

Could psychedelic drugs be a new treatment option for people with depression?

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After being relegated to the fringes of legitimate scientific inquiry for nearly five decades, an increasing number of researchers, including Javier González-Maeso, Ph.D., and Mario de la Fuente Revenga, Ph.D., both in the Department of Physiology and Biophysics at the Virginia Commonwealth University School of Medicine, are exploring whether psychedelics, or related compounds, could be a new treatment option for

people with depression.

Major depression is one of the most common mental health issues in the United States, according to the National Institute of Mental Health, affecting an estimated 17.3 million adults. Treatment usually involves counseling/therapy, medication or a combination of both. However, these options take time to produce meaningful results and have high failure rates.

"Patients with depression need to receive antidepressants for weeks or even months to start to see the first therapeutic effects. Not only that—within that period of time, the risk of suicide goes up," said González-Maeso, an associate professor.

Fast-acting antidepressant effects

Researchers in the U.S. and Europe have shown that a single dose of psilocybin, the psychoactive compound in so-called "magic mushrooms," has fast-acting antidepressant effects—generally within hours. These effects also appear to last much longer than traditional antidepressants.

In one study cited by González-Maeso, 80 percent of people diagnosed with terminal cancer and depression who received a single dose of psilocybin continued to show improvements in their mood after six months.

"This does not mean that the average Joe feeling blue will be able to go to the closest pharmacy to get his dose of therapeutic mushrooms any time soon," said de la Fuente, a postdoctoral fellow in González-Maeso's lab.

That is because despite showing promise as a treatment for mood and substance abuse disorders in the 1950s and '60s, the Drug Enforcement

Administration cracked down on psychedelics such as LSD and psilocybin in 1970, making them some of the most tightly controlled substances in the country.

It took until the year 2000 for the Food and Drug Administration to grant permission for psilocybin research to resume, and it was only recently that positive results from these studies have made headlines.

Still, psychedelics are considered controlled substances that have "no currently accepted medical use and a high potential for abuse" and are classified as Schedule I drugs.

As a result, "it will take rock-hard [scientific evidence](#) before they can be used by physicians," de la Fuente said.

A major component of that evidence will come from uncovering how psychedelic compounds produce antidepressant effects. This is exactly what de la Fuente and González-Maeso are trying to uncover—the underlying changes that psychedelics promote in the brain, both at a molecular and structural level.

Rewiring the brain

One possible mechanism behind psychedelics' observed antidepressant activity that the pair is investigating involves changes to the way the brain is wired—a process involving the creation of new synapses.

Synapses are the most basic structures that neurons use to communicate with each other. Previous research has shown that people experiencing depression often have fewer synaptic connections, especially in areas of the brain responsible for regulating mood and cognition, such as the frontal cortex.

As part of their preclinical research, González-Maeso and de la Fuente have found that when mice are given a single dose of a [psychedelic](#) compound, it not only reduces behaviors associated with depression but also increases the number of synapses in their frontal cortexes. González-Maeso presented these findings at the inaugural meeting of the International Society for Research on Psychedelics in New Orleans in October.

Relief without the 'trip'

González-Maeso and de la Fuente hope that by identifying the long-lasting changes that psychedelics trigger in the brain, they might be able to develop purely clinical versions of these drugs.

"If we understand at a molecular level how psychedelics induce antidepressant activity, we could design much better therapeutic drugs than we currently have in the clinic," González-Maeso said. "The ultimate goal is to find drugs that induce antidepressant effects without inducing psychosis-like effects."

González-Maeso and de la Fuente already have provisional U.S. patents for two such compounds that they plan to test for their antidepressant potential.

"Psychedelics have been a banned field for decades," de la Fuente said. "Now, with a more open attitude, we have all of the technological advances that we've accumulated over this time to apply to a growing field that almost nobody has explored before. From a scientific point of view, it is essentially the 'promised land' and will hopefully yield results that will make a real difference in the clinic."

Provided by Virginia Commonwealth University

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