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Synapses
Acrylic

My painting represents neuroplasticity, the brain's ability to adapt, induced by psychedelics. The main shapes are inspired by synapses because that is primarily where psychedelic effects lie. The sharper shapes and edges represent the struggles and repressed traumas one may face in drug assisted therapy to achieve growth, which I illustrated through the floral-like patterns. I like to treat the paint like sculpting clay, I am simply shaping the piece and letting my brushstrokes guide me. With each stroke, the artwork evolves, capturing the time and care I put into its creation. Ultimately, this painting serves as a visual representation of my exploration. I prioritized the journey over the destination, focusing solely on the act of creation rather than fixating on the final product. For me, it's a meditative practice to simply paint and let the painting guide me. I start with more mute colors and as I develop the work I start to bring in brighter colors. The work is made up of several layers of design that I built up to create the final product. In essence, my painting reflects the relationship between neuroplasticity, therapeutic introspection, and the transformative power of psychedelics. As I navigate intricate designs, I invite the viewer to embark on intrinsic exploration, where the boundaries between mind and medium dissolve.

Psychedelic Therapy:

A Gateway to Healing and Transformation

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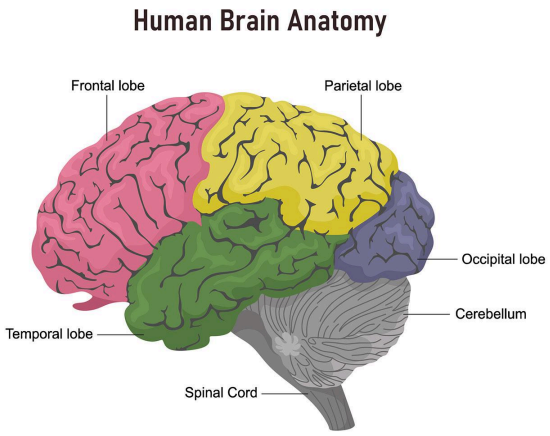
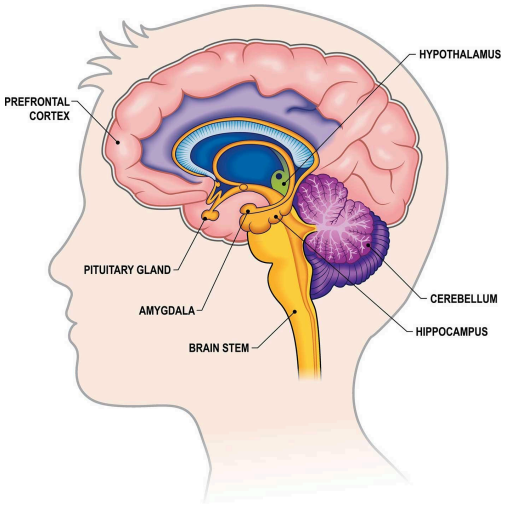
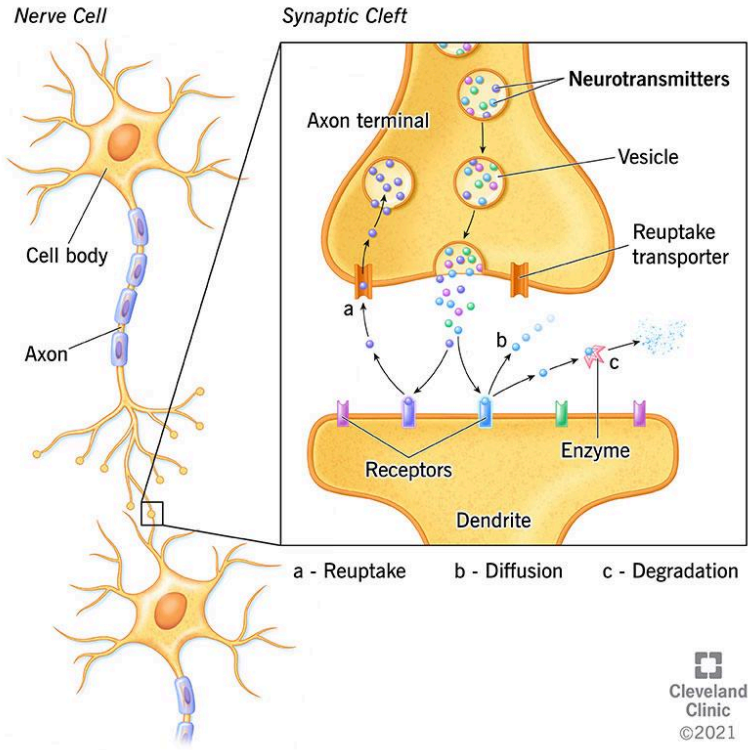
Psychedelic Therapy: A Gateway to Healing and Transformation

Imagine losing your successful career to chronic pain, along with losing the father of your children to cancer after a recent divorce, and then moving into two different homes, all in the span of two years. How would one overcome that challenge and continue to mother two children? According to University Hospitals, the top five stressors are the death of a loved one, divorce, moving, major illness or injury, and job loss ("The Top 5 Most Stressful," 2015). My mother faced all five. I watched as she became a shell of herself, unable to do the things that once brought her joy. Despite her awareness of her depressive state, she lacked the capacity and ability to change. My father wasn't the only one I lost when he died. Her PTSD and depression worsened as she fell deeper into a cycle of negativity with no way to break free. That is, until she began ketamine-assisted psychotherapy once a week. Although we were skeptical at first, the changes I witnessed in my mom were pivotal to her recovery. Once chained to her bed, she began to wake up early again and exercise, something she used to love. She also started cooking again, and I was able to taste the foods from my childhood memories. Now, finally, I began to truly see my mother again for the first time in three years. Psychedelic treatment changed her life for the better, and her story does not stand alone.





To understand the effects and benefits of psychedelics, it's essential to understand the brain. The main parts of the brain impacted by psychedelics are parts of the frontal lobe, limbic system, and default mode network (DMN). Psychedelics primarily affect a section of the frontal lobe, the prefrontal cortex (PFC). The PFC, responsible for learning, creativity, ordering events, and working memory, makes up a third of the outer layer of the brain. Additionally, it's often linked with limbic cortices (Goyal). The three main areas of the limbic system affected by psychedelics include the amygdala, thalamus, and hypothalamus. The amygdala regulates emotion, memory, fight-or-flight responses, and the brain reward system. The thalamus acts as a relay station, receiving sensory information and sending it to the cerebral cortex. Finally, the hypothalamus controls homeostasis and memory (Cherry). The final part of the brain affected is the DNM, a collection of areas active at inactive moments and is mainly responsible for daydreaming, introspective thinking, and remembering one’s past or future (Buckner).



Neurons communicate electrically using signals called action potentials and chemically through neurotransmitters in the junction between neurons, known as the synapse. An action potential causes the first neuron to release a neurotransmitter. The neurotransmitter, then, can either help (excite) or hinder (inhibit) the next neuron from firing its action potential. Neurons reside in the cell membrane, which serves as the barrier between a cell's inside and outside, allowing positive or negative ions to enter and exit the cell. The inside of a cell is more negative than the outside, with a resting membrane potential of approximately -70 mV. The membrane potential constantly fluctuates depending on the sum of inputs from the axons of other neurons. When the total of inhibitory and excitatory inputs cause the neuron's membrane potential to rise to -50mV, referred to as the “action potential threshold,” action potential at the presynaptic terminal releases neurotransmitters into the synaptic cleft, a gap between presynaptic axon terminal and postsynaptic dendrite. Then, when the transmitter binds to the postsynaptic receptor,

the signal changes back into an electrical one and continues to the next neuron ("Action Potentials").

Some important neurotransmitters include amino acids such as glutamate and gamma aminobutyric acid (GABA) and monoamines such as serotonin, dopamine, and norepinephrine. Glutamate, the most common excitatory transmitter, moderates thinking, learning, and memory. In contrast, the most common inhibitory transmitter, GABA, regulates brain activity to prevent problems with anxiety, irritability, concentration, sleep, seizures, and depression. Monoamines are responsible for consciousness, cognition, attention, and emotion. Dopamine plays a requisite role in the reward system, along with facilitating feelings of pleasure. Similarly, serotonin also regulates mood in addition to sleep patterns, anxiety, sexuality, appetite, and pain. Finally, Norepinephrine increases blood pressure and heart rate and modulates alertness, arousal, decision-making, attention, and focus ("Neurotransmitters," 2022).

Psychedelics have the power to change the way the brain sends messages. In fact, throughout the 20 years before psychedelics were banned, research into hallucinogens thrived. Some drugs classified as psychedelics include LSD, DMT, psilocybin, MDMA, and ketamine. Psychedelics increase neuroplasticity, a property essential to learning, memory, recovery, and adaption. Neuroplasticity refers to the ability to build and remodel synapses. Disruption of neuroplasticity leads to mood disorders and addiction. Neuroplasticity consists of dendritogenesis, the growth of dendrites, synaptogenesis, the production of synapses, and neurogenesis, the integration of new neurons into the central nervous system. People frequently become imprisoned in the same thought patterns, and breaking out can often appear virtually impossible. Psychedelics provide a way out of that seemingly endless cycle and can catalyze

long-lasting improvements mentally. But how? What is the efficacy of psychedelic usage for modern-day medical treatment?

One theory argues that psychedelics are "psychoplastogens," substances that rapidly stimulate plasticity, thereby creating a space for neuroplastic changes that can free someone from the negative feedback loops of depression and PTSD. The psychedelic experience takes place in a highly plastic brain, giving more power to reshape neural circuitry. On a molecular level, psychedelics evoke changes in gene and protein expression, which cause the formation and modification of synapses and dendrites. Hallucinogens promote the Brain Derived Neurotrophic Factor (BDNF) which regulates neuronal growth and synaptic plasticity. Psychedelics stimulate the serotonin 5 hydroxytryptamine A receptors' pyramidal neurons post-synaptically, along with neurons that release GABA. By exciting the pyramidal neurons, they increase levels of extracellular glutamate, which stimulates the AMPA receptors, inducing neurogenesis. Induced neurogenesis and neuroplasticity mainly depend on the presence of 5-HT2a and 5-HT1a receptors (Calder.) Animal studies show psychedelics upregulate plasticity-related genes in the prefrontal cortex to foster the growth of synapses and dendritic spines in the frontal lobe. Why is neuroplasticity important? Depression is categorized by reduced cortical neuroplasticity, synapse atrophy, and reduced ability to regulate limbic areas in the prefrontal cortex (Calder). An increase in neuroplasticity has the ability to counteract these effects. Alongside psychotherapy, psychedelics help with mood disorders and addiction. Patients claim mood improvements following treatment due to enhanced dendritic and synaptic growth in PFC neurons. PFC regulates emotion through connections with the amygdala and other subcortical regions. PTSD, social anxiety disorder, and generalized anxiety are linked to fewer synaptic connections between the medial PFC and amygdala. Ayahuasca and psilocybin both promote cognitive flexibility and

increase mindfulness, a form of regulation through the PFC and ACC. Psychedelics evoke a plastic mental state allowing for significant brain development.

There are 3 main types of psychedelics, classified by their chemical structure or mode of action: serotonergic hallucinogens, dissociative anesthetics, and entactogens. Hallucinogens, such as LSD, psilocybin, and mescaline, produce psychotic-like symptoms, changes in mood, and differences in perception of self and surroundings. They act upon serotonin and dopamine receptors, causing the "high." LSD has been found to improve frontal development, memory retrieval, and reinforcement learning by enhancing reward sensitivity (Calder). Frontal development and memory retrieval allow patients to overcome traumas and move forward from whatever position they may be stuck in. Additionally, enhanced reward sensitivity can allow patients to break the cycle of addiction. Studies from the late 1950s and 1960s examined LSD's efficacy in the treatment of a broad variety of conditions including alcoholism, opioid dependence, pain, neurosis, and cancer-related anxiety, among others. LSD was also shown as an aid in facilitating creativity and problem solving in healthy volunteers. The effects can vary widely, but include altered mood, perception, cognition, hallucinations, as well as experiences described as insightful and transcendent. Psilocybin, first isolated in 1958 and found in over 100 species of mushrooms, produces similar effects at higher dosages. PET scans on humans show psilocybin increases glutamate signaling in the PFC, strengthens cortico-hippocampal synapses, improving memory, and activates the Default Mode Network (DMN), responsible for daydreaming and self-related thoughts (Blackmore). In addition, it also reduces blood flow in the same areas of the brain as long-term meditators when meditating, which allows for a mindful, intrinsic state. A study examining psilocybin in nine individuals with treatment-resistant obsessive-compulsive disorder (OCD) demonstrated improvement of OCD symptoms at four,

eight, and twenty-four hours post-psilocybin administration across a range of doses from 0.025 mg/kg (very low dose) to 0.3 mg/kg (higher dose). In addition to helping OCD, psilocybin also can aid symptoms of depression. Results from an open-label pilot study in which 12 participants with unipolar treatment-resistant major depression received a low (10 mg) and high (25 mg) dose of psilocybin in a supportive setting a week apart showed psilocybin may function as a rapid-acting antidepressant with sustained therapeutic benefits. After high-dose psilocybin administrations, significant reductions relative to baseline Quick Inventory of Depressive Symptoms scores occurred. Scores on the Beck Depression Inventory showed complete remission in 8 of the 12 participants at one week and 5 participants at 3 months after high-dose psilocybin administration. Finally, mescaline, found in some cacti, has a longer duration of action and acts less potent than other hallucinogens. In 1896, German chemist Arthur Heffter isolated mescaline from Lophophora williamsii, a small cactus native to northern Mexico and the southwestern United States. Chemist and pharmacologist Alexander Shulgin altered the mescaline molecule to create more potent synthetic hallucinogens, which became popular recreationally. Contemporary research is limited (Garcia-Romeu).

Dissociative anesthetics, including phencyclidine (PCP) and ketamine, act as antagonists of the vV-mcthyl-D-aspartate (NMDA) subtype of the glutamate receptor. Enhanced spinogenesis induced by ketamine is associated with depression reduction (Calder). Ketamine was first synthesized in 1962 PCP as a battlefield anesthetic. Ketamine reached high levels of recreational use since its adoption as a club drug in the 1990s. As a result, ketamine was classified as a schedule III drug in 1999 in the US. Depending on how the drug is administered, intravenously, orally, intramuscularly, or intranasally, the effects can last a couple of minutes to a couple of hours. Low doses intranasally induce visual hallucinations and dissociative and

stimulant effects, with higher doses intensifying these effects. A qualitative interview study of 90 infrequent, frequent, and ex-ketamine users revealed the most appealing aspects of ketamine use to be melting into the surroundings, visual hallucinations, out-of-body experiences, and "giggliness." The dissociative perceptual effects and personal meaningfulness classify it as a psychedelic. In the 1980s and 1990s over 1000 alcoholics were treated with ketamine psychedelic therapy without complications like ketamine abuse. Patients continued to abstain 2 and 3 years post-treatment. High-dose ketamine produced greater levels of heroin abstinence in 14 out of the 16 patients with those who underwent more sessions showing greater abstinence at the 1-year follow-up. Ketamine's antidepressant effects generally last from 3 to 7 days and persist as long as two weeks; however, ketamine is largely eliminated from the body within 3 hours of administration. Despite the short time it stays in the system, the effects can permanently alter connections in the brain. Ketamine has shown a clinical response rate of 40% to 60% at 24 hours post-infusion in treatment-resistant populations suffering from both unipolar (MDD) and bipolar depression and has also exhibited notable antisuicidal properties (Garcia-Romeu).

Some psychedelic drugs, classified as entactogens, produce weaker, more subtle effects than classic hallucinogens, one being MDMA. MDMA was first synthesized in 1912 as a mild short-acting drug that increases the capacity for introspection, empathy, and intimacy. Additionally, it temporarily frees the mind from depression, anxiety, and defensiveness without drastic changes to sense of self, body image, and awareness. It was popularized in Europe and the US during the 1970s. Taken in doses of 75-175 mg by mouth, the effects take 45 min to start and last 2-4 hours. Similar to other psychedelics, bad trips can occur when other drugs are accompanying it. There have been no reports of craving or withdrawal when used in a medical sense. Patients report losing defensive anxiety and feeling more emotionally open. One patient

states after treatment, “I have been able to experience myself more fully… to feel my feelings… to be totally with myself… to experience the ease of expressing myself when I’m in touch with myself.” It allows patients to get in touch with feelings normally unavailable to them and to feel less defensive, which, in turn, improves their relationships with others and strengthens trust and capacity for intimacy. On May 31, 1985, the Drug Enforcement Association placed MDMA on Schedule 1 of the Controlled Substance Act. Since then, the only government-approved scientific study with MDMA consisted of a phase 1 dose response in Spain surrounding patients with chronic PTSD. The main concern in MDMA is the potential neurotoxicity to serotonin nerve terminals; however, PET scans that measured serotonin transporter binding sites in a trial where naive MDMA subjects received a therapeutic dosage of MDMA showed no effect (Grinspoon).

Although the benefits of psychedelics, there is a complicated legal history behind them. During the 1940s, LSD and other psychedelics were considered safe and useful in psychiatric medicine. However, due to LSD’s growing popularity recreationally in the 1960s, myths that LSD contained deadly poisons and caused chromosome damage and birth defects began to spread. Unlike other new studies where there is an uprise in interest and natural skepticism, after the 1960s, there was a hostile response to hallucinogens based solely on subjective ideas. This led to the United Nations (UN) Single Convention on Narcotic Drugs in 1961 and the UN Convention on Psychotropic Substances in 1971, which placed tight restrictions on psychedelics and other drugs in 183 countries (Garcia-Romeu). The *International Narcotics Control Board* now disputes these restrictions because the decision was not based on medical facts. In the US, sacred plants like ayahuasca, peyote, and more are defined as drugs with a high abuse risk and no accepted medical use under section 1 of the Controlled Substance Act of 1970, even though entheogens are low-risk substances. LSD and MDMA cause less harm to the body than nicotine

and alcohol, both of which are legalized. The amount of harm done is determined by mindset and setting, yet even so, no cases of lethal overdose exist with classical hallucinogens. The US National Institute on Drug Abuse (NIDA) has confirmed statements claiming hallucinogen "overdose" leads to psychosis and death are false. Psychedelics have more to offer than danger. In a survey, "67% of volunteers rated their experience with psilocybin to be either the single most meaningful experience of his or her life or among the top five most meaningful experiences of his or her life" (Blainey).

Despite the surge of popularity in the 1940s, many communities around the world have used psychedelics in their practices for centuries; however, many prefer to use the terms "entheogens" and "sacred plants." The word "hallucinogen" implies the plant induces illusions, and the word "psychedelic" reflects hedonistic use in the 1960s. In contrast, "entheogen" means "to generate god within" in Greek, which denotes the vision-producing substances used in shamanism or religion. Many cultures incorporate these substances in their practices; the ancient Hindu and Buddhist use cannabis (Tetrahydrocannabinol), ancient Mesoamericans and Mazatec shamans in Mexico consume mushrooms (Psilocybin), the Native American Church and aboriginal groups in the South American Andes use the northern Mexican peyote cactus (Mescaline), the Bwiti religion of West Central Africa consume iboga root (Ibogaine), and the Brazilian religion of Santo Daime ingest a drink called Ayahuasca (N, N Dimethyltryptamine). Santo Daime devotees, called daimistas, refer to Ayahuasca as the "vine of the soul" and make it from various Amazonian native plants. According to Mark Blainey in "Forbidden Therapies," "Entheogenic practitioners believe that the ritualistic consumption of entheogenic plants helps them to achieve spiritual and existential insights that beget positive improvements to their health" (Blainey 4). This has been proven true as psychiatrists conclude Santo Daime members

are generally healthy. Rituals, referred to as “works,” last 2-12 hours and include dancing, meditating, and singing along with the ayahuasca.

The numerous positive effects outweigh any negative possibilities, contrary to the fear surrounding psychedelics, Dangers with entheogens arise commonly among people with schizophrenia or psychotic episode-prone tendencies, on medications such as SSRIs, or who ingest in uncontrolled environments. The psychedelic experience varies based on numerous factors such as the person, setting, mental state, and more (Grinspoon). The Daime trials set an example for a controlled environment for practice. Preindustrial cultures using psychedelics tolerated the ambiguity of psychedelic healing and embraced its healing potential. MDMA serves as an effective catalyst for treating PTSD, Ketamine treats MDD, the peyote ritual treats alcoholism among American indigenous people, Ibogaine has been used therapeutically to treat opiate withdrawal and drug dependence, and Ayahuasca has been used to treat addiction. Neuroplastic changes in dopaminergic neurons in the mesolimbic pathway cause addiction; however, due to inhibitory neurons from the PFC that carry 5-HT2A receptors, psychedelics are more likely to have an adverse effect on addiction (Calder).

Addiction expert and award-winning author Dr. Gabor Maté treats his patients (addicts to street drugs like heroin and cocaine) with ayahuasca-assisted therapy. One of his patients credits Ayahuasca with healing her psychological wounds to help her overcome addiction, “Ayahuasca saved my life... It enabled me to look at all those dark things I buried long ago... to unleash them and the pain, so that I could move forward” (Blainey). By allowing her to fully process the pain or “dark things” she felt unable to think through normally, ayahuasca allowed her the space to cope and move on. Dr. Maté explains, “Ayahuasca is not a drug in the Western sense, something you take to get rid of something. Properly used, it opens up parts of yourself that you usually

have no access to. The parts of the brain that hold emotional memories connect with and activate the parts that modulate insight and awareness, so you see past experiences in a new way (Blainey). Psychedelics are not solely responsible for noticed effects; they simply act as a catalyst for that positive change by providing the right state of mind.

Psychedelic means “mind-manifesting,” which acts as an accurate term for its therapeutic qualities. Ketamine and its derivative, esketamine, are currently the only classic psychedelics approved by the FDA to be used as dissociative anesthetics, a subtype of hallucinogen that causes feelings of detachment. The experience serves as a time for self-exploration, religious insight, and relief for somatic and neurotic systems. Patients claim psychedelics reduced feelings of guilt, depression, anxiety, and boosted feelings of self-acceptance and tolerance. Psychotropic therapy consists of two types. The first, psycholytic, meaning “mind-loosening,” explores the psychodynamic unconscious and consists of several small dose sessions with LSD or Mescaline. It's primarily used for neurotic and psychosomatic disorders. Patients are often asked to focus on their interpretation of drug-induced visions and symbolic psychodramas. Psychedelic therapy, the second type, makes use of a mystical experience using large doses (200mcg or more) in a single session. Treatments often consist of a combination of both types. One example of a patient is a 55-year-old man with a fairly normal life who had a serious mental breakdown. He had symptoms of anxiety, neurotic depression, decreased self-confidence, and insomnia. He became unfit for work for months. After 15 treatments with LSD, his anxiety peaked, and he claimed to feel as if he was experiencing being born. The session ended with him achieving “a double sense of the world.” Another patient who had 23 LSD treatments over the course of 5 months attributed all her growth to the treatments despite previously undergoing 4 years of psychoanalysis. A 40-year-old worker and alcoholic for 4 years got sent to hospital from jail

after drinking for 10 days. He was also anxious and depressed; however, after psychedelic-assisted therapy, he felt like a changed person, “I felt as if 10 tons had fallen from my shoulders… Everything looked better all around me… I changed my mind from alcohol towards Christ and the rose came back into my life” (Grinspoon). For him, treatment provided a spiritual experience, allowing him to grow and escape the pain that once haunted him. After therapy, his score for neurotic traits on the Minnesota Multiphasic Personality Inventory dropped from 88th percentile to 10th. In addition, when checked up a year later he still remained sober. Early studies reported up to 50% of alcoholics recovered and stayed sober a year or two later. Nevertheless, more studies revealed the harsh results that it often only helps short term because of how common sporadic and periodic relapses are. Psychedelic treatment has been proven to help for at least a year with alcoholism, and with further research and partnership with psychotherapy, it could possibly help for longer (Grinspoon). In the Native American church, peyote (mescaline) has been used to help treat alcoholism for decades. Early observational studies of peyote use by the Native American Church (NAC) concluded that religious use of peyote seemed safe and may prove effective in the treatment of alcoholism (Garcia-Romeu). A 1965 experiment provided the psychedelic experience for the dying at the Spring Grove State Hospital in Maryland and the Maryland Psychiatric Research Institute. The results showed that of people struggling with fear of death, pain, and depression, one-third improved drastically, one-third moderately, and one-third not at all after receiving LSD or dipropyltryptamine (DPT). University of Arizona in Tucson FDA approved a small double-blind placebo-controlled pilot study. Researchers administer psilocybin to 10 patients with Obsessive Compulsive Disorder (OCD). This study marked the first time in 25 years the FDA approved psilocybin to be given to patients.

The discovery of LSD in 1943 by Albert Hofman, a Swiss chemist, brought hallucinogens to the forefront of medical research. LSD induced a psychosis-like state, and its similarity to serotonin 5 hydroxytryptamine evoked the hypothesis that 5-HT plays a role in schizophrenia. This started the study on the neuronal basis of drug-induced altered state of consciousness (ASC) and how it relates to natural psychoses. According to Dittrich, the 3 dimensions of drug-induced ASC include oceanic boundlessness, anxious ego-dissolution, and visionary resacralization. Dittrich defines oceanic boundlessness as the dissolution of ego boundaries associated with positive emotions ranging from heightened mood to sublime happiness and serenity or grandiosity. Anxious ego-dissolution includes thought disorder, loss of autonomy and self-control variously associated with arousal, anxiety, and paranoid ideations, and lastly, visionary resacralization, referring to auditory and visual illusions, hallucinations, and altered meaning of perception. Both psilocybin and ketamine produce either a loss of ego boundaries associated with positive emotions or negative ego-disintegration associated with thought disorder and loss of autonomy and self-control. Extensive lesion and drug studies in rodents show sensorimotor gating, functions that regulate sensory information and allow for coherent thought, subject to considerable adaptation from cortical, limbic, striatal, pallidal, and thalamic structures, including cortico-striato-pallido-thalamic (CSPT) circuitry. Animal studies indicate that hallucinogens, amphetamines including MDMA, and NMDA antagonists disrupt sensorimotor gating in rats by interacting with different components of the CSPT loop. The "thalamic filter hypothesis of psychosis," advanced by Carlsson and Carlsson, proposes that corticostriatal pathways exert a modulatory influence on the thalamic gating of sensory information to the cerebral cortex. An impairment of thalamic filtering results in sensory overload of the cortex, which includes the breakdown of integrative cortical functions, positive

symptoms such as delusions, hallucinations, thought disturbances, persecution, and loss of a coherent ego experience, and negative symptoms, such as emotional and social withdrawal, resulting from efforts to protect from input overload. The limbic cortico-striato-thalamic-cortical (CSTC) feedback loops are involved in memory, learning, and self-nonself discrimination and linked exteroceptive perception with internal stimuli of the value system. The filter function of the thalamus is supposed to protect the cortex from exteroceptive sensory information overload and internal overarousal (Vollenweider).

As discussed here, psychedelics have the ability to change lives and the potential to steer modern therapies and medical treatments. Moreover, a deeper understanding of the brain's intricate neurochemistry reveals how psychedelics exert their therapeutic effects, targeting key areas such as the prefrontal cortex, limbic system, and default mode network. By enhancing neuroplasticity and promoting the formation of new synaptic connections, these substances create opportunities for profound psychological insight and growth. Historically, psychedelics have faced unjust stigma and regulatory barriers despite their potential to alleviate suffering and promote spiritual and existential insights. However, emerging research and cultural shifts challenge outdated perceptions, paving the way for advancement in psychedelic medicine. By fostering an environment of openness, education, and responsible use, we can harness the full therapeutic potential of these remarkable substances, offering hope to individuals like my mother and countless others who seek relief from the burdens of mental illness and trauma.

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