TIFR study uses psychedelic drug to trace neuron that can reduce anxiety

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New Delhi: The word 'psychedelic' evokes images of wild, mind-bending trips straight out of the 1960s. But what if the same 'trippy' substances used in drugs like LSD and magic mushrooms could be harnessed to treat mental health issues? A new study may have unlocked the way.

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"People's first reaction to psychedelics is often alarmist. But substances like LSD, a synthetic psychedelic, psilocybin, found in magic mushrooms, and mescaline, derived from cacti, have been used extensively by traditional healers for thousands of years—by ancient tribes from the Amazonians to the Incas in Central and South America—long before they became symbols of rebellion," says Vidita Vaidya, a neuroscientist and professor of biological sciences at TIFR who led the project.

Targeting the ventral hippocampus could help reduce anxiety at both cellular and neural levels, she says. “And using a psychedelic drug as a tool to achieve this opens the door to more targeted treatments for anxiety disorders, as well as the development of psychedelic-inspired medications for treatment-resistant mental health conditions like PTSD and depression without triggering hallucinations,” she adds.

The drug used in their study is a synthetic one called DOI, designed by Alexander Shulgin in 1984. “Because of regulatory hurdles in India, we can’t import LSD or psilocybin to work with. That’s why we worked with DOI, which is potent but isn’t a common street drug and hasn’t been abused like LSD or psilocybin. However, it belongs to the same umbrella of psychedelics which alter states of reality,” says Vaidya, whose journey with DOI dates back to her days as a PhD student. “I’ve looked at it from multiple angles. It has profound, diverse effects — as an antidepressant, it produces hallucinations, reduces anxiety. We’ve also studied its ability to change mitochondria (the energy that cells need to function). Our main question was, how does DOI reduce anxiety?”

To confirm that it actually does, the team used an ‘elevated plus maze’—an apparatus with open and closed arms used to measure anxiety in rodents. “We observed whether after being injected with DOI, they’d explore more open and risky areas. And they did. This was the first step, it confirmed that DOI reduces anxiety in rats and mice.”

But there were still gaps in understanding “where in the brain” this was happening. “When my student Prachi Tiwari expressed her desire to delve deeper into this for her PhD thesis, I told her, ‘this is a meaty problem that’ll need multiple approaches,’ but she was determined,” says Vaidya.

What started five years ago as a challenge, grew into a collaborative effort that extended far beyond their TIFR lab as a multi-institutional study with researchers from Cornell, Yale, and Columbia universities, all working together. “So, it became an international effort as we brought in peers from all these universities to conduct experiments that our collaborators could help us answer faster,” says Vaidya. After several trials on rodents, the ventral hippocampus was identified as a key target for DOI in reducing anxiety.

But they still faced a challenge. “It’s a part of the brain with millions of different cell types. We suspected it might be a specific group of neurons but weren’t sure,” says Vaidya. That’s when Cornell helped identify a “PV-positive neuron” that was hyperactive when the drug was present.

Vaidya broke it down with a simple analogy: “Think of the brain as a map of Mumbai. We knew that DOI worked, kind of like knowing something is happening in a busy city like Mumbai. But we didn’t know exactly where. So, we had to search neighbourhood by neighbourhood—until we found Marine Drive, which represents the ventral hippocampus. Even then, it wasn’t just any building, but the specific Art Deco ones. That’s our PV-positive neurons. Once we knew that, we could target just those neurons, to get the anxiety-reducing effect without needing the whole drug.”

The discovery was significant, given that these neurons reduce anxiety without triggering hallucinations. “By understanding how these psychedelics work at a deeper level, we can design drugs that target those parts of the brain responsible for reducing anxiety without unwanted effects like hallucinations. Some colleagues are already designing psychedelic-inspired drugs that don’t produce hallucinations or motor effects.”

Vaidya, whose scientific career has centred on the 'neurobiology of emotion' has been discussing her findings with experts at NIMHANS, to move the research from lab to clinical trials. "But India currently lacks clinical trials for psychedelic-assisted therapy...Australia, Europe and the US are moving forward with major, carefully controlled trials," says Vaidya.

Biju Viswanath, additional professor of psychiatry at NIMHANS, specialising in the effects of psychotropics on neural stem cell lines, said current medications for anxiety and depression take weeks to be effective and leave patients at risk during that waiting period. "Especially since around 50% of patients don't respond to existing pharmacological treatments," he said. "Exploring a new class of agents using animal models is a promising approach."

But he cautions that clinical trials in India may still be far off due to their high abuse potential. Vaidya shares his frustration. "Our regulatory knots make it hard to conduct this kind of research in India," she says, as she prepares to present this research at the 2025 Gordon Research Conference on Neurobiology of Psychedelics at Rhode Island. "We need to stop playing catch-up...Right now, we have too few psychedelic researchers. That's not good for a nation facing a growing mental health crisis."

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