Psychedelics are a Promising Therapy, but They Can Be Dangerous for Some

While drugs like ketamine and psilocybin are largely considered safe, here’s what to know about who should be cautious.



**By Dana G. Smith**

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When Dr. Charles Nemeroff first met his patient, the 32-year-old woman had already been to see several psychiatrists. Initially, the woman, whose identity has been concealed to protect her privacy, had experienced paranoid and racing thoughts, insisting there were listening devices in her phone and that people were watching her; she even sold her home in an attempt to get away from them. After being given antipsychotic drugs, her mania and psychosis abated, but they were replaced by debilitating depression.

“By the time she came to me, she said, ‘I have no feelings whatsoever. I have no mood variation. I am completely empty,’” said Dr. Nemeroff, who is chair of the department of psychiatry and behavioral sciences at the University of Texas at Austin Dell Medical School.

While the woman had been treated for mild depression for over 10 years, she’d previously maintained a rich social life and fulfilling career. This — the psychosis followed by the deep depression — was something completely different. And it was triggered by her use of psychedelics.

Eight months earlier, the woman had tried hallucinogenic mushrooms for the first time with friends and had such a great time that she took them again the next day. The second time, though, something went terribly wrong.

“She had a full blown psychotic episode for the first time in her life,” said Dr. Nemeroff, who published the woman’s story as a case report in [The American Journal of Psychiatry](https://ajp.psychiatryonline.org/doi/full/10.1176/appi.ajp.22010073) in December. Her friends, who took the same drugs she did both days, had no lasting ill effects.

Psychedelics have surged in popularity in recent years: 1.4 million Americans tried hallucinogens for the first time in 2020, according to the [National Survey on Drug Use and Health](https://www.samhsa.gov/data/sites/default/files/reports/rpt35325/NSDUHFFRPDFWHTMLFiles2020/2020NSDUHFFR1PDFW102121.pdf). This enthusiasm is partly attributed to clinical trials showing that the drugs, most notably psilocybin and ketamine, [hold real promise](https://www.nejm.org/doi/full/10.1056/nejmoa2032994) in treating some mental health disorders, particularly depression.

There has also been a shift in how the drugs are presented in popular culture and the media, like in Michael Pollan’s [best-selling book](https://www.nytimes.com/2022/07/15/arts/television/how-to-change-your-mind-netflix-michael-pollan.html) and Netflix series, “How to Change Your Mind.” Two states, Oregon and Colorado, have now legalized psilocybin for therapeutic use, and more are expected to follow suit.

As these drugs gain mainstream acceptance, more and more people will likely consider taking them, both therapeutically and recreationally. Experts who study these substances strongly urge that people only use them in supervised therapeutic settings, such as in a clinical trial or at an established ketamine clinic, partly because of safety concerns and partly because they are illegal outside of these confines. Realistically, though, many people will use them elsewhere.

Psychedelics have an extremely low chance of lethal overdose and there is little likelihood of addiction. As a result, they have been classified by experts as some of the [least harmful](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(10)61462-6/fulltext) recreational drugs. But that doesn’t mean they are entirely without risk. Because of this, psilocybin trials and ketamine clinics have strict exclusion criteria to try to protect people who have physical or psychological vulnerabilities.

If you’re considering using these drugs, here’s what to know about when they could potentially be dangerous.

## **Serious psychiatric disorders**

When it comes to significant side effects, experts’ primary worry about ketamine, psilocybin and other hallucinogens, like LSD or ayahuasca, is that they can trigger a psychotic or manic episode. Because these drugs (with the exception of ketamine) are not approved for use by the Food and Drug Administration, the safety data on them is scarce. Instead, most of the basis for this concern stems from anecdotal evidence.

What little data does exist suggests that the chances of psychosis developing in the general population is low. [One survey](https://www.nature.com/articles/s41598-021-94421-z) of over 1,000 self-reporting recreational psychedelic users did not find a link between drug use and [schizophrenia-like symptoms](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5775125/). [Another study](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0063972) similarly showed no connection between past psychedelic use and current psychosis or other psychiatric disorders.

However, experts say the risk of psychedelics triggering a psychotic or manic episode is likely elevated for people who have a personal or family history of schizophrenia or bipolar disorder. Consequently, people with these histories are excluded from psilocybin clinical trials and treatment at ketamine clinics.

“I had many patients that would give me the story that they were more or less fine, they took LSD, and they’ve had schizophrenia since,” said Dr. Bryan Roth, a pharmacology professor at the University of North Carolina at Chapel Hill. “My guess is they had some underlying predisposition to schizophrenia and it sort of tipped them over the edge.”

Dr. Nemeroff agreed: “I think the issue with these very powerful medications is that there are probably people who are genetically vulnerable to a major psychiatric illness, but they haven’t reached the threshold yet. And then what these medications might do is unleash it.”

Backing up these concerns, one of the few studies looking at psychedelic use in [people with bipolar disorder](https://journals.sagepub.com/doi/pdf/10.1177/02698811221131997) found that one-third reported that their symptoms worsened after taking psilocybin recreationally, and 3 percent had to seek emergency medical care.

As a result, Dr. Roth said, “Anybody with a serious psychiatric disorder — like schizophrenia, bipolar disorder — should not take psychedelics.”

## **Cardiovascular concerns**

Psychedelics’ emerging legal status also means there is very little research about their physical safety. Experts do know that psilocybin and ketamine raise blood pressure and heart rate, so out of an abundance of caution, people with heart conditions, such as uncontrolled high blood pressure, heart disease and arrhythmias, are advised not to take them.

During carefully monitored clinical trials, where dosage is supervised and patients are screened, the drugs “appear to be safe from a cardiac standpoint,” said Dr. Jeremy Ruskin, a professor of medicine at Massachusetts General Hospital who specializes in cardiology. Whether they are as safe for people who are at high risk in uncontrolled settings is unknown.

One reason that psychedelics appear to be safer than many other drugs is because the majority of users take them infrequently, meaning there’s little concern that potential damage could accumulate over time. However, experts say there is a second, hypothetical cardiovascular risk if the drugs are taken every day or every week.

Most hallucinogens are thought to produce their psychedelic effects by activating a specific serotonin receptor called 5-HT2A (except ketamine, which primarily works via the glutamate system). The drugs also act on a sibling serotonin receptor, 5-HT2B, which has been linked to valvular heart disease. [Research](https://www.nejm.org/doi/10.1056/NEJMp068265) has shown that medications that activate this receptor — which include some used to treat Parkinson’s disease and migraines, as well as the infamous diet drug [fen-phen](https://pubmed.ncbi.nlm.nih.gov/9688104/) — cause valvular damage in roughly 25 percent of people who take them. Two small studies of frequent, heavy users of MDMA (another psychedelic-related drug that activates 5-HT2B) [showed the same signs of heart disease](https://pubmed.ncbi.nlm.nih.gov/17950805/).

Dr. Roth said that the risk of developing valvular problems from doing psychedelics a few times “is almost probably zero.” But he is worried about people who [microdose](https://www.nytimes.com/2022/02/28/well/mind/microdosing-psychedelics.html) — taking tiny amounts of the drugs — several times a week.

## **Other safety concerns**

There are a few other notable risks pertaining to medications or medical history that potential users of psychedelics should be aware of.

First, the drugs substantially alter brain activity, so it’s possible they could [trigger a seizure](https://www.sciencedirect.com/science/article/pii/S0376871622003234) in someone with epilepsy.

In addition, Dr. Celia Morgan, a professor of psychopharmacology at the University of Exeter in England, said that people who’ve had a traumatic brain injury should consult with their doctor before using ketamine, because the drug can increase intracranial pressure.

“If you’ve got anything in your brain that’s raising the pressure, then you raise the pressure further, you could end up with a horrible hemorrhage,” she explained.

In terms of medication interactions, people on antidepressant drugs that affect serotonin levels should be careful about taking psilocybin because too much of the neurochemical can cause a potentially fatal reaction known as serotonin syndrome. Dr. Roth said the risk is greatest for people taking monoamine oxidase inhibitors (M.A.O.I.s); it’s less clear for the more commonly prescribed selective serotonin reuptake inhibitors (S.S.R.I.s, like Prozac). Just in case, psilocybin clinical trials typically require participants to go off their antidepressants first.

For ketamine, the biggest risk is taking it while you’re also on drugs that depress the central nervous system, like opiates, muscle relaxants or benzodiazepines, because those medications could enhance or prolong ketamine’s sedative effect.

Finally, although the general risk for dependence on psychedelics is extremely low, for ketamine it is not nonexistent. Dr. Morgan said that using the drug multiple times a week and wanting more after it wears off would be red flags for addiction.

“I think it’s got enormous value,” she said. “But we’re going to miss that if we’re not mindful of the risks.”