designed the study this way, thinking that might be helpful."

**More information:** Jacob S. Aday et al. Predicting Reactions to Psychedelic Drugs: A Systematic Review of States and Traits Related to Acute Drug Effects, *ACS Pharmacology & Translational Science* (2021). [DOI: 10.1021/acsptsci.1c00014](https://doi.org/10.1021/acsptsci.1c00014)

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