

Mental Health and Psychedelics

Berkeley
Center for the
Science of
Psychedelics

press.psychedelics@berkeley.edu

In 2019, over a billion people were living with a mental health disorder.¹ Suicide accounted for more than 1 in 100 deaths, and 58 percent of suicides were committed by individuals under age 50. But available treatment has failed to address this prevalence. Worldwide, seventy-one percent of those with psychosis do not receive mental health services. Even in high-income countries, only a third of people with depression have access to formal treatment.² This disparity has widened during the COVID-19 pandemic: depression and anxiety increased by 25 percent globally in the first year of the pandemic alone.³ In 2022, a World Health Organization report on mental health called on policy makers to step up investments in mental health research and treatment, and to diversify and scale up care options.⁴ The need for mental health care is rising as interest in psychedelic therapy grows.

For thousands of years, Indigenous peoples have used psychedelics for spiritual and medicinal purposes. In the 1950s and 1960s, researchers began experimenting with psychedelics to treat psychiatric conditions, starting with tests on whether LSD could be used in psychotherapy to treat alcohol addiction and for trauma.⁵ Early evidence supported the therapeutic potential of psychedelics and their limited medical risks. However, following the passage of the Controlled Substances Act in 1970, the federal government halted most of this research.⁶

Since the 1990s, a steady resurgence in psychedelic research has provided new evidence that many substances can be used in conjunction with therapy to treat a range of psychiatric conditions. Other research on substances like psilocybin also suggest enduring improved well-being for healthy users after psychedelic experiences. Even more research is expanding our neuroscientific understanding of the effects of these substances on our nervous system.⁷ This may help contribute to development of therapies for patients whose conditions have resisted more traditional treatment. Much of this work is still ongoing.

Here's what the research tells us so far about the effects of the major psychedelic substances on our mental health.

Classic Psychedelics

While conditions like depression and anxiety can reduce functional connectivity between certain brain regions, some research suggests that classic psychedelics can help temporarily rewire the brain and promote neuroplasticity by increasing and strengthening those connections.⁸

Psilocybin

In 2000, researchers at Johns Hopkins received federal and institutional approvals to run a non-therapeutic trial, giving psilocybin to healthy human volunteers who had never taken a psychedelic. That led to a landmark 2006 publication, "Psilocybin Can Occasion Mystical-type Experiences Having Substantial and Sustained Personal Meaning and Spiritual Significance." Since then, studies have suggested that, in combination with therapy, psilocybin can be used to alleviate depression,⁹ anxiety and depression in cancer patients,¹⁰ substance abuse disorders,¹¹ and post-traumatic stress disorder.¹² Researchers are also investigating the use of psilocybin to treat anorexia nervosa¹³ and the psychological distress that can accompany neurodegenerative diseases like Alzheimer's and other forms of dementia.¹⁴

In some healthy research volunteers, psilocybin has been shown to increase "nature relatedness"¹⁵ and overall well-being and life satisfaction.¹⁶

Ayahuasca

Research suggests that ayahuasca could be used in carefully structured settings to treat addiction,¹⁷ depression, and anxiety. Some users report that after taking ayahuasca they feel more creative,¹⁸ more loving and empathetic, see improvement in their memory and concentration, and generally have a more positive mood.¹⁹ Long-term use of ayahuasca has been shown to produce changes in brain chemistry and personality.²⁰

DMT

Although the acute drug experience is short when it's injected or its vapor is inhaled, research suggests that DMT can have significant impacts. Studies show it could play a role in neuroregeneration²¹ and that it reduces chronic inflammation in the central nervous system. It also has been shown to reduce anxiety and depression in rats.²²

5-MeO-DMT

Anecdotal reports and early studies suggest 5-MeO-DMT (which is also short acting when its vapor is inhaled) could help treat anxiety and depression, but further research is needed to determine its safety and effectiveness.^{23, 24}

LSD

Research suggests that LSD combined with therapy can be effective in reducing anxiety in people with a life-threatening illness,²⁵ and in treating alcoholism,²⁶ obsessive compulsive disorder,²⁷ and cluster headaches.²⁸ Studies (some ongoing) have investigated whether microdosing LSD – taking small amounts that don't cause perceptual changes – could help treat chronic pain,²⁹ depression,³⁰ and inflammation caused by neurodegenerative diseases,³¹ but there is debate over the extent to which the apparent benefits of microdosing are due to LSD or due to a placebo effect.³²

Mescaline

Mescaline, a long-acting psychedelic, was first isolated by the German chemist and physician Arthur Heffter in 1897,³³ and in the 1950s the drug was used experimentally to simulate and study schizophrenia.³⁴ Research suggests mescaline could be effective in combination with therapy for treating addiction to alcohol³⁵ and other drugs³⁶ as well as reducing anxiety and depression³⁷

Non-Classic Psychedelics

This category includes substances whose effect profiles overlap with those of the classic psychedelics but that don't interact as prominently, or at all, with serotonin 2A receptors in the brain. Instead, these psychedelics interact with other neurotransmitter systems, including dopamine and glutamate, and often have effects outside of the general profile of the classic psychedelics.

Ibogaine

Ibogaine's potential to interrupt drug addiction was first recognized in 1962 by Howard Lotsof, at the time a heroin addict who experimented with ibogaine.³⁸ Since then, numerous studies have shown ibogaine can help treat addiction to heroin and other opioids.³⁹ However, ibogaine can be dangerous. There are numerous reports in the scientific literature of fatal cardiac events after taking ibogaine. Other side effects range from nausea and tremors to (less commonly) psychosis and mania to seizures and comas.⁴⁰ Because ibogaine can cause an irregular heartbeat, it can be particularly risky for people with preexisting cardiac problems or when mixed with other drugs.⁴¹

Ketamine

Ketamine is used widely as an anesthetic, especially on the battleground when equipment is not available to administer standard anesthesia, in children, and in animals. It is also sometimes used to treat chronic pain.⁴² At lower doses, ketamine can alter one's perception and sense of time and space. Over the last twenty years, numerous studies have suggested that ketamine can be used to treat chronic depression,⁴³ bipolar depression,⁴⁴ obsessive-compulsive disorder,⁴⁵ anxiety,⁴⁶ and post-traumatic stress disorder.⁴⁷ While some participants in clinical trials reported

side effects including headache, dizziness, nausea, blurred vision, drowsiness, and poor memory, but these symptoms resolved quickly after treatment sessions⁴⁸ Chronic ketamine use has been associated with neurodegeneration in newborn rhesus monkeys⁴⁹ and with kidney disease. Some people become addicted to ketamine, a dependency which can be very difficult to overcome.

MDMA

In 2010, researchers published the results of the first clinical trial that showed MDMA could be used alongside therapy to treat post-traumatic stress disorder.⁵⁰ Subsequent studies suggest it's also effective at reducing anxiety in autistic adults⁵¹ and in people with life-threatening illnesses,⁵² as well as in treating eating disorders⁵³ and substance abuse disorders.⁵⁴

In 2021, researchers at several sites across the United States, Canada, and Israel published the results of a phase III clinical trial using MDMA-assisted therapy to treat PTSD. The trial studied ninety participants and found that the treatment was safe and that MDMA relieved many, or in some cases most, of the symptoms for the majority of patients who received it.⁵⁵

Salvia divinorum

Salvinorin A, a chemical found in *Salvia divinorum*, interacts with kappa-opioid receptors, which play a role in pain perception. Because of this, researchers hypothesize that it could be used to treat disorders characterized by perceptual distortions like schizophrenia and bipolar disorder.⁵⁶ Other studies suggest that salvinorin A may have cognitive-enhancing effects, making it a possible treatment for neurodegenerative diseases including Alzheimer's disease.⁵⁷ Researchers have also conducted pre-clinical trials using salvia to treat cocaine addiction.⁵⁸

New Research

Around the world, hundreds of new and ongoing research studies and clinical trials are testing how psychedelic substances interact with our bodies and exploring the possible benefits of therapies on physical health. For example, recent research has found that many of the classic psychedelics, including psilocybin, LSD, DMT, and MDMA have potent anti-inflammatory effects.⁵⁹ One recent study found that treating asthmatic rats with psychedelic compounds could prevent and reverse lung inflammation.⁶⁰

New studies are also focusing on how psychedelics affect general behavior, mood, cognition, and brain function and health, and are using psychedelics as tools to better understand fundamental properties of the mind and brain.⁶¹ Researchers are also digging into how psychedelics contribute to neuroplasticity, or the brain's ability to change, to better help psychiatric patients with conditions resistant to most medications and therapies.⁶²

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