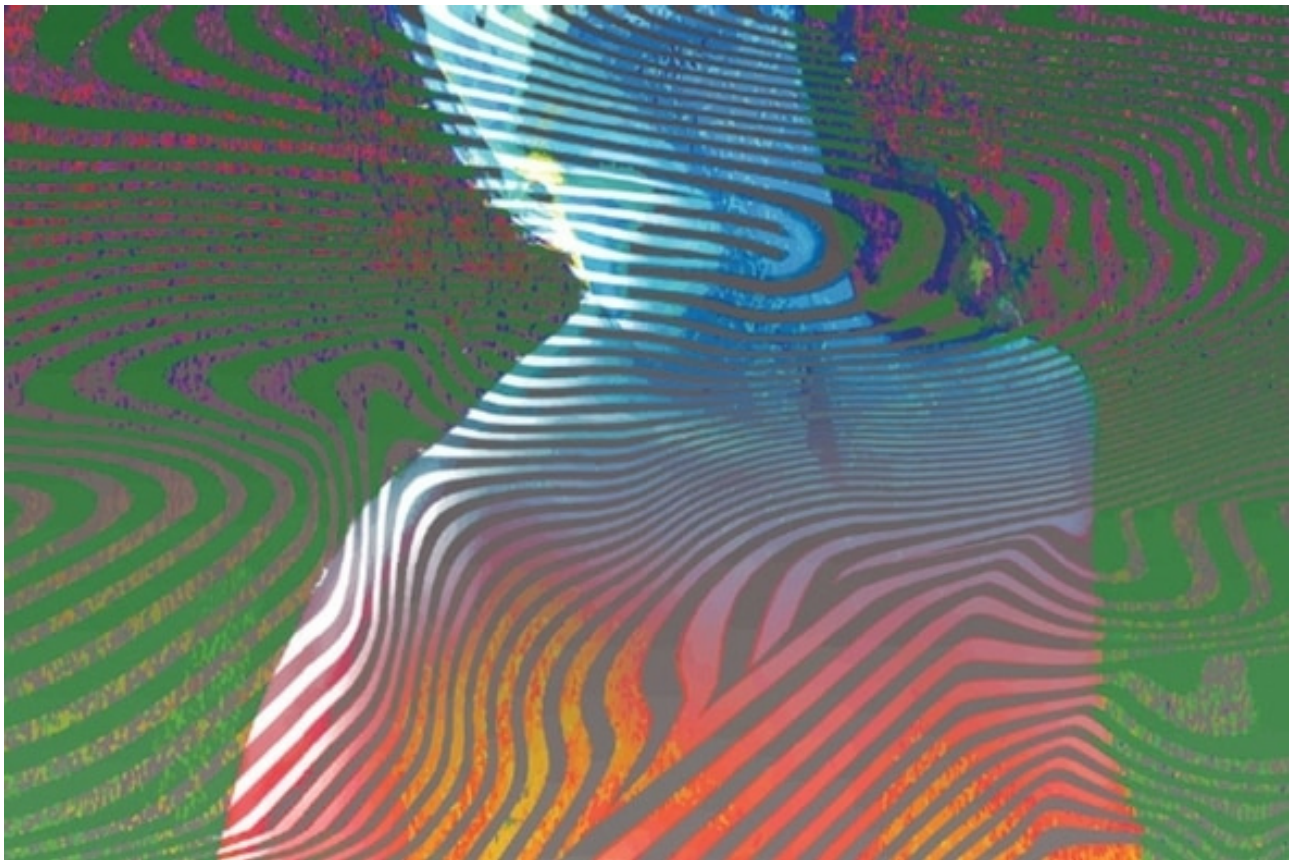
MENTAL HEALTH

A Trip inside the Schizophrenic Mind

Researchers are investigating how hallucinogens might be used to model—and develop treatments for—psychosis

By Taylor Beck on March 1, 2017



Credit: George Peters Getty Images

LSD, “magic” mushrooms and mescaline have been banned in the U.S. and many other countries since the 1970s, but psychedelic medicine is making a comeback as new therapies for depression,

nicotine addiction and anxiety. The drugs have another scientific use, too: so-called psychotomimetics, or mimics of psychosis, may be useful tools for studying schizophrenia. By creating a brief bout of psychosis in a healthy brain, as indigenous healers have for millennia, scientists are seeking new ways to study—and perhaps treat—mental illness.

“We think that schizophrenia is a group of psychoses, which may have different causes,” says Franz Vollenweider, a psychiatrist and neuroscientist at the University of Zurich. “The new approach is to try to understand specific symptoms: hearing voices, cognitive problems, or apathy and social disengagement. If you can identify the neural bases of these, you can tailor the pharmacology.”

Vollenweider and his colleagues have found an existing drug for anxiety that blocks specific effects of psilocybin, the psychoactive ingredient in magic mushrooms. When healthy people were given the drug before tripping, they did not report visual hallucinations and other common effects, according to a study published in April 2016 in *European Neuropsychopharmacology*. The effort is part of a burgeoning movement in pharmacology that seeks to induce psychosis to learn how to treat it.

And schizophrenia desperately needs new treatments. Seventy-five percent of afflicted patients have cognitive problems. And most commonly used drugs do not treat the disorder's “negative” symptoms—apathy, social withdrawal, negative thinking—nor the cognitive impairments, which best predict how well a patient will fare in the long term.

Psychedelics such as LSD, psilocybin mushrooms and mescaline

(derived from the peyote cactus) all act on serotonin, a neurotransmitter tied to mood. Brain imaging of schizophrenic brains has revealed that networks involved in introspection and those for external attention bleed into one another, as they do in healthy brains on psychedelics. By finding drugs that block this boundary-blurring effect, scientists hope to home in on the biological basis of psychosis and help to prevent it.

“If someone is hallucinating, it may not matter if the person is experiencing hallucinations through Parkinson's disease, schizophrenia or a manic episode,” says Mitul Mehta, a neuropharmacologist and psilocybin researcher at King's College London, who was not involved in the Swiss study.

The goal of the study was to prevent the deluge of serotonin activation and the resulting hallucinations caused by magic mushrooms, using two nonhallucinogenic chemicals shaped similarly to LSD. The researchers recruited 36 people, each of whom took part in four sessions in the laboratory separated by at least two weeks. They divided people into two groups, each of which tested a different candidate antipsychedelic drug: buspirone, a drug prescribed for anxiety, or ergotamine, one used to treat migraines. The study participants took one of the antipsychedelics followed by psilocybin, a placebo followed by psilocybin, an antipsychedelic followed by a placebo or two placebos in a row. Three hours after taking the drug cocktails, the subjects reported their psychedelic experiences on a standardized questionnaire that measures dimensions of hallucinatory states, including euphoria, visual hallucinations and delusions.

Buspirone prevented some psychotic effects of psilocybin, the researchers found. They hypothesize that by binding to serotonin

1A receptors, which pair with and counteract the serotonin 2A (psilocybin) receptor, buspirone restrained the visual hallucinations, flood of memories and imaginative thinking commonly triggered by psilocybin. The drug had no impact on other psychedelic symptoms such as the anxious sense of ego dissolution or the fear of going insane that some people experience, nor did it prevent decreased alertness during the trip.

The psychotic effects blocked by buspirone are also common in early schizophrenia and Parkinson's. The first approved drug for treating psychosis in Parkinson's, pimavanserin, acts by blocking the serotonin 2A receptor. Vollenweider previously found that a blood pressure drug, ketanserin, blocks the serotonin 2A receptor and prevents virtually all psilocybin effects, but it has not been tested for schizophrenia. Eventually such medicines might not treat the catchall disease “schizophrenia” but alleviate a patient's specific symptoms.

ABOUT THE AUTHOR(S)

Taylor Beck