

A REVIEW ON BEHAVIOURAL NEUROBIOLOGY OF PSYCHEDELIC DRUGS

Supreetha Srinivasan^{1*}, Shubamalya L. G.², Nirmita S. B.³ and Kirthika N.⁴

¹Masters in Applied Psychology, Bharathiyar University, Coimbatore.

²Pharm D, Rao's College of Pharmacy, Venkatachalam, SPSR Nellore, AP -524320.

^{3,4}Pharm D, PSG College of Pharmacy, Peelamedu, Coimbatore, TN -641004.

Article Received date: 25 June 2024

Article Revised date: 05 July 2024

Article Accepted date: 25 July 2024



*Corresponding Author: Supreetha Srinivasan

Masters in Applied Psychology, Bharathiyar University, Coimbatore.

Email ID: drshubamalyapharmd@gmail.com

ABSTRACT

Psychedelic substances' remarkable effects on human mind and behaviour have sparked a fresh interest in science. The behavioural neurobiology of psychedelics is examined in this study, with particular attention paid to their mechanisms of action, which include effects on brain plasticity and serotonin receptor modulation. We describe their historical background, including everything from their use in antiquity to contemporary scientific research, and we divide them into two groups: classical (like LSD and psilocybin) and atypical (like MDMA and ketamine). Potential therapeutic uses in mental health issues are explored with behavioural impacts, such as changed perception and cognition. We also discuss the difficulties that are currently facing safety, regulations, and ethical issues. Lastly, future prospects in clinical applications and research are examined, with a focus on how psychedelics may change the way that mental therapy paradigms are used.

KEYWORDS: Psychedelic drugs, behavioural neurobiology, serotonin receptors, therapeutic applications, mental health disorders.

INTRODUCTION

Drugs that cause altered states of consciousness, sometimes referred to as hallucinogens or psychedelics, are compounds that frequently cause sensory distortions, alterations in perception, and increased introspection. They can cause significant alterations in mood and cognitive processes, as well as tactile, auditory, and visual hallucinations.

Psychedelic substances mainly affect the brain's serotonin receptors, namely the 5-HT_{2A} receptor, which modifies cognitive functions and sensory experiences. The experiences that can arise from this interaction range from intense mystical or spiritual experiences to difficult and perhaps upsetting psychological repercussions, which are commonly referred to as "bad trips."

The therapeutic potential of psychedelics has garnered renewed attention in recent times. Treatment outcomes for a range of mental health issues, such as depression, anxiety, PTSD, and drug use disorders, have been encouragingly demonstrated by research. As a result, their legal standing and their uses in contemporary medicine have been re-examined.

Additionally important to the study of consciousness and the human mind are psychedelics. They are of tremendous interest to both neuroscience and psychology because they offer novel insights into the nature of human perception and cognition as well as the functioning of the brain.^[1,2,3]

HISTORICAL OVERVIEW OF PSYCHEDELIC DRUGS

The history of psychedelic substances crosses centuries and cultural boundaries, demonstrating the significant influence these drugs have had on medicine, spirituality, and human civilization.

Ancient and Indigenous Use

- **Prehistoric and Ancient Times:** It seems from archaeological evidence that psychoactive plants and fungi have been utilized by humans for a very long time. The usage of these chemicals in shamanic and religious rites is documented in ancient literature and rock art.
- **Indigenous Cultures:** Psychedelics have long been used for spiritual and medicinal purposes in many traditional societies. For example, the indigenous

tribes of the Amazon basin have utilized Ayahuasca, a drink containing DMT, for spiritual and therapeutic purposes, while the Mazatec people of Mexico have used psilocybin mushrooms in religious rites.

Early Scientific Exploration

- **19th Century:** Western scientists started investigating the effects of psychoactive drugs in the late 1800s. For instance, the mescaline-containing plant peyote was investigated for its hallucinogenic qualities.
- **Early 20th Century:** Systematic scientific research on psychedelics began in the early 1900s. After mescaline was created in 1919, several studies looked into its psychological effects.^[4,5]

Mid-20th Century: The Psychedelic Renaissance

- **1940s and 1950s:** People became increasingly interested in LSD after Albert Hofmann discovered it in 1938 and it began to have psychedelic effects in 1943. Research on the therapeutic potential of LSD and other psychedelics in psychiatry was conducted extensively in the 1950s. Their application in the treatment of anxiety, depression, and alcoholism has been studied.
- **1960s:** The use of psychedelics, especially LSD, for recreational purposes gained popularity during the 1960s counterculture movement. They were promoted for use in extending awareness and investigating the mind by notable individuals such as Timothy Leary. Still, the legalization of psychedelics was brought about by political and social opposition over their widespread recreational use.

Late 20th Century: The Dark Ages

- **1970s to 1990s:** In the United States, the Controlled Substances Act of 1970 designated psychedelics as Schedule I substances, meaning they had a high potential for abuse and no recognized medical value. This led to the Dark Ages of the late 20th century. As a result, there was a sharp drop in research, marking what is sometimes called the "Dark Ages" of psychedelic study.

21st Century: The Psychedelic Renaissance

- **2000s to Present:** The 2000s to the Present: In the late 20th and early 21st centuries, there was a resurgence of interest in psychedelics. Innovative research from establishments like Imperial College London, Johns Hopkins University, and others started delving into the therapeutic possibilities of psychedelics once more.
- **Breakthrough Research:** Prominent research showed that psychedelics were effective in treating a range of mental health issues, which sparked a

renewed interest in the field from scientists and medical professionals. The FDA designated psilocybin and MDMA as "Breakthrough Therapy" for depression and PTSD, respectively.

Recent Developments

- **Legislative Changes:** A number of states have started to decriminalize or legalize the use of psychedelics for therapeutic and medical purposes. For example, in 2020 Oregon became the first state in the United States to authorize psilocybin therapy.
- **Ongoing Research:** Research on the safety, therapeutic potential, and mechanisms of action of different psychedelics is still ongoing. Microdosing, the use of psychedelics at sub-perceptual levels to improve mental and emotional health, is another topic of study.^[6,7,8]

TYPES OF PSYCHEDELICS

Psychedelic drugs can be broadly classified into different categories based on their chemical structures, mechanisms of action, and sources. Below are the classifications and types of psychedelic drugs.

Classical Psychedelics

Classical psychedelics primarily interact with the serotonin (5-HT) receptors in the brain, particularly the 5-HT_{2A} receptor. These include

1. LSD (Lysergic acid diethylamide)

- **Source:** Synthetic
- **History:** Discovered by Albert Hofmann in 1938.
- **Mechanism of Action:** Potent agonist at the 5-HT_{2A} receptor.
- **Effects:** Profound alterations in perception, mood, and thought; visual hallucinations.

2. Psilocybin

- **Source:** Natural (found in magic mushrooms, particularly in the genus *Psilocybe*)
- **History:** Used in traditional rituals by indigenous cultures.
- **Mechanism of Action:** Converted to psilocin in the body, which acts as a partial agonist at the 5-HT_{2A} receptor.
- **Effects:** Euphoria, altered thinking processes, and changes in perception.

3. Mescaline

- **Source:** Natural (found in peyote cactus, San Pedro cactus)
- **History:** Traditionally used in Native American religious ceremonies.
- **Mechanism of Action:** Agonist at the 5-HT_{2A} receptor.
- **Effects:** Visual hallucinations, altered states of consciousness, and emotional experiences.

Atypical Psychedelics

Atypical psychedelics may interact with different neurotransmitter systems and have unique effects compared to classical psychedelics.

1. MDMA (3, 4-Methylenedioxyamphetamine)

- **Source:** Synthetic.
- **History:** Developed in the early 20th century, popularized in the 1980s as a recreational drug.
- **Mechanism of Action:** Increases the release of serotonin, dopamine, and norepinephrine.
- **Effects:** Euphoria, increased sociability, and empathy; mild perceptual changes.

2. Ketamine

- **Source:** Synthetic
- **History:** Developed in the 1960s as an anaesthetic.
- **Mechanism of Action:** NMDA receptor antagonist.
- **Effects:** Dissociative anaesthesia, out-of-body experiences, and hallucinations.

- **Characteristics:** Chemically manufactured, often with precise dosages and purities.

2. Natural Psychedelics

- **Examples:** Psilocybin (magic mushrooms), Mescaline (peyote cactus), DMT (in ayahuasca brew), Salvinorin A (*Salvia divinorum*).
- **Characteristics:** Extracted or derived from natural sources, variability in potency due to environmental factors.

The categorization of psychedelic substances aids in comprehending their various effects, modes of action, and their medical applications. The distinct qualities that each class of psychedelics has to offer support their wide range of uses in therapeutic and recreational contexts. The complex understanding of these compounds is still developing as study advances, illuminating both their possible advantages and disadvantages.^[9,10,11,12]

Synthetic vs. Natural Psychedelics

1. Synthetic Psychedelics

- **Examples:** LSD, MDMA, Ketamine, 2C-B, DMT (N, N-Dimethyltryptamine, when synthesized in a laboratory).

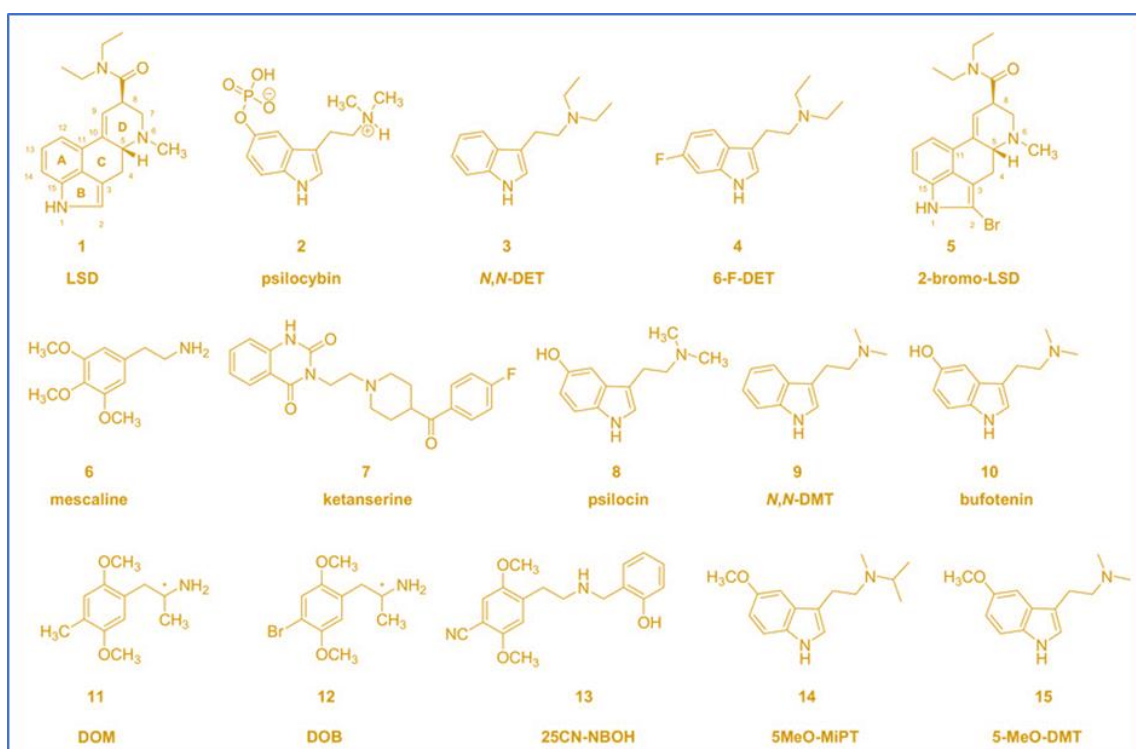


Figure 1: Chemical structures of LSD and some classic hallucinogenic compounds.

IMPORTANCE OF PSYCHEDELIC DRUGS IN MODERN MEDICINE AND PSYCHIATRY

In contemporary medicine and psychiatry, psychedelic substances have garnered renewed interest because of their potential therapeutic benefits in the treatment of a range of mental health disorders.

1. Treatment-Resistant Mental Health Disorders:

When traditional therapies fail, psychedelics such as MDMA and psilocybin (found in magic mushrooms) have demonstrated potential in treating illnesses like treatment-resistant depression, PTSD, and anxiety disorders.

2. **Neuroplasticity and Brain Connectivity:** Studies indicate that psychedelics may improve brain connectivity and foster neuroplasticity, which may have therapeutic benefits that extend beyond the short-term psychedelic experience.
3. **Mindfulness and Spiritual Insight:** During psychedelic sessions, many users describe having profound spiritual experiences and increased mindfulness, which can help with existential suffering, emotional healing, and personal growth.
4. **Safety and Efficacy:** Psychedelics have demonstrated a comparatively safe profile when compared to conventional psychiatric drugs when given in controlled environments and under appropriate medical supervision.
5. **Research Advancements:** To maximize treatment success and reduce side effects, ongoing research is investigating novel ways to utilize psychedelic chemicals, frequently in conjunction with psychotherapy.
6. **Public Interest and Support** As a result of expanding public support and lobbying, clinical trials and studies including psychedelics are receiving more financing and regulatory support.

All things considered, psychedelics represent a promising new area in contemporary medicine and psychiatry for treating difficult mental health issues, even though more research is required to completely grasp their mechanisms and possible applications.^[13,14,15]

NEUROBIOLOGY/MECHANISM OF ACTION OF PSYCHEDELIC DRUGS

The main way that psychedelic drugs work in the brain is by interfering with different neurotransmitter systems. The most well-known and extensively researched mechanism focuses on the 5-HT_{2A} receptor and other serotonin (5-HT) receptors. But other neurotransmitter systems and receptors also have important functions.

1. Interaction with Serotonin Receptors (5-HT_{2A} and Others)

5-HT_{2A} Receptors

- **Primary Target:** The brain's 5-HT_{2A} receptors are the main site of action for psychedelic substances like mescaline, DMT, psilocybin, and LSD.
- **Effects:** Perception, emotion, and cognitive function are all affected when 5-HT_{2A} receptors are activated. The prefrontal cortex, which is engaged in complex activities and higher-order thinking, has a high concentration of this receptor.

Other Serotonin Receptors

- **5-HT_{1A}:** Certain psychedelics also have an effect on 5-HT_{1A} receptors, which can affect anxiety and mood.
- **5-HT_{2C}:** Involved in mood, anxiety, and feeding behaviour regulation. The way that psychedelics interact with these receptors may be a factor in their overall psychotropic effects.^[16,17]

2. Modulation of Neural Plasticity Synaptic Plasticity

- **Growth of New Synapses:** Research has indicated that psychedelics stimulate the formation of new synapses and dendritic spines, especially in the prefrontal cortex. This may improve neuronal transmission and connection.
- **BDNF (Brain-Derived Neurotrophic Factor):** Psychedelics have the ability to upregulate the expression of this protein, which helps synapses and neurons survive and grow and promotes brain plasticity.

Long-Term Potentiation (LTP)

- Psychedelics may improve long-term potentiation (LTP), a mechanism essential to learning and memory that fortifies neuronal connections.^[18,19]

3. Alteration of Default Mode Network (DMN) Activity

Default Mode Network (DMN)

- When the mind is at rest and not focused on the outside world, as it is during daydreaming, self-referential thinking, and introspection, the default mental network (DMN) is activated.
- **Psychedelics' Effect:** In general, psychedelics lower DMN activity and connection. The sense of ego dissolution, in which the distinction between the self and the outside world becomes hazy, is linked to this decrease in DMN activity.
- **Implications:** Because excessive DMN activity and rigid self-referential thought patterns are typical in illnesses like depression and anxiety, altered DMN activity may result in significant changes in perception and consciousness and may thus contribute to the therapeutic benefits of psychedelics in these circumstances.

4. Other Neurotransmitter Systems Involved

- **NMDA Receptors:** Ketamine and PCP, two dissociative hallucinogens, primarily function as antagonists at NMDA receptors, altering glutamate transmission, which is essential for brain communication and synaptic plasticity.
- **Dopamine Release:** The stimulating and mood-enhancing effects of many psychedelics, especially

MDMA, are also attributed to an increase in dopamine release.

- **Norepinephrine:** Psychedelics have the ability to alter norepinephrine secretion, which in turn affects alertness and arousal.
- **GABA:** Interactions with the GABAergic system, which controls neuronal excitability and preserves the equilibrium between excitation and inhibition in the brain, may occur.

Although psychedelic drugs affect several neurotransmitter systems, 5-HT_{2A} receptor activation is the main mechanism via which they work. Significant alterations in perception, mood, and cognitive function result from this interaction. Moreover, psychedelics interact with other neurotransmitter systems such as glutamate, dopamine, and norepinephrine, change the activity of the default mode network, and encourage brain plasticity. Their distinct psychotropic qualities and perhaps therapeutic advantages are a result of these combined effects.^[20,21,22]

BEHAVIORAL EFFECTS OF PSYCHEDELIC DRUGS

1. Altered Perception

- **Visual Hallucinations:** Enhanced hues, patterns, and fractal-like visuals are among the striking visual modifications that users frequently describe seeing. Usually, the visual impacts of substances like psilocybin and LSD are more pronounced.
- **Auditory Changes:** Sounds could get distorted or more vivid. Additionally, users may experience synesthesia, which is the perception of colours or shapes in sounds.
- **Time Perception:** One's perception of time can be significantly affected; for example, minutes can appear to be hours, and vice versa.

2. Emotional Changes

- **Euphoria:** A lot of psychedelics, especially MDMA, can cause very strong emotions of joy and contentment.
- **Emotional Release:** Catharsis or emotional release is a common experience reported by users. Emotions of both a positive and negative nature may be involved.
- **Empathy and Connection:** Enhanced emotions of love, empathy, and kinship are frequently experienced, particularly while using MDMA, commonly referred to as the "empathogen."^[23,24]

3. Cognitive Effects

- **Altered Thinking:** It is possible for thought processes to become more fluid and non-linear.

Users might have fresh insights and ideas as well as changed problem-solving skills.

- **Introspection:** Deeper introspection and self-reflection are prevalent and can result in important realizations and insights for the individual.
- **Ego Dissolution:** Higher dosages of classical psychedelics may cause a diminished feeling of self or ego. This may result in a transcendental experience or a sensation of unity with the universe.

4. Behavioral Changes

- **Increased Sociability:** It's well known that psychedelics, such as MDMA, enhance sociability and a sense of intimacy with people.
- **Reduced Anxiety:** Psychedelics have been shown to help some people feel less anxious and more at ease. But for others, especially in unfamiliar or stressful situations, they might cause worry and paranoia.
- **Enhanced Creativity:** Users frequently mention feeling more imaginative and creative. This can show up as creative expression or creative problems.

5. Therapeutic Potential

- **Treatment of PTSD:** By enabling patients to revisit painful memories with less fear and improved emotional processing, MDMA has demonstrated potential in the treatment of PTSD.
- **Depression and Anxiety:** Psilocybin and other psychedelics are being researched for their ability to cure anxiety and depression that is resistant to treatment, particularly in patients who are terminally ill.
- **Addiction:** Studies have looked into the use of psychedelics as treatments for a variety of addictions, and some suggest they may be able to lessen reliance on substances like alcohol and nicotine.

6. Spiritual and Mystical Experiences

- **Spiritual Insights:** A lot of users talk about having had mystical or deeply spiritual experiences, such as feeling like they are a part of the cosmos or a higher force.
- **Mystical-type Experiences:** It's common to have feelings of awe, veneration, and oneness. For the person, these can be incredibly transformational and significant events.

7. Long-term Behavioural Effects

- **Lasting Changes in Attitude and Behaviour:** A few users mention sustained adjustments to their behaviours, attitudes, and personality traits, such as

a decrease in neuroticism and an increase in openness.

- **Improved Mental Health:** Research has indicated that psychedelic encounters can result in long-lasting changes in mental health, such as a decrease in the symptoms of anxiety and depression.

Psychedelic substances have a wide range of behavioural effects, which can differ greatly according on the substance, dosage, context, and individual. Modified perception, emotional shifts, cognitive effects, social shifts, and increased creativity are some of these consequences. Additionally, there is great therapeutic promise for the use of psychedelics in the treatment of a variety of mental health issues as well as the promotion of deep spiritual and mystical experiences. For psychedelic use to have as many positive impacts as possible while reducing its hazards, it is imperative to comprehend these behavioural consequences.^[28,29,30]

THERAPEUTIC APPLICATIONS

Psychedelic substances have demonstrated encouraging therapeutic potential for treating a range of mental health issues. The potential advantages of these therapies have been the subject of increased research in recent years, especially when treating illnesses that have shown resistant to traditional medicines.

1. Treatment-Resistant Depression

- **Psilocybin:** Research has shown that psilocybin produces quick and long-lasting antidepressant effects. This is especially true for people with severe depression who have not responded to standard therapies. It indicates that psilocybin enhances emotional processing and brain plasticity.

2. Anxiety Disorders

- **PTSD (Post-Traumatic Stress Disorder):** MDMA-assisted psychotherapy has demonstrated encouraging outcomes in PTSD clinical trials. MDMA helps people manage traumatic experiences by lowering fear reactions and improving communication and trust.

3. Substance Use Disorders

- **Addiction:** The potential of psychedelics, such as ibogaine (derived from the iboga plant) and ayahuasca (containing DMT), to cure substance addiction, including that to opioids, cocaine, and alcohol, has been studied. These drugs could provide users a better understanding of the reasons behind and behaviours associated with addiction.

4. End-of-Life Anxiety and Existential Distress

- **Terminal Illness:** The potential of psilocybin therapy to lessen anxiety and depression in individuals with terminal illnesses has been investigated. It can enhance people's quality of life

in the time they have left over and assist them in accepting their mortality.^[31,32,33]

5. Obsessive-Compulsive Disorder (OCD)

- **LSD and Psilocybin:** According to some initial study, psychedelics may be able to alleviate OCD symptoms by encouraging flexibility in cognition and unending inflexible thought patterns.

6. Autism Spectrum Disorders (ASD)

- **MDMA:** Research on MDMA-assisted therapy for ASD patients has been preliminary, with an emphasis on reducing social anxiety and strengthening relationships with others.

7. Cluster Headaches

- **LSD and Psilocybin:** LSD and psilocybin have demonstrated efficacy in lowering the frequency and intensity of cluster headaches, a crippling ailment that frequently defies medical intervention.

Mechanisms of Action in Therapy

- **Neuroplasticity:** The formation of new synaptic connections and the rearrangement of brain networks are among the processes that are facilitated by psychedelics. This can support the development of fresh viewpoints and assist in breaking negative mental habits.
- **Emotional Processing:** Psychedelics frequently aid in introspection and deep emotional processing, enabling people to face and resolve traumatic experiences or unresolved emotional problems.
- **Spiritual and Transpersonal Experiences:** Deeply spiritual or mystical experiences brought on by psychedelics may have a positive therapeutic effect by enhancing feelings of purpose, meaning, and connectivity.

Even though psychedelic-assisted treatment has a lot of potential, more research is necessary to determine its safety, effectiveness, and optimal applications in therapy. The potential for psychedelic research to transform mental health care in the next years is highlighted by the changing legal environment and growing acceptance of this field of study.^[34,35]

RISKS AND LEGAL ISSUES

There are a number of hazards and concerns associated with integrating psychedelics into therapeutic methods, which should be carefully considered. Although there is encouraging research on their therapeutic potential, safety, legality, and ethical issues remain major concerns. The following are some of the main dangers and issues surrounding psychedelics:

1. Safety Concerns

- **Psychological Vulnerability:** Especially in people who are prone to mental health difficulties,

psychedelics can cause strong and erratic psychological experiences, such as anxiety, paranoia, and psychosis.

- **Physiological Effects:** Certain psychedelics, such as MDMA and ketamine, may cause unfavourable physiological consequences, including higher blood pressure, accelerated heart rate, and an increased risk of dehydration or hyperthermia.
- **Risk of Misuse and Dependence:** While traditional psychedelics like LSD are not thought to be addictive, drugs like MDMA carry a risk of abuse and dependence, particularly when used recreationally.

2. Legal and Regulatory Issues

- **Schedule I Classification:** According to international drug control treaties, several psychedelics are categorized as Schedule I substances, which restricts their use in clinical and legal study.
- **Regulatory Hurdles:** It is difficult to get regulatory approval for psychedelic research and therapy because of legal limitations, stigma, and public safety concerns.^[36,37]

3. Ethical Considerations

- **Informed Consent:** Because psychedelic experiences are powerful and unpredictable, obtaining informed consent in psychedelic therapy is difficult. Therapists have a duty to fully advise their patients of the advantages and disadvantages.
- **Integration and Support:** In order to assist people digest powerful psychedelic experiences and lessen the possibility of negative psychological impacts, proper integration support is essential.

4. Public Perception and Stigma

- **Historical Stigma:** Due to its history of countercultural connotations and recreational usage, psychedelics continue to have a stigma that influences both public perception and professional acceptability.
- **Media Representation:** Informed public conversation can be impeded and misconceptions can be reinforced by sensationalized media coverage and false information regarding psychedelics.

5. Lack of Long-term Research

- **Long-term Effects:** It is difficult to comprehend the possible long-term advantages and hazards of psychedelic therapies due to the paucity of long-term research on their safety and effectiveness.

Addressing Risks and Controversies

- **Clinical Guidelines and Protocols:** To guarantee safety, effectiveness, and consistency in therapeutic outcomes, standardized clinical guidelines and protocols for psychedelic-assisted therapy are being developed.
- **Regulatory Reform:** Pushing for changes to regulations to allow more room for research and to give eligible patients legal access to psychedelic treatments.
- **Professional Training:** Offering therapists specific training in psychedelic-assisted therapy to improve their ability to support clients and manage psychedelic experiences.
- **Public Education:** Encouraging evidence-based instruction and awareness initiatives to debunk stereotypes, lessen stigma, and promote knowledgeable public discussion regarding psychedelics and their possible medical uses.^[38,39,40]

FUTURE DIRECTIONS

The prospective future prospects of psychedelic substances are being driven by growing understanding of their medicinal potential and continued research. Psychedelic substances are anticipated to have a future shaped by the following major areas and developments.

1. Advancing Clinical Applications

- **Expansion of Indications:** Psychedelic therapies are being investigated further for mental health conditions other than depression and PTSD, such as anxiety disorders, addiction, OCD, and neurodevelopmental disorders like autism.
- **Integration into Mainstream Healthcare:** Appropriate steps are being taken to incorporate psychedelic therapies into mainstream healthcare systems by means of regulatory approvals, clinical guidelines, and professional training for healthcare providers.

2. Enhancing Therapeutic Protocols

- **Optimization of Treatment Protocols:** Improving the sustainability, safety, and effectiveness of psychedelic-assisted therapies through the refinement of therapeutic protocols. Investigating the best dosage schedules, therapeutic modalities, and integrating techniques are all part of this.
- **Combination Therapies:** Researching the synergistic benefits of combining supportive therapies, adjunct drugs, or psychotherapy techniques with psychedelics in order to maximize therapeutic outcomes and meet a range of patient demands.^[41,42]

3. Mechanistic Insights

- **Neurobiological Mechanisms:** Improving knowledge of the neurobiological processes underlying the effects of psychedelics, such as changes in brain connections, interactions with neurotransmitter systems, and stimulation of neuroplasticity.
- **Molecular and Cellular Effects:** Examining the molecular and cellular alterations brought about by psychedelics at the genetic and synaptic levels in order to provide light on the long-term effects on the nervous system and the mechanisms underlying therapeutic action.

4. Personalized Medicine

- **Individualized Approaches:** Creating individualized treatment plans based on genetic information, biomarkers, and mental health history in order to reduce risks, maximize therapeutic benefits, and forecast treatment responses.

5. Regulatory and Policy Developments

- **Regulatory Reform:** Pushing for changes to regulations to allow for more chances for study, legal access to psychedelics for therapeutic purposes, and integration with medical systems.
- **Public Education and Awareness:** Raising awareness among the general public and among professionals by promoting evidence-based policy decisions, reducing stigma, and educating the public.

6. Technological Innovations

- **Digital Therapeutics:** Enhancing the delivery of psychedelic therapy, tracking treatment progress, and facilitating therapeutic integration through the use of digital health technology, such as virtual reality and digital biomarkers.

7. Ethical and Social Considerations

- **Ethical Guidelines:** Developing best practices and ethical standards for psychedelic therapy and research, such as informed consent, patient safety, privacy, and fair access to care.

8. Global Perspectives

- **Global Research Collaborations:** Promoting global cooperation and information exchange to further psychedelic research, take cultural issues with account, and increase access to psychedelic treatments worldwide.^[43,44,45]

CONCLUSION

In summary, this review has delved into the complex terrain of behavioural neurobiology surrounding psychedelic substances, exposing their significant impacts on both behaviour and brain function. By understanding the mechanisms of action pertaining to serotonin receptors, neuronal plasticity, and changed

brain connectivity, scientists have discovered the ways in which these chemicals elicit modifications in perception, emotional states, and possible therapeutic advantages. Recent scientific discoveries have rekindled interest in spite of historical stigma and legal obstacles, opening the door for novel therapies for mental health conditions like addiction, PTSD, and depression. Future research on tailored therapeutic techniques that combine psychotherapy and psychedelics to maximize results while resolving safety issues is promising. To guarantee responsible use and fair access, ethical considerations, legal frameworks, and public views must, nevertheless, keep pace with the field's evolution. Psychedelic medications have the potential to revolutionize psychiatric therapy and deepen our understanding of brain function, but only if they can overcome these obstacles and welcome future developments.

REFERENCES

1. Nichols DE. Psychedelics. *Pharmacol Rev.*, 2016 Apr; 68(2): 264-355. doi: 10.1124/pr.115.011478. Erratum in: *Pharmacol Rev.*, 2016 Apr; 68(2): 356.
2. Raj P, Rauniyar S, Sapkale B. Psychedelic Drugs or Hallucinogens: Exploring Their Medicinal Potential. *Cureus.*, 2023 Nov 13; 15(11): e48719.
3. Psychiatry & the psychedelic drugs. Past, present & future. Rucker JJ, Iliff J, Nutt DJ. *Neuropharmacology*, 2018; 142: 200–218.
4. Rodríguez Arce JM, Winkelman MJ. Psychedelics, Sociality, and Human Evolution. *Front Psychol.*, 2021 Sep 29; 12: 729425.
5. Baggott M. J. Psychedelics and creativity: a review of the quantitative literature. *PeerJ PrePrints*, 2015; 3: e1202v1.
6. Doblin RE, Christiansen M, Jerome L, Burge B. The Past and Future of Psychedelic Science: An Introduction to This Issue. *J Psychoactive Drugs*, 2019 Apr-Jun; 51(2): 93-97.
7. Lee M, Shlain B: *Acid Dreams: The Complete History of LSD: The CIA, The Sixties, and Beyond.* New York, Grove Press, 1992.
8. Siegel JS, Daily JE, Perry DA, Nicol GE. Psychedelic Drug Legislative Reform and Legalization in the US. *JAMA Psychiatry*, 2023 Jan 1; 80(1): 77-83.
9. Vollenweider FX, Smallridge JW. Classic Psychedelic Drugs: Update on Biological Mechanisms. *Pharmacopsychiatry*, 2022 May; 55(3): 121-138.
10. Wojtas A, Gołombiowska K. Molecular and Medical Aspects of Psychedelics. *International Journal of Molecular Sciences*, 2024; 25(1): 241.
11. Classic psychedelic use is associated with reduced psychological distress and suicidality in the United States adult population. Hendricks PS, Thorne CB, Clark CB, Coombs DW, Johnson MW. *J Psychopharmacol*, 2015; 29: 280–288.
12. The neural basis of psychedelic action. Kwan AC, Olson DE, Preller KH, Roth BL. *Nat Neurosci.*, 2022; 25: 1407–1419.

13. Barber GS, Aaronson ST. The Emerging Field of Psychedelic Psychotherapy. *Curr Psychiatry Rep.*, 2022 Oct; 24(10): 583-590.
14. Schlag AK, Aday J, Salam I, Neill JC, Nutt DJ. Adverse effects of psychedelics: From anecdotes and misinformation to systematic science. *Journal of Psychopharmacology*, 2022; 36(3): 258-272.
15. Elsey JWB. Psychedelic drug use in healthy individuals: A review of benefits, costs, and implications for drug policy. *Drug Science, Policy and Law*, 2017; 3.
16. Vollenweider FX. Brain mechanisms of hallucinogens and entactogens. *Dialogues Clin Neurosci*, 2001 Dec; 3(4): 265-79.
17. Kwan AC, Olson DE, Preller KH, Roth BL. The neural basis of psychedelic action. *Nat Neurosci.*, 2022 Nov; 25(11): 1407-1419.
18. Winkelman MJ The Mechanisms of Psychedelic Visionary Experiences: Hypotheses from Evolutionary Psychology. *Front. Neurosci.*, 2017; 11: 539.
19. Dohmatob E, Dumas G, Bzdok D. Dark control: The default mode network as a reinforcement learning agent. *Hum Brain Mapp.*, 2020 Aug 15; 41(12): 3318-3341.
20. Zorumski CF, Izumi Y, Mennerick S. Ketamine: NMDA Receptors and Beyond. *J Neurosci.*, 2016 Nov 2; 36(44): 11158-11164.
21. Ly C, Greb AC, Cameron LP, Wong JM, Barragan EV, Wilson PC, Burbach KF, Soltanzadeh Zarandi S, Sood A, Paddy MR, Duim WC, Dennis MY, McAllister AK, Ori-McKenney KM, Gray JA, Olson DE. Psychedelics Promote Structural and Functional Neural Plasticity. *Cell Rep.*, 2018 Jun 12; 23(11): 3170-3182.
22. Sayin, Umit. A Comparative Review of the Neuro-Psychopharmacology of Hallucinogen-Induced Altered States of Consciousness: The Uniqueness of Some Hallucinogens. *Neuro Quantology*, 2012; 10.
23. Hysek CM, Schmid Y, Simmler LD, Domes G, Heinrichs M, Eisenegger C, Preller KH, Quednow BB, Liechti ME. MDMA enhances emotional empathy and prosocial behavior. *Soc Cogn Affect Neurosci.*, 2014 Nov; 9(11): 1645-52.
24. Halberstadt AL, Geyer MA. Effect of Hallucinogens on Unconditioned Behavior. *Curr Top Behav Neurosci.*, 2018; 36: 159-199.
25. Lear MK, Smith SM, Pilecki B, Stauffer CS, Luoma JB. Social anxiety and MDMA-assisted therapy investigation: a novel clinical trial protocol. *Front Psychiatry.*, 2023 Jul 14; 14: 1083354.
26. Lyubomirsky, S. Toward a New Science of Psychedelic Social Psychology: The Effects of MDMA (Ecstasy) on Social Connection. *Perspectives on Psychological Science*, 2022; 17(5): 1234-1257.
27. Krediet E, Bostoen T, Breeksema J, van Schagen A, Passie T, Vermetten E. Reviewing the Potential of Psychedelics for the Treatment of PTSD. *Int J Neuropsychopharmacol.*, 2020 Jun 24; 23(6): 385-400.
28. Sjöström DK, Claesdotter-Knutsson E, Kajonius PJ. Personality traits explain the relationship between psychedelic use and less depression in a comparative study. *Sci Rep.*, 2024 May 3; 14(1): 10195.
29. Nour, Matthew & Evans, Lisa & Carhart-Harris, Robin. Psychedelics, Personality and Political Perspectives. *Journal of Psychoactive Drugs*, 2017; 49: 1-10.
30. Bălăeț M. Psychedelic Cognition-The Unreached Frontier of Psychedelic Science. *Front Neurosci.*, 2022 Mar 15; 16: 832375.
31. Barber GS, Aaronson ST. The Emerging Field of Psychedelic Psychotherapy. *Curr Psychiatry Rep.*, 2022 Oct; 24(10): 583-590.
32. Davis AK, Barrett FS, May DG, et al. Effects of psilocybin-assisted therapy on major depressive disorder: a randomized clinical trial. *JAMA Psychiat.*, 2021; 78(5): 481-489.
33. Hendricks PS, Thorne CB, Clark CB, Coombs DW, Johnson MW. Classic psychedelic use is associated with reduced psychological distress and suicidality in the United States adult population, 2015; 0(0).
34. Ledwos N, Rodas JD, Husain MI, Feusner JD, Castle DJ. Therapeutic uses of psychedelics for eating disorders and body dysmorphic disorder. *J Psychopharmacol.*, 2023 Jan; 37(1): 3-13.
35. de Vos CMH, Mason NL, Kuypers KPC. Psychedelics and Neuroplasticity: A Systematic Review Unraveling the Biological Underpinnings of Psychedelics. *Front Psychiatry.*, 2021 Sep 10; 12: 724606.
36. Pilecki, B., Luoma, J.B., Bathje, G.J. *et al.* Ethical and legal issues in psychedelic harm reduction and integration therapy. *Harm Reduct J.*, 2021; 18: 40.
37. Azevedo N, Oliveira Da Silva M, Madeira L. Ethics of Psychedelic Use in Psychiatry and Beyond—Drawing upon Legal, Social and Clinical Challenges. *Philosophies*, 2023; 8(5): 76.
38. Viña, Sean. Stigma, Psychedelics Use, and the Risk of Reduced Formal Mental Health Care. *Stigma and Health*, 2024.
39. Schlag AK, Aday J, Salam I, Neill JC, Nutt DJ. Adverse effects of psychedelics: From anecdotes and misinformation to systematic science. *J Psychopharmacol*, 2022 Mar; 36(3): 258-272.
40. van Elk M, Fried EI. History repeating: guidelines to address common problems in psychedelic science. *Ther Adv Psychopharmacol*, 2023 Sep 25; 13: 20451253231198466.
41. Zaretsky TG, Jagodnik KM, Barsic R, Antonio JH, Bonanno PA, MacLeod C, Pierce C, Carney H, Morrison MT, Saylor C, Danias G, Lepow L, Yehuda R. The Psychedelic Future of Post-Traumatic Stress Disorder Treatment. *Curr Neuropharmacol.*, 2024; 22(4): 636-735.
42. Acero VP, Cribas ES, Browne KD, Rivellini O, Burrell JC, O'Donnell JC, Das S, Cullen DK. Bedside to bench: the outlook for psychedelic

- research. *Front Pharmacol.*, 2023 Oct 2; 14: 1240295.
43. Kelly JR, Gillan CM, Prenderville J, Kelly C, Harkin A, Clarke G, O'Keane V. Psychedelic Therapy's Transdiagnostic Effects: A Research Domain Criteria (RDoC) Perspective. *Front Psychiatry.*, 2021 Dec 17; 12: 800072.
 44. Banushi B, Polito V. A Comprehensive Review of the Current Status of the Cellular Neurobiology of Psychedelics. *Biology.*, 2023; 12(11): 1380.
 45. Olson, David. The Subjective Effects of Psychedelics May Not Be Necessary for Their Enduring Therapeutic Effects. *ACS Pharmacology & Translational Science*, 2020.