Undergraduate

Let's Take a TRIP into Mental Health

BY ANNA CASTELLO

HISTORY OF PSYCHEDELICS

In 1943, Swiss scientist Albert Hoffman voyaged into a lysergic acid diethylamide, or LSD, "acid trip". Upon taking approximately 250 mg of LSD, about twice the typical dose one would take today, Hoffman recorded feeling dizzy and having the desire to laugh, as well as a "most severe crisis."[1,2] His experience inspired him to outsource LSD to any researcher interested in studying the compound. As interest in the compound grew, researchers began to investigate similarly shaped molecules that have been used for thousands of years in many Indigenous cultures: psilocybin found in mushrooms, mescaline found in cacti, and N,N-dimethyltryptamine (DMT) found in the psychoactive drink ayahuasca (see *Figure 1*). They found that these molecules have similar chemical structures to serotonin, a neurotransmitter in our brain responsible for the regulation of mood, sleep, and other processes. Due to this structural similarity, these compounds can enter the bloodstream and act as agonists—chemicals that bind to a receptor (in this case, mainly the 5-HT2A and 5-HT2B receptors in the brain) and incite a biological response.[3] These hallucinogenic drugs, known as the "classic psychedelics," have the power to drastically alter one's perception of reality for anywhere between three to twelve hours, depending on the drug, dose, and person.

On May 13th, 1957, *Life* magazine published an article titled "The Discovery of Mushrooms That Cause Strange Visions," introducing many Americans to psychedelics for the first time. Featured in the article, a New York banker recounts his experience with a medicine woman named Marie Sabine who performed a mushroom based healing ritual.[4] This story spread and by the 1960s, the government opened a federally funded trial at the Spring Grove Mental Health Facility in Catonsville, Maryland to test whether LSD could help with treating mental disorders.[5]

News of the trial's promising results spread across the United States, fascinating scientists and the public alike. This sentiment, however, abruptly changed as psychedelics became entwined with the counterculture movement. The movement's strong anti-Vietnam and anti-government ideals threatened Nixon's government, leading to a mass demonization of psychedelics in the media and by the government. These compounds quickly became classified as Schedule 1 drugs: a category of drugs considered to have "high potential for abuse" and "no currently accepted medical use," making them entirely illegal.[6] Even *Life* magazine reversed their stance on psychedelics, labeling them an "exploding threat."[7] This vilification of psychedelics included "educational" and government funded films warning of the risk of chromosomal damage, birth defects, fatal accidents, suicide, psychosis, and brain damage—most of which have been disproved.[8]

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In fact, research suggests that psychedelics are neither toxic nor physically or chemically addictive, and there seems to be no evidence suggesting that chromosomal damage and birth defects are caused by psychedelic use.[8] In reality, the most common danger currently associated with these compounds comes from illegally purchased psychedelics laced with drugs such as PCP or methamphetamine. Though, very infrequently, LSD psychosis, which mirrors symptoms of schizophrenia, can develop in individuals who are predisposed to psychosis. However, a study surveying 20,000 psychedelic users found no significant association between psychedelics and mental illnesses, demonstrating how rare such a psychotic break due to psychedelics is.[9,10]

THE DMN AND DEPRESSION

Psychedelics are thought to affect a region of the brain called the default mode network (DMN). The DMN is composed of several brain regions that are active when an individual is not focused on stimuli from the outside world. These regions have been studied by

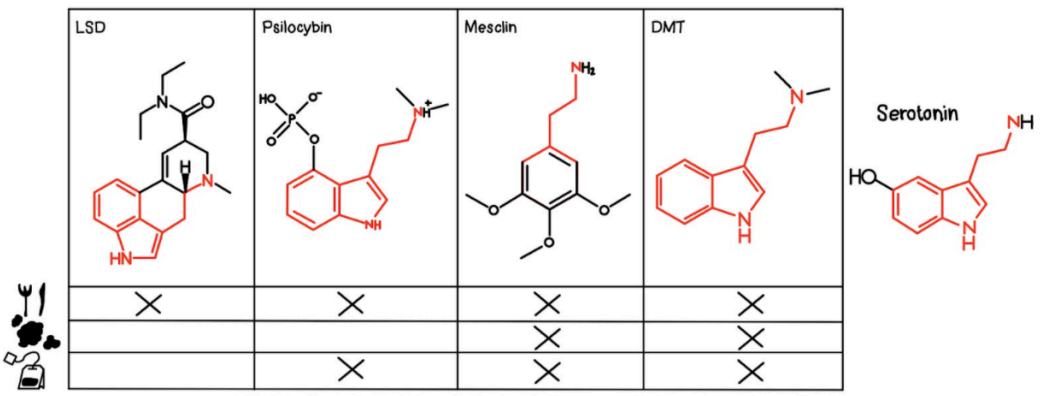

Figure 1: Chemical structure of classic psychedelics compared to serotonin. *These are the chemical structures of the classic psychedelics. Due to their similar shape, they bind to 5-HT, or serotonin, receptors in a similar manner. Depending on the psychedelic, they can be eaten, smoked, or drunk in a brew.*

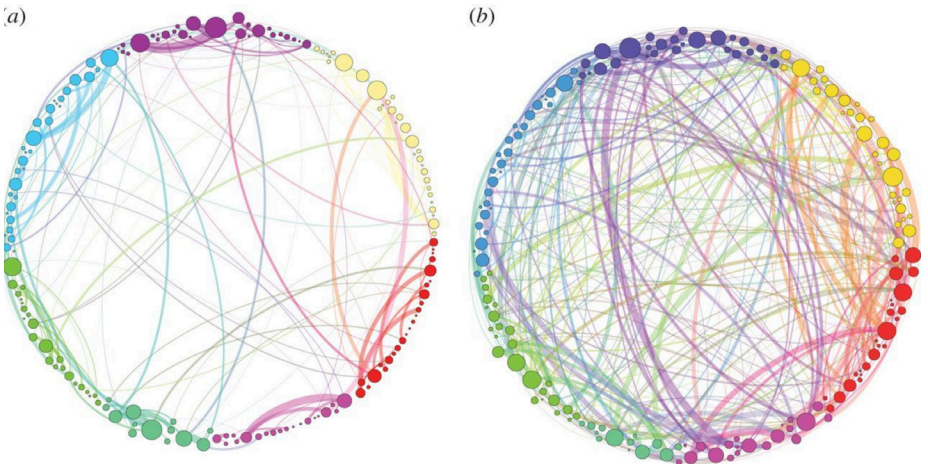

Figure 2: Connectivity in a placebo brain and one on psilocybin. *The image on the left is a representation of the connections a brain makes when not on psilocybin, while the representation on the right is that of someone on psilocybin. Clearly the one on the right has significantly more connections which help rewire the brain and its old thoughts and habits, helping combat mental illnesses.*

using functional MRIs that measure small changes in blood flow which occur with brain activity. The DMN can be thought of as the self, unaffected by a person's surroundings, and is responsible for mind-wandering, planning the future, and looking at the past. Dysfunction of the DMN has been found in people suffering from major depressive disorder, bipolar disorder, schizophrenia, and other mental illnesses.[11] With depression being one of the leading mental health issues globally, psychedelics' effects on the DMN make them a promising therapeutic drug. In fact, a 2017 study looked at the brains of 19 patients with treatment-resistant depression by using fMRI to examine changes in blood flow before and after treatment with psilocybin. All 19 patients reported feeling less depressed after one week of treatment, and nearly half of patients reported less depression after five weeks. The study also found decreased cerebral blood flow in the temporal cortex, including the amygdala—which controls anger, fear, sadness, and aggression.[12]

Interestingly, however, this study found increased activity in the DMN, a surprising result given that increased activity was previously found to be a marker for depressed mood.[13] Multiple studies have actually found depression to be linked to either higher or lower levels of activity of the DMN.[13,14,15,16] It is irregular DMN activity levels that depress mood—this is a lesser known fact that could explain why there are inconsistencies within studies on how psychedelics affect DMN activity. Clearly, the mechanism by which psychedelics alter the brain to help with depression in a therapeutic setting is not fully understood yet. Fortunately, as the stigma associated with psychedelics decreases, many more research institutions are starting to take a closer look at the neural mechanisms affected by these drugs.

PSYCHEDELICS AND ADDICTION

Depression is not the only affliction psychedelics can remedy. Currently, psychedelics are being explored for remedying addiction as well. Addictive compounds work by short-wiring the reward system in the brain through the release of "feel-good" neurotransmitters such as dopamine. These neurotransmitters saturate the nucleus accumbens, a region in the brain responsible for pleasure and therefore impulse control.[17] Psychedelics seem to hijack this process, rewiring the brain and making new neural connections—and thus developing in individuals the ability to overcome alcoholism and other forms of addiction (see *Figure 2*).[18] Though more research on the mechanisms by which psychedelics accomplish this is necessary, studies suggest that psychedelics aid addiction recovery tremendously.

For instance, a Johns Hopkins study looked at 15 psychiatrically healthy cigarette addicts who had all previously attempted to quit smoking. They were subjected to a 15 week program where they would ingest increasing amounts of psilocybin accompanied by cognitive behavioural therapy, with the goal in mind to quit smoking. Eighty percent of the participants remained smoking free 6 months after the study. A follow up to this study found that high levels of smoking abstinence was maintained even a year and a half after the treatment. This is an incredible success rate as the current tools to quit smoking, both pharmacological and behavioural, provide, on average, a mere 35% success rate. Though this pilot study was not perfect, it highlights the possibilities that psychedelics can offer.[19,20]

"Surprisingly, one component that seems to be crucial for psychedelics to have a therapeutic effect is the desire for the trip to be transformative"

Surprisingly, one component that seems to be crucial for psychedelics to have a therapeutic effect is the desire for the trip to be transformative. There is substantial evidence from the '60s and '70s when individuals commonly used both psychedelics and smoked cigarettes that demonstrates the importance of intention. Because these individuals had no intention to quit smoking, they remained cigarette smokers long after stopping the use of hallucinogens. Researchers believe psychedelic users must make a con-

scious decision to use these compounds as a tool to stop smoking in order for the trip to have the desired effect. In fact, many experts agree that the original method of consuming psychedelics with guides and shamans might indeed be the best way to reach psychological breakthroughs. Though today's psychologists, psychiatrists, and mental health workers can not be directly compared to shamans and light workers, as shamans have extensive roles in the community that go beyond guiding people through a psychedelic experience, the importance of guidance is not something that is being ignored in today's clinical setting.

MANY MORE TRIPS TO GO

Research is not at the point where psychedelics can be fully prescribed outside clinical studies since there is still a lot to be discovered on how these drugs interact with the brain. However, we are definitely on the edge of a psychedelic renaissance, promising intriguing, new understanding of the brain and one's psyche.

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IMAGE REFERENCES

1. *Banner:* made by author.
2. *Figure 1:* made by author.
3. *Figure 2:* Petri, Expert, P., Turkheimer, F., Carhart-Harris, R., Nutt, D., Hellyer, P. J., & Vaccarino, F. (2014). Homological scaffolds of brain functional networks. *Journal of the Royal Society Interface*, 11(101), 20140873–20140873. https://doi.org/10.1098/rsif.2014.0873