Medical Xpress

Psychedelic science holds promise for mainstream medicine

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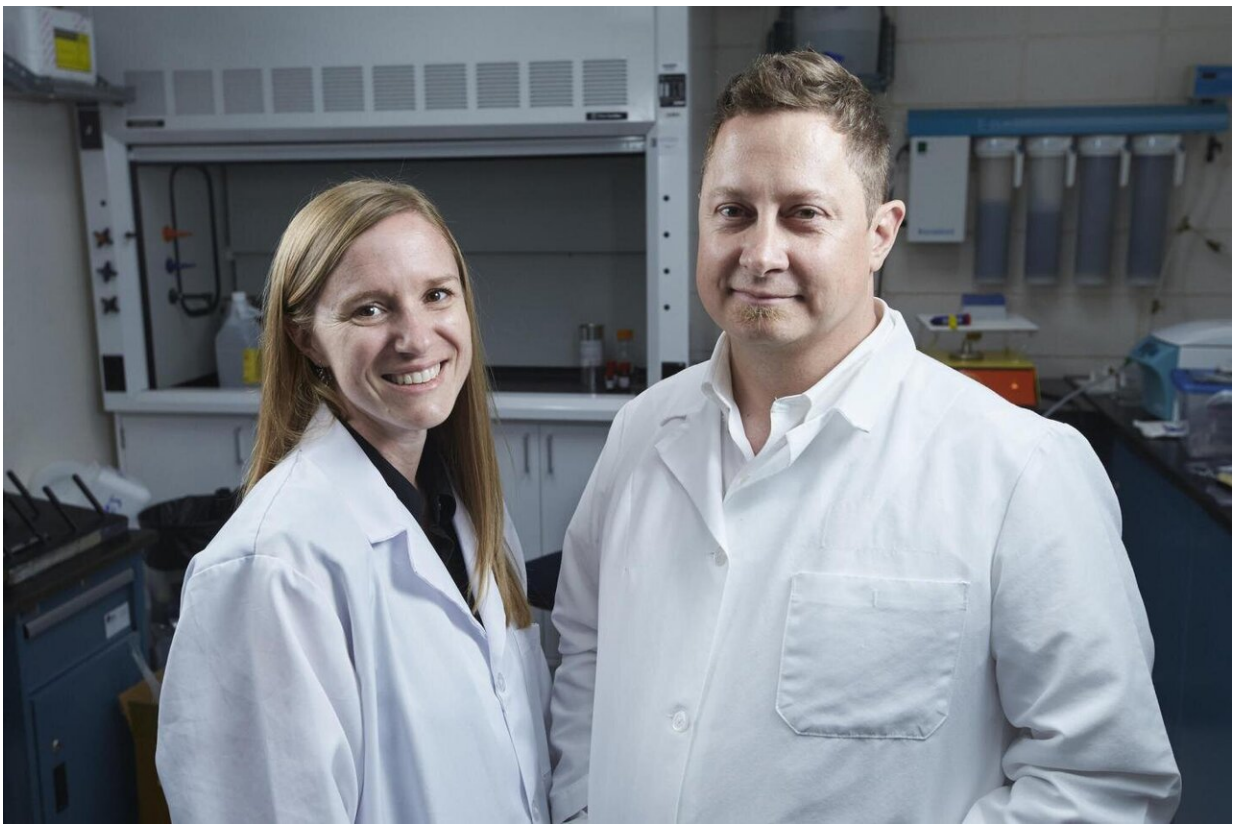

UNLV neuroscientists Dustin and Rochelle Hines join rising number of researchers studying possible medical benefits of psychedelics; their work on brain activity recently published by Nature: *Scientific Reports*. Credit: Josh Hawkins/UNLV Photo Services

Psychedelic healing may sound like a fad from the Woodstock era, but

it's a field of study that's gaining traction in the medical community as an effective treatment option for a growing number of mental health conditions.

While the study of psychedelics as medicine is inching toward the mainstream, it still remains somewhat controversial. Psychedelics have struggled to shake a 'counterculture' perception that was born in the 1960s, a view that had stymied scientific study of them for more than 50 years.

But that perception is slowly changing.

Mounting research suggests that controlled treatment with psychedelics like psilocybin mushrooms, LSD, and MDMA—better known as ecstasy—may be effective options for people suffering from PTSD, anxiety disorders, and depression. The U.S. Food & Drug Administration recently granted 'breakthrough therapy' status to study the medical benefits of psychedelics. And two years ago this month, the FDA approved a psychedelic drug—esketamine—to treat depression.

An increasing number of states and municipalities are also grappling with calls to decriminalize psychedelic drugs, a move that UNLV neuroscientist Dustin Hines says could further the recent renaissance in psychedelic science.

"The resurgence in interest in psychedelic medicine is likely related to multiple factors, including decreasing societal stigma regarding drugs like hallucinogens and cannabis, increasing awareness of the potential therapeutic compounds found naturally occurring in plants and fungi, and the growing mental health crisis our nation faces," says Hines. "Because of the intersection between the great need for innovation and wider social acceptance, researchers have started to explore psychedelics as novel treatments for depressive disorders, including work with

compounds that have been used for millennia."

In the Hines lab at UNLV, husband and wife researchers Dustin and Rochelle Hines are uncovering how psychedelics affect brain activity. Their work, published recently in *Nature: Scientific Reports*, shows a strong connection in rodent models between brain activity and behaviors resulting from psychedelic treatment, a step forward in the quest to better understand their potential therapeutic effects.

We caught up with the Hineses to learn more about the evolution of psychedelic science—which actually dates back thousands of years—their research (which doesn't date back as long), misconceptions about this emerging field of study, and what to expect next.

The scientific study of psychedelics holds great promise for people suffering with mental illness. Where do we stand?

Dustin Hines: It's estimated that 1 in 5 American adults suffer from some type of mental illness. And while not all require pharmacological treatment, unfortunately there's been limited progress in advancing novel therapies for depressive disorders in 50 or more years.

Rochelle Hines: It's also worth noting that available therapies for major depression are only effective in specific segments of the depressed population. That's what makes the study of psychedelic compounds so fascinating. Recent clinical studies have empirically demonstrated that these compounds can exert rapid antidepressant effects—essentially bringing into the clinic a practice that Mesoamerican and other cultures have used for thousands of years. But there are still quite a few regulatory barriers that limit even research use of psychedelics. We're hopeful that as the public view of psychedelic compounds changes, so

too will the federal regulations that currently govern their study.

Current therapies for mental health disorders can take weeks to become effective. Recent research, including your own, shows the potential for psychedelic compounds to work much more quickly. What do we know about how this happens?

Rochelle: Clinical research on the use of psychedelics as therapeutics suggests that they work by altering the connectivity, or communication, between brain regions. Multiple studies suggest that the connectivity of cortical sensory regions and other brain areas is strengthened. Studies have also reported alterations in the patterns of brain activity during psychedelic treatment in patients with depression.

Dustin: Our recent studies support the evidence for changes in patterns of brain activity, and provide additional detail into specific patterns of brain activity that are generated during psychedelic treatment. The brain activity patterns that we've characterized are related to specific behaviors known to occur following treatment with psychedelic hallucinogens. These findings support the idea that generation of specific brain activity patterns may be a key aspect of the beneficial effects that psychedelic compounds exert.

In your research, you discuss the long history of hallucinogens for ritualistic practices. What did these cultures know that we don't, and how does your work draw upon this ancient evidence?

Rochelle: Modern medicine—which includes our research team—is reinvestigating psychedelic practices with a 5,000-plus year history.

Mesoamerican practitioners are known to engage in specific processes that were honed over millennia of skilled use, often including the addition of nicotine to their ritualistic and therapeutic practices with psychedelics. At present, very little research has investigated the synergistic effects of psychedelics and nicotine.

Dustin: Despite this long history and recent clinical promise, we still really don't know just how these drugs actually work on the brain to influence mood. This knowledge is essential to optimize their therapeutic potential. In our study of brain activity in a rodent model, we found that nicotine enhanced both the brain's slow waveform as well as behavioral arrest, both hallmark aspects of the response to psychedelic hallucinogens. We're now working on studies examining the synergy between psychedelics and nicotine, and whether nicotine enhances the anti-depressant effects of psychedelics.

Rochelle: We're also investigating the cellular and molecular mechanisms that underlie the specific changes in brain activity following treatment with psychedelics. With this understanding, we may be able to further refine the clinical utility, applicability, and efficacy of psychedelic hallucinogens as medicines.

As researchers who study the possible therapeutic benefits of psychedelics, what are some of the biggest misconceptions you've encountered? How can further scientific study combat them?

Dustin: Microdosing of psychedelics—where users gain benefit, though not the prototypical "high" from small amounts the drugs is a practice that's been in the news a lot lately. While there are some data suggesting that low doses can exert beneficial effects, the idea that a person can purchase controlled substances without clarity on the content of

psychoactive ingredients and regulate their own dosing with precision is in my opinion misguided. By conducting research to examine both purified and synthetic compounds, we can more accurately establish dosing.

Rochelle: There's a long-standing belief that these drugs are addictive. However, much of the research suggests that these drugs don't result in maladaptive patterns of substance use behavior. To the contrary, some research actually suggests that these compounds may be effective in treating substance use disorders. More research on the effects of these compounds in models may provide better clarity on not only the acute effects, but the effects of repeated dosing.

Dustin: An important point to drive home with all of this is that psychedelics are powerful psychoactive drugs, and they should not be used for therapeutic purposes without an experienced practitioner.

The context surrounding the use of psychedelics as a therapy is emerging, but further research into the clinical use of psychedelics is needed to establish procedures and protocols that we hope will ultimately support positive outcomes for patients.

More information: April Contreras et al, Behavioral arrest and a characteristic slow waveform are hallmark responses to selective 5-HT2A receptor activation, *Scientific Reports* (2021). DOI: 10.1038/s41598-021-81552-6

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