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Psychedelics: A Paradigm Shift in Neuropsychiatry and Therapeutic Frontiers

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ABSTRACT

Psychedelics have emerged as transformative agents in the realm of neuropsychiatry, offering unprecedented therapeutic potential for mental health conditions once considered refractory to conventional treatments. Compounds such as psilocybin, LSD, and MDMA interact with serotonin receptors to modulate neural plasticity, network connectivity, and emotional processing, resulting in profound alterations in consciousness and perception. These mechanisms underpin their efficacy in addressing disorders like depression, anxiety, PTSD, and substance use disorders, as demonstrated by a growing body of clinical evidence. This review delves into the neurobiological foundations of psychedelics, emphasizing their ability to foster adaptive rewiring of neural circuits and enhance introspective insights. Beyond their therapeutic applications, psychedelics challenge traditional paradigms by bridging the divide between pharmacology and experiential healing, offering a holistic approach to mental well-being. While the therapeutic promise is immense, psychedelics also raise critical questions regarding safety, regulatory frameworks, and the need for carefully structured therapeutic settings. This article synthesizes the latest advancements in psychedelic research, highlights ongoing challenges, and explores the future directions of this rapidly evolving field, ultimately positioning psychedelics as a revolutionary frontier in neuropsychiatry and personalized medicine.

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Introduction

Psychedelic drugs belong to a class of drugs that alter a person's sensory perception, causing a shift in their understanding of reality. These drugs, known as hallucinogens, can influence a person's thoughts and emotions (Nichols, 2016). Some psychedelics are man-made, while others are naturally occurring and contain compounds derived from plants and fungi. These substances can induce hallucinations, which may feel real but are actually subconscious thoughts (Carhart-Harris and Goodwin, 2017).

Individuals may experience auditory, visual, or tactile sensations that aren't present in reality. Some psychedelic drugs can cause a sense of detachment from one's body and surroundings (Halberstadt and Geyer, 2011).

These types of drugs which might effect our mood if a person is tripping over these hallucinogens they might experience good or bad trips (Schultes and Hofmann, 1980) . These drugs are used for millennia in both spiritual or medicinal contexts, so many clinical successes have been seen interested in the developing of psychedelic therapies mechanism that can account for these phenomenological and therapeutics properties remain unknown (EMCDDA, 2023).

Psychedelics have been used in ritual and religious contexts across diverse cultures for centuries (Schultes, 1969). Notably, there has been a recent trend of increasing recreational use of psychedelics in Europe and the United States, as evidenced by the European Drug Monitor (Passie et al., 2002).

Psychedelics disrupt communications between chemical networks throughout a person's brain. Serotonin, which controls various functions in a person, may be affected by psychedelic drugs, leading to hallucinations. Classic serotonergic psychedelics are small molecules that produce acute effects on perception, mood, and cognition by activating serotonin 2A receptors (5-HT2ARs) (Vollenweider and Kometer, 2010).

Drugs like LSD, PCP, psilocybin, peyote that alter sensory perceptions comes under the classification of psychedelics (Nichols and Grob, 2021).

LSD

The LSD is a lysergic acid diethylamide made from lysergic acid which is a strong mind controlling drugs, this looks clear where people swallow these acid tablets

These LSD makes people live in their own reality which is away from the reality which might last from 9-12 hrs (National Institute on Drug Abuse, 2019).

PEYOTE

It is a spineless cactus ingredient which is termed mescaline which is a naturally occurring in the cactus which is found in the crown of the cactus which might last around 12 hrs it is one of the ancient psychedelic (Halpern, 2004).

PSILOCYBIN

Which comes from the mushrooms which are also known as magic mushroom which is found in the tropical and tropical regions of US and other states in South America and Mexico these mushrooms contain substances like psilocybin which is 0.5% in the magic mushroom as these mushrooms are bitter

psilocybin chocolates have been popular which was developed using the mushrooms and chocolate together with less bitter taste (Passie et al., 2002).

PCP

PCP stands for phenylcyclohexyl piperidine which is also known as phencyclidine or angel dust which might be found in liquid or powder or tablets (National Institute on Drug Abuse, 2015).

How do psychedelics work

Psychedelic drugs induce a transient state in patients, enabling them to better process memories, emotions, and past trauma. This state allows them to reemerge with a fresh perspective on these experiences, which can be liberating and therapeutic. This concept is known as psychedelic-assisted therapy (Carhart-Harris RL and Goodwin, 2017).

Adverse effects of psychedelics

Mydriasis (dilated pupils), increased body temperature, increased heart rate, excessive sweating, loss of weight, insomnia, xerostomia (dry mouth), tremors, ataxia (loss of coordination), tachypnea (rapid breathing), and numbness (Johnson et al., 2008).

Contraindications in psychedelic treatment

It's crucial to prioritize safety and well-being when considering the use of any substance, especially psychedelics. Certain individuals should exercise extreme caution or avoid them altogether. Pregnant women should avoid psychedelics due to potential risks to the developing fetus. Additionally, individuals with a history of epilepsy or other seizure disorders should avoid psychedelics, as these substances can lower the seizure threshold and increase the likelihood of seizures. Furthermore, there's a risk to cardiovascular diseases associated with psychedelic use. Responsible psychedelic use requires understanding and respecting its contraindications to ensure the health and safety of all individuals. Consulting a qualified healthcare professional is essential to assess whether psychedelic use is appropriate and to receive personalized advice tailored to your individual medical history and circumstances (Halpern and Pope, 2003).

Psychedelics, by activating serotonin receptors in the brain, can potentially lead to a life-threatening condition known as serotonin syndrome.

Individuals with a history of substantial trauma who lack fundamental coping skills or have not developed a safety plan (such as the stabilization phase of trauma treatment) should refrain from using psychedelics for the same reason they should avoid cognitive processing therapy or prolonged exposure. Psychedelics can trigger the reliving of traumatic experiences and the exposure of repressed traumatic memories, which can result in significant emotional distress (Brierley DI and Davidson, 2012).

Applications of psychedelics

Clinical research has focused on the potential of psychedelics to alleviate mental health conditions such as post-traumatic stress disorder (PTSD), treatment-resistant depression (TRD), and substance use disorders (Carhart-Harris and Goodwin, 2017).

Mechanisms of action of psychedelics

Classic psychedelics typically refer to serotonergic hallucinogenic substances, such as lysergic acid diethylamide (LSD), psilocybin (the psychoactive compound in magic truffles and mushrooms), and N,NDimethyltryptamine (DMT). These drugs have a common mechanism of action, consisting of partial agonism for

the serotonin 5-HT2A G protein-couple receptors (Halberstadt and Geyer, 2013).

LSD and psilocybin induces cross-tolerance, whereby the efficacy of the drugs decreases after repeated dosages

The 5-HT2A receptor is involved in learning and memory, pain perception, and the sleeping/ waking cycle (Nichols, 2016).

5-HT2A receptors can be found in the so-called pyramidal neurons in layer 5 of the neo-cortex, in the thalamus, and in the reticular nucleus, which are involved in visual perception A high concentration of 5-HT2A receptors can also be found in so-called higher-order association areas in the brain, such as the temporo-parietal junction and the medial prefrontal cortex. Psychedelics activate the TAAR1 receptor, which in turn exerts an inhibitory effect on dopaminergic activity. These receptor-mechanisms may underlie the therapeutic effects of psychedelics on addiction and depression by affecting the sensitivity to reward and stress at a pharmacological level

Pharmacological level,
The neural level
The psychological level

The Psychological level

Psychedelics are often reported to induce a complex, dynamic, and multifaceted experience that is difficult to concisely convey (**Carhart-Harris and Friston, 2019)**. Below we detail some of the most prominent psychological effects that have been associated with the acute subjective effects of psychedelics, including

Altered and affective states,
changes in cognition,
belief change,
social effects,
behavior change (**Nichols, 2016)**.

Altered and affective states

One of the key characteristics of psychedelics is their potential to induce an altered state of consciousness, including mystical experiences, feelings of awe, ego dissolution, and an enhanced perception of emotions. Mystical-type experiences are characterized by feelings of unity, transcendence of space and time, a noetic quality, ineffability, paradox, and sacredness, as well as positive feelings of bliss, joy, wonder and awe (**Griffiths et al, 2006; MacLean et al., 2012)**.

Cognition

Psychedelics generally impair attention and cognitive control, but they've also been proposed to enhance psychological and cognitive flexibility. Numerous studies have demonstrated that psychedelics can increase psychological flexibility, which can be defined as the adaptive response individuals can use to respond to various stressors in a value-driven manner (**Barnett et al., 2018)**. It has been observed that psychological flexibility mediates the effects of psychedelic-induced experiences and reduces anxiety and depression (**Ly et al.,2018)**.

Beliefs

Psychedelic experiences can trigger attributions of supernatural encounters and increase suggestibility, resulting in changes in metaphysical beliefs, worldviews, and the perception of enhanced feelings of meaning (**Pahnke, 1966)**. Many people have vivid encounters with seemingly (to some) supernatural entities and otherworldly realities during their psychedelic experiences (**Griffiths et al.,2011)**.

Social connection

Psychedelics exert strong social effects, including feelings of connectedness, communities, and empathy. Classic psychedelics often induce strong feelings of connectedness with other

people, with nature and with humanity (**Forstmann and Sagioglou**, 2017; **Carhart-Harris et al.,2018)**.

Behaviour

Finally, following on the observed psychedelic-induced increase in neuroplasticity, it has been suggested that psychedelics offer a therapeutic window of opportunity for learning new healthy habits and behavior change (**Schenberg, 2018)**. Combined with behavior change programs, such as cognitive behavioral therapy, psychedelics might offer a strong potential for fostering a healthier lifestyle, including improved diet, physical exercise, and mindfulness practices (**Nutt et al., 2020)**.

Tolerance and Addiction

Psychedelics do not appear to be addictive. Addiction is defined as chronic use of a substance despite negative consequences (**Nichols**, 2016; **Johnson et al., 2018)**.

However, some hallucinogenic drugs may lead to tolerance and some people report experiencing withdrawal effects when they stop using such substances (**Bonson and Murphy, 1995)**.

LSD use can lead to tolerance, which means people require more of the substance in order to achieve the same effects. This can be risky due to the unpredictable effects that the drug may have (**Halberstadt, 2015)**.

Cross-tolerance to other substances can also occur. Developing a tolerance to LSD means that people will experience a decreased reaction to some substances, including mescaline and psilocybin (**Isbell** et al., 1956; **Strassman, 1995)**.

Table 1. Uses of Pyschedilics

Psychiatric Disorders	Psychological Disorders
Chronic pain	CLUSTER HEAD ACHE
PTSD	Mood disorders
Substance use disorders	Psychological distress linked to life threatening illness

Conclusion

Psychedelics represent a groundbreaking advancement in the landscape of neuropsychiatry, redefining therapeutic approaches to mental health conditions. By harnessing their unique capacity to modulate neural plasticity, reconfigure dysfunctional brain networks, and facilitate profound introspection, psychedelics offer a promising alternative for conditions that have eluded conventional treatments. Their ability to merge pharmacological efficacy with transformative experiential healing sets them apart as a holistic and revolutionary tool in mental health care.

However, the path to integrating psychedelics into mainstream medicine demands careful navigation of ethical, regulatory, and safety considerations. The need for standardized protocols, well-defined therapeutic settings, and long-term impact assessments is paramount to ensuring their safe and effective use. As research continues to illuminate the intricate mechanisms underlying their effects, psychedelics hold the potential to not only treat mental health disorders but also enhance our understanding of consciousness and the human psyche.

In conclusion, psychedelics herald a paradigm shift in neuropsychiatry, offering a unique convergence of science, medicine, and introspec-

tion. Their judicious application could mark the dawn of a new era in personalized mental health care, fostering resilience, well-being, and a deeper connection to the self and others.

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Conflict of interest

The authors declare that there are no conflicts of interest relevant to this review.

References

Barnett BS, Siu WO, & Pope HG. Jr. A comprehensive review of the effects of psychedelics on cognition. *Journal of Psychoactive Drugs* **2018;** *50*(3): 1–11.

Bonson KR, & Murphy DL. Alterations in the function of 5-HT2A receptors after chronic administration of serotonergic hallucinogens. *Neuropsychopharmacology* **1995;** *13*(1): 65–85.

Brierley DI, Davidson C. Developments in harmine pharmacology—implications for ayahuasca use and drug-dependence treatment. *Prog Neuropsychopharmacol Biol Psychiatry.* 2012; 39(2): 263-272.

Carhart-Harris RL, & Friston KJ. REBUS and the Anarchic Brain: Toward a Unified Model of the Brain Action of Psychedelics. *Pharmacological Reviews* **2019;** *71*(3), 316–344.

Carhart-Harris RL, *et al.* Psilocybin with psychological support for treatment-resistant depression: six-month follow-up. *Psychopharmacology* **2018;** *235*(2): 399–408.

Carhart-Harris RL, Goodwin GM. The Therapeutic Potential of Psychedelic Drugs: Past, Present, and Future. *Neuropsychopharmacology.* 2017; 42(11): 2105-2113.

Carhart-Harris RL, Goodwin GM. The Therapeutic Potential of Psychedelic Drugs: Past, Present, and Future. *Neuropsychopharmacology.* 2017; 42(11): 2105-2113.

Carhart-Harris RL, Goodwin GM. The therapeutic potential of psychedelic drugs: Past, present, and future. Neuropsychopharmacology. 2017; 42(11): 2105-2113.

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). European Drug Report 2023: Trends and Developments. Luxembourg: Publications Office of the European Union; 2023.

Forstmann M, & Sagioglou C. Lifetime experiences with classic psychedelics predict pro-environmental behavior through an increase in nature relatedness. *Journal of Psychopharmacology* **2017;** *31*(8): 975–988.

Griffiths RR, *et al.* Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology* **2006;** *187*(3): 268–283.

Griffiths RR, *et al.* Psilocybin occasioned mystical-type experiences: Immediate and persisting dose-related effects. *Psychopharmacology* **2011;** *218*(4): 649–665.

Halberstadt AL, Geyer MA. Serotonergic hallucinogens as translational models relevant to schizophrenia. *Int J Neuropsychopharmacol.* 2013; 16(10): 2165-2180.

Halberstadt AL, Geyer MA. Serotonergic hallucinogens as translational models relevant to schizophrenia. Int Neuropsychopharmacol.

2011; 14(6): 720-731.

Halberstadt AL. Recent advances in the neuropsychopharmacology of serotonergic hallucinogens. *Behavioural Brain Research* **2015;** *277: 99–120.*

Halpern JH, Pope HG Jr. Hallucinogen persisting perception disorder: what do we know after 50 years? *Drug Alcohol Depend.* 2003; 69(2): 109-119.

Halpern JH. Hallucinogens and dissociative agents naturally growing in the United States. *Pharmacol Ther.* 2004; 102(2): 131-138.

Isbell H, Belleville RE, Logan CR, & Wilkerson HL. Studies on lysergic acid diethylamide (LSD-25). *AMA Archives of Neurology and Psychiatry* **1956;** *76*(4): 468–478.

Johnson MW, Griffiths RR, Hendricks PS, & Henningfield JE. The abuse potential of medical psilocybin according to the 8 factors of the Controlled Substances Act. *Neuropharmacology* **2018;** *142: 143–166.*

Johnson MW, Richards WA, Griffiths RR. Human hallucinogen research: guidelines for safety. *J Psychopharmacol.* 2008; 22(6): 603-620.

Ly C, *et al.* Psychedelics promote structural and functional neural plasticity. *Cell Reports* **2018;** *23*(11): 3170–3182.

MacLean KA, Leoutsakos JM, Johnson MW, & Griffiths RR. Factor analysis of the Mystical Experience Questionnaire: A study of experiences occasioned by the hallucinogen psilocybin. *Journal of Scientific Exploration* **2012;** *26* (3): 358–382.

National Institute on Drug Abuse. *Hallucinogens and Dissociative Drugs Research Report.* National Institutes of Health; 2015.

National Institute on Drug Abuse. *Hallucinogens DrugFacts*. National Institutes of Health; 2019.

Nichols DE, Grob CS. Hallucinogens: Neurochemical, Behavioral, and Clinical Perspectives. 3rd ed. Oxford: Oxford University Press; 2021.

Nichols DE. Psychedelics. Pharmacol Rev. 2016; 68(2): 264-355.

Nichols DE. Psychedelics. *Pharmacol Rev.* 2016; 68(2): 264-355.

Nichols DE. Psychedelics. *Pharmacological Reviews* **2016;** *68*(2): 264–355.

Nichols DE. Psychedelics. *Pharmacological Reviews* **2016;** *68*(2): 264–355.

Nutt D, *et al.* Psychedelic therapy for psychiatric disorders: What we know and what we need to know. *Neuropharmacology* **2020;** *142: 41–49.*

Pahnke WN. Drugs and mysticism: An analysis of the relationship between psychedelic drugs and the mystical consciousness. *Journal of Religion and Health* **1966;** *5*(3): 175–208.

Passie T, Halpern JH, Stichtenoth DO, Emrich HM, Hintzen A. The pharmacology of psilocybin. Addiction Biology. 2002; 7(4): 357-364.

Passie T, Seifert J, Schneider U, Emrich HM. The pharmacology of psilocybin. *Addict Biol.* 2002; 7(4): 357-364.

Schenberg EE. Psychedelic-assisted psychotherapy: A paradigm shift in psychiatric research and development. *Frontiers in Pharmacology* **2018;** *9: 733.*

Schultes RE, Hofmann A. The Botany and Chemistry of Hallucinogens. 2nd ed. Springfield, IL: Charles C. Thomas Publisher; 1980.

Strassman RJ. Human psychopharmacology of N, N-dimethyltryptamine (DMT): A review. *Journal of Nervous and Mental Disease* **1995;** *183* (3): 181–192.

Vollenweider FX, Kometer M. The neurobiology of psychedelic drugs: Implications for the treatment of mood disorders. Nat Rev Neurosci. 2010; 11(9): 642-651.

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