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PSYCHEDELIC RENAISSANCE IN PSYCHIATRY: EMERGING EVIDENCE FOR PSILOCYBIN, KETAMINE, AND MDMA IN MENTAL HEALTH TREATMENT

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ABSTRACT

Psychedelics (serotonergic hallucinogens) are potent psychoactive drugs that impact many cognitive functions and change mood and perception. They don't cause addiction or dependence and are generally regarded as physically harmless. The increasing prevalence of mental health conditions such as anxiety, depression, and post-traumatic stress disorder (PTSD) throughout the world highlights the critical need for faster-acting and more efficient therapies.[1] Interest in psychedelic pharmacology has increased recently, especially in relation to the medicinal potential of psilocybin, ketamine, and 3,4-methylenedioxymethamphetamine (MDMA). These drugs, which were once disregarded because of social and legal restrictions, are currently undergoing thorough clinical trials and have shown encouraging results in lowering the symptoms of anxiety, depression, and trauma-related disorders that are resistant to therapy. Psilocybin, ketamine, and MDMA's distinct pharmacological effects and potential to revolutionize psychiatric treatment paradigms are examined in this review along with their mechanisms of action, clinical efficacy, and safety profiles. When used in controlled, therapeutic settings, both compounds can promote long-term psychological healing and provide quick symptom relief, even though they work through different neural pathways, such as serotonin receptor agonism, NMDA receptor antagonism, and improved emotional processing. Although there are still issues with accessibility, long-term safety, and ethical issues, new research makes psychedelic-assisted therapy an intriguing new avenue for mental health treatment.[2]

KEYWORDS: MDMA, psilocybin, ketamine, LSD, psychedelics, and hallucinogens.

INTRODUCTION

Psychedelic drugs (a neologism combining the terms "psyche" and "Delon") relate to the class of drugs in question and mean "mind-revealing." Since "hallucinogens" may be deceptive in emphasizing these substances' hallucinogenic qualities, I prefer to use this name. I use the term "psychedelics" to describe substances that have significant serotonin 2A receptor agonist qualities and can significantly and uniquely alter consciousness.[3] LSD is the quintessential or "reference-standard" psychedelic. A significant public health issue, psychiatric problems impact approximately 350 million individuals globally and impose social and economic expenses. Despite immense efforts to identify pathophysiological factors, our knowledge of psychiatric disorders and how to treat them is still lacking. Research on psychedelics is reviving in the clinical and research areas after an extended lead due to laws that placed these substances under a restrictive regulated drug schedule.[4] This is particularly true when it comes to their potential therapeutic use in treating mental illnesses. Since the 1960s, hallucinogenic substances have generally been divided into two categories: "dissociative anesthetics" and "serotonergic classic hallucinogens," sometimes known as "psychedelics." By functioning as agonists of the 5-HT2A receptor, classic hallucinogens mainly use the 5-HT system to produce their pharmacological effects.[5]

Ketamine and other "dissociative anesthetics," on the other hand, are however, classified as hallucinogens even though they are thought to function on the glutamatergic system rather than the 5-HT system and do not cause the same stated "trip" as psychedelics.[6] Ketamine has been shown to be effective in treating resistant depression in both humans and experimental animals in several research studies conducted in the past ten years. Additionally, studies have indicated that psilocybin and LSD may have antidepressant and mood-modulating effects, respectively, and that they may alter functional brain connectivity. Entactogens are other substances, such as 3,4-methylenedioxymethamphetamine (MDMA). Although they have psychotropic effects, their mode of action differs from that of hallucinogens. In addition to being effective in treating PTSD, MDMA has been shown to improve sociability in both people and animals.[7]

BACKGROUND AND HISTORY: PSYCHEDELICS' ASCENT AND DECLINE IN PSYCHIATRY

Psychedelics' Ascent in Psychiatry (1940s–1960s)

Early Discovery and Exploration (1930s–1940s)

- **The discovery of LSD:** At Sandoz Pharmaceuticals, Swiss chemist **Albert Hofmann** created **lysergic acid diethylamide (LSD**) for the first time in 1938. It wasn't until 1943, however, that its psychedelic qualities were identified after Hofmann inadvertently consumed a small quantity and felt its effects. This incident turned into one of the pivotal events in the history of psychedelics.
- **Research on Psychedelics Begins:** Scientists, notably **Stanley Krippner** and **Timothy Leary of Harvard**, started testing LSD and other drugs like **mescaline** and **psilocybin** for their potential as medicines in the 1940s and 1950s.[8]

The 1950s–1960s were the Golden Age

- **Psychotherapy and Mental Health Treatment:** Psychedelics were widely used by **psychiatrists** to treat a variety of mental health conditions in the 1950s and 1960s, such as **schizophrenia, addiction, anxiety, and depression**. Numerous early clinical trials were encouraging, and thousands of research studies were carried out, mostly in the US and Europe.[9]

- **LSD** was used in both "psychedelic therapy" (which entailed higher dosages intended to produce deep experiences) and "psycholytic therapy," which involved patients taking minimal doses of the drug while interacting with a therapist.[10]
- **The Harvard Psilocybin Project (1960s):** At Harvard University, Timothy Leary and **Richard Alpert** (later Ram Dass) began psilocybin research. They conducted experiments to see how the medication would affect awareness and behavior, which sparked curiosity in its possible medicinal applications.[11]
- **The Rise of Popular Culture:** Psychedelics became embedded in the cultural zeitgeist as the 1960s unfolded. Widespread public interest in the possibilities of LSD and other substances was caused by the counterculture movement, which was personified by individuals like **Ken Kesey** and The **Merry Pranksters**. Even the Beatles' experiments with LSD contributed to the drug's widespread acceptance.[12]

The Fall (1970s): Psychedelics in Psychiatry

The Backlash and the Counterculture

- Psychedelics were widely associated with the **counterculture** and **anti-establishment movement** by the late 1960s. A movement for regulation and, ultimately, criminalization of these substances resulted from this association as well as growing worries about public health and safety.[13]
- The increasing use of psychedelics by young people was viewed by the American government and conservative social groups as a danger to social stability and order. This caused a **moral panic** and led to requests for strict regulation.[14]

The Controlled Substances Act (1970)

- LSD, psilocybin, mescaline, and other psychedelics were categorized under Schedule I, which is a category for drugs judged to have a high potential for abuse and no recognized medical use, in response to the growing popularity of psychedelics and their viewed threat to public order. In effect, this stopped research and significantly limited the use of psychedelics in clinical settings.[15]

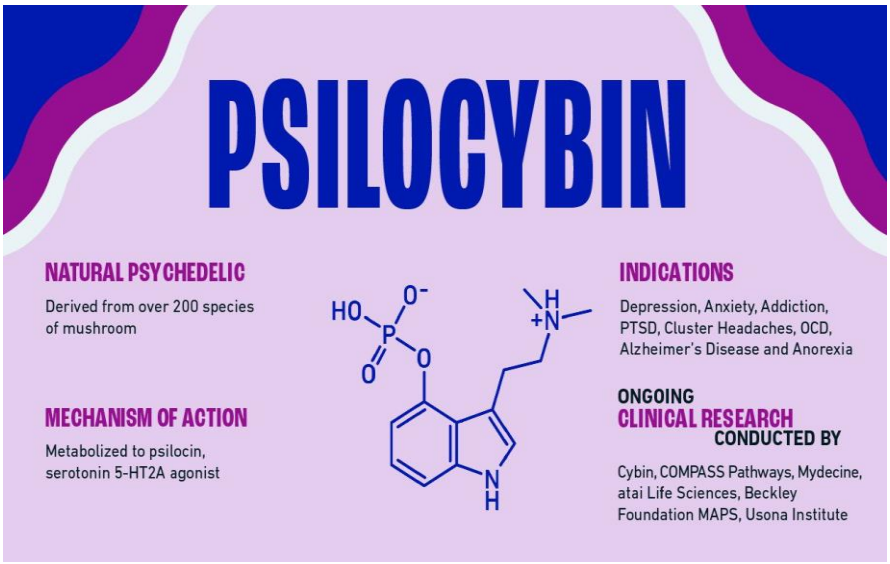
Modern Research (2000s–Present)

- **The Johns Hopkins Center** for Psychedelic and **Consciousness Study** was founded in 2019 after **Johns Hopkins University** returned to the field of **psychedelic** study in the early 2000s.
- According to **research,** drugs like **psilocybin** and **MDMA** can significantly improve mental health, including **substance use disorders**, **anxiety, and depression** that is resistant to treatment.[16]
- **Fast-Tracking by the FDA:** Both **psilocybin** (for depression) and **MDMA** (for PTSD) have received **breakthrough** therapy designations from the FDA in recent years, hastening the licensing process for their possible medical applications.[17]

1. PSILOCYBIN

More than 200 different species of mushrooms, including Psilocybe cubensis, Psilocybe cyanescens, and Psilocybe mexicana, generate the naturally occurring hallucinogenic psilocybin. Although it has been illegal in the majority of developed nations for almost fifty years, it has recently been decriminalized in a few of US cities, including Denver, Colorado. Psilocybin belongs to a class of chemicals known as indolamines, which also contains more prevalent endogenous neurotransmitters like serotonin and DMT and LSD (see below).[18] Its metabolite, psilocin, is produced when it is dephosphorylated. Because of its structural resemblance to serotonin, it can readily activate the serotonin 5-

HT2A receptor and penetrate the blood-brain barrier. It is believed that the hallucinogenic effects of psilocybin are caused by this receptor activation. Increased perception, bright imagery, complex hallucinations, and temporal distortions are some examples of these dose-dependent effects.[19] Many ideas explain how psilocybin causes psychedelic effects in the brain, such as changes in thalamic gating and increases in prefrontal cortex activity.



There is currently no approved use of psilocybin to treat any illnesses. Yet it is being tested for several conditions, such as:

- Alzheimer's disease
- depression
- anxiety
- PTSD
- OCD
- CLUSTER headaches

One of the first studies to directly compare the antidepressant effects of a psychedelic and an antidepressant—in this case, the selective serotonin reuptake inhibitor (SSRI) escitalopram—was conducted with psilocybin in May 2021. Researchers at the Centre for Psychedelic Research at Imperial College London organized this historic investigation.[20]

This demonstrated that psilocybin could complement the SSRI's antidepressant effects. Researchers at the Centre for Psychedelic Research at Imperial College London organized this historic investigation.

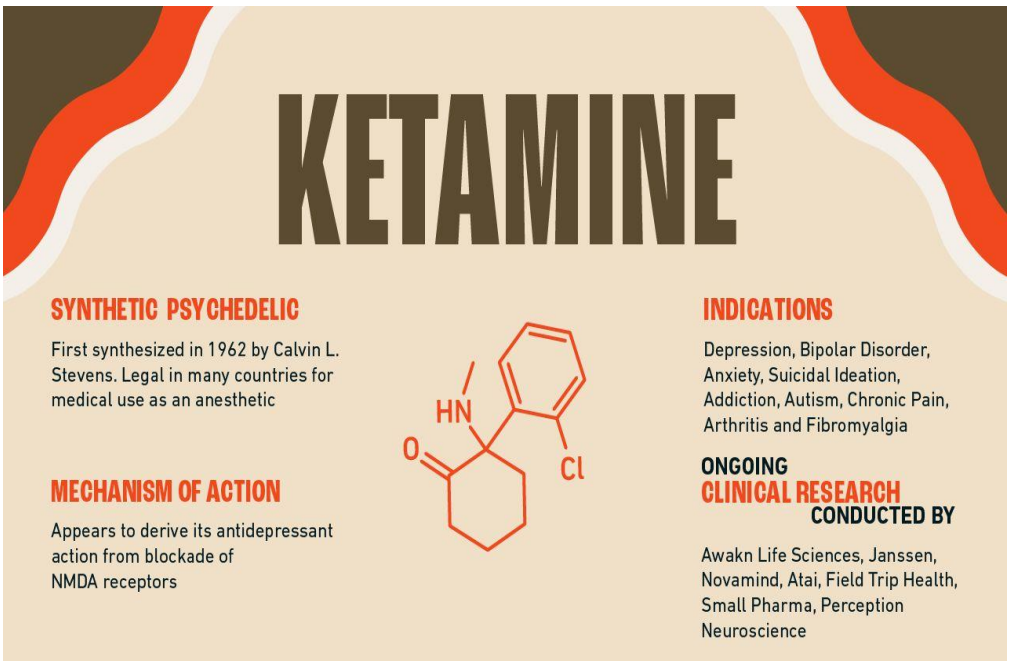
This demonstrated that psilocybin could complement the SSRI's antidepressant effects. Although the research only included 59 participants, it was not sufficiently powered to identify a significant difference, despite the findings suggesting that psilocybin may have a deeper and faster effect.[21]

2. KETAMINE

The first ketamine was created by Calvin L. Stevens in 1962. For several reasons, ketamine differs slightly from the other compounds on this list:

1. Although subanesthetic dosages can have psychedelic effects, its primary function is as an anesthetic.

2. Because of its anesthetic qualities, it can be legally prescribed. Ketamine has been approved as a medication for anesthesia in both human and veterinary medicine in more than 60 countries.
3. It should come as no surprise that there are more ongoing trials for ketamine than any other psychedelic drug, with over 100 listed on the EU Clinical Trials Register alone. This is because ketamine is a recognized prescription and confronts significantly fewer legal barriers than some of the other chemicals on our list.[22]
4. This psychedelic is the first to be authorized for the treatment of mental illnesses. In 2019, the FDA granted a license for Janssen Pharmaceuticals, Inc.'s ketamine-derived nasal spray Spravato to treat treatment-resistant depression.
5. Ketamine is a racemic mixture, which is a combination of two chemical structures that are mirror images of one another. Esketamine and arketamine are the names of these two substances.
6. Esketamine, the only ingredient in Spravato, was chosen as the main subject of research because it more strongly stimulates NMDA receptors. However, arketamine is also being researched and may have a longer half-life and less potential for addiction.[23]



The precise mode of action of ketamine is unknown. Blockade of neuronal receptors known as NMDA receptors seems to be the source of its antidepressant activity, but selective block of NMDA receptors on GABAergic interneurons and inhibition of AMPA receptors may also be involved.

Ketamine, the only psychedelic with a license, is being researched for a few conditions, such as

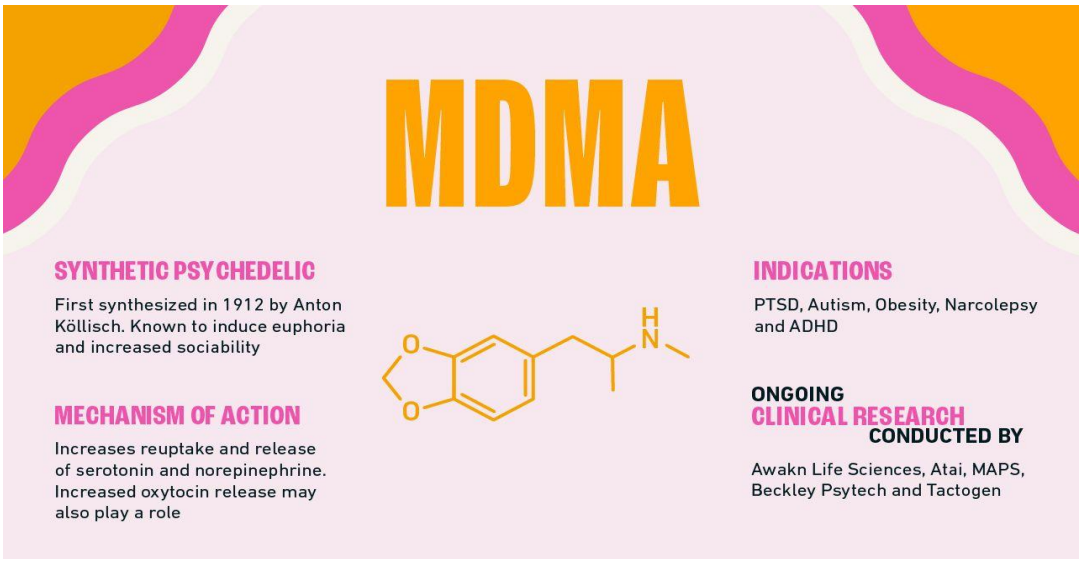
- Depression
- Bipolar disorder
- anxiety
- Suicidal thoughts
- Addiction
- Autism spectrum disorder[24]

3. 3,4-METHYLENEDIOXYMETHAMPHETAMINE (MDMA)

Anton Kollisch synthesized MDMA for the first time in 1912. Increased sociability and euphoria are known side effects. Pharmacologist David Nichols called the medicine an "entactogen" (meaning "producing a touching within") due to its pro-social effects.[25] Ecstasy, which is MDMA that is frequently mixed with other substances, has been used recreationally by clubbers and ravers for decades.

Although MDMA is not a traditional psychedelic and does not directly cause hallucinations, it can produce similar effects to psilocybin and LSD, such as depersonalization and changed perception and thinking. Its chemical structure is similar to that of methamphetamine. Although increased oxytocin release could possibly play a role, it is believed to work by boosting the reuptake and release of serotonin, dopamine, and norepinephrine.[26]

In 2017, the FDA granted MDMA Breakthrough Therapy Designation, despite its image as a party drug. The FDA granted the Multidisciplinary Association for Psychedelic Studies (MAPS) this classification to study the use of MDMA in treating PTSD, allowing the FDA to expedite several aspects of the clinical trials process.



The following organizations are carrying out ongoing research:

- Awakn Life Sciences
- Atai
- MAPS
- Beckley Psytech
- Tatogen

MAPS published the findings of their MDMA clinical trial for PTSD earlier this year. Rounds of psychotherapy were combined with MDMA in this trial. 32% of patients who received a placebo were no longer eligible for a PTSD diagnosis following three sessions of this treatment. However, this rate skyrocketed to 67% for individuals who had received MDMA.[27]

Jennifer Mitchell of the University of California, San Francisco, who was the lead author of the report that detailed MAPS's success, stated that the "unique ability of MDMA to raise compassion and understanding while tamping down fear is probably what enables it to be so effective."

Patients with the dissociative subtype of PTSD seem to benefit from it the most. Because of the trauma that led to their PTSD, members in this group frequently display depersonalization. According to Mitchell, MDMA can assist those who have mentally detached themselves from a trauma in facing and overcoming it if they have the correct attitude and an environment that is supportive enough.[28]

CLINICAL EVIDENCE AND TRIALS

1. PSILOCYBIN

Obsessive–compulsive disorder

In a double-blind study, nine subjects (two women and seven men) with obsessive-compulsive disorder (OCD) and at least one serotonin reuptake inhibitor treatment failure (mean 3.4 ± 1.9 treatment failures) were given up to four doses of psilocybin orally (one dose per test session) [Moreno et al. 2006]. Psilocybin was given in three different doses: low (100 µg/kg), medium (200 µg/kg), and high (300 µg/kg). A very low dose (25 µg/kg) was added at random and in a double-blind fashion at any point following the initial dose (100 µg/kg). The subjects' mean baseline Yale–Brown Obsessive–Compulsive Scale (YBOCS) score was 24.1 ± 5.9, and they satisfied the DSM-IV criteria for OCD. Prior to drug consumption, as well as four, eight-, and twenty-four-hours following ingestion, YBOCS and Visual Analog Scales (VAS) scores were obtained to assess the overall severity of OCD symptoms.

Six subjects got all doses, seven got the very low and medium levels, and all subjects got the low dose. In one or more sessions, all individuals showed YBOCS score reductions ranging from 23% to 100%. Furthermore, after taking at least one psilocybin dose, 88.9% of participants sustained a decrease in YBOCS scores of at least 25%, and 66.7% maintained a fall of at least 50% after 24 hours. One volunteer reported improvement during the 6-month follow-up, and two individuals indicated improvement over the next week. All individuals tolerated psilocybin well, and VAS scores decreased during the trial.[29]

Anxiety associated with advanced-stage cancer

The safety and possible therapeutic benefits of psilocybin in treating psychological distress related to the existential crisis of terminal illness were evaluated in a double-blind, randomized, placebo-controlled research study [Grob et al. 2011]. Oral psilocybin (0.2 mg/kg) or the active placebo niacin (250 mg) was administered in a double-blind manner to twelve subjects (11 women) with advanced-stage cancer who were also diagnosed with acute stress disorder, generalized anxiety disorder, anxiety disorder caused by cancer, or adjustment disorder with anxiety according to the DSM-IV. Each experimental session was preceded by, followed by, and two weeks following the administration of the Beck Depression Inventory (BDI), the Profile of Mood States (POMS), and the State-Trait Anxiety Inventory (STAI). For six months following the last session, the BDI, POMS, and STAI were given once more at monthly intervals.

Eleven of the twelve participants finished the four-month follow-up, eight finished the six-month follow-up, and all twelve completed the three-month follow-up. Two participants passed away from their cancer during the trial, while two others became too sick to continue. At the 1- and 3-month follow-ups, there were notable declines in STAI scores, and at the 6-month follow-up, there were notable declines in BDI scores. All patients tolerated psilocybin well, and no

discernible alterations were seen in POMS ratings. Ten of the twelve participants had passed away from their cancer by the time the study was submitted in 2010.[30]

Tobacco dependence

The effects of moderate (20 mg/70 kg) and high (30 mg/70 kg) dosages of psilocybin were evaluated in an open-label trial in 15 nicotine-dependent smokers (mean age of 51 years; ten men and five women) [Johnson et al. 2014]. In addition to smoking an average of 19 cigarettes a day for an average of 31 years, participants had an average of six prior lifetime quit attempts. Psilocybin was administered to volunteers during weeks five (moderate dosage), seven (high dose), and thirteen (high dose) of a 15-week cognitive behavioral therapy smoking cessation program (participants were allowed to repeat the moderate dose on sessions two and three). Between the 30 days before study intake and the 6 months following the first psilocybin session (at week 5 of treatment), changes in the average number of cigarettes consumed each day were compared. Urinary cotinine levels and exhaled carbon monoxide (CO) were measured at intake, weekly during the intervention, and at the 6-month follow-up to gauge recent smoking.[31]

Every participant finished the research. At the 6-month follow-up, 80% (12 of 15) of individuals were abstinent based on the Timeline Follow-Back (TLFB) and biomarker data (breath CO, urine cotinine). Significant decreases in breath CO levels, urine cotinine, and self-reported daily smoking were noted in the entire sample from intake to the 6-month follow-up. Additionally, yearning [measured by the Smoking Abstinence Self-Efficacy scale (SASE)] and temptation to smoke [measured by the Questionnaire on Smoking Urges (QSU)] were considerably decreased at all time periods.[32] Confidence to abstain (SASE) increased considerably from the time of intake until the 6-month follow-up, while withdrawal scores (measured by the Wisconsin Smoking Withdrawal Scale (WSWS)) peaked one week after psilocybin and then sharply declined over the course of the 6-month follow-up. There were no notable side effects noted during psilocybin sessions.[33]

2. KETAMINE

For nearly twenty years, ketamine's antidepressant qualities have been recognized . Subanesthetic doses of ketamine (0.5 mg/kg, infused over 40 min) have been shown in a number of placebo-controlled clinical trials to be effective in treating depression and suicidal thoughts in MDD patients who are not responding to selective serotonin reuptake inhibitors.[34] Ketamine's quick therapeutic onset, which may be measured at 4 hours, and its effectiveness for more than a week following a single infusion are what distinguish it in depressed patients. At one day following therapy, single ketamine infusions are linked to a therapeutic response rate of 50%–70%.[35]

Although the overall response rate seems to be equivalent to single-dose infusions, new data have indicated that repeated treatments have the capacity to maintain an antidepressant effect. Repeated ketamine injections reduced suicidal thoughts by 69% in open-label research. Ketamine does, however, carry a high risk of addiction, and prolonged use is linked to notable bladder and neurological toxicity. Not enough is currently known about the physiological processes behind ketamine's induction and maintenance of long-lasting effects in humans to develop comparable medications with increased safety and durability. As previously mentioned, ketamine's antidepressant action has long been linked to mTORC1 activation and NMDAR antagonistic interactions.[36]

It appears that ketamine's mechanism of action as an antidepressant is more complicated than its action on NMDARs, as other NMDAR antagonists have not demonstrated clinical efficacy comparable to ketamine for MDD Unexpected

outcomes have recently been obtained from clinical trials evaluating some of the predictions made by NMDAR-based models.[37] A recent clinical study, for instance, showed that peripheral coadministration of rapamycin to treatment-resistant MDD patients improved rather than inhibited the antidepressant effect of ketamine about the mTORC1 pathway, indicating a more intricate interaction between these medications in humans. However, in deceased cases of MDD, the mTORC1 signaling pathway is downregulated in the PFC and hippocampal regions which is consistent with the signaling system's relevance for MDD treatment. As may be expected given the variety of ketamine's pharmacological targets, other signaling systems, including opioid receptors may potentially be involved. We may be able to improve ketamine therapy and create new treatments based on its mechanism by changing our viewpoint from receptor-based mechanisms to a neural-systems-level examination.[38]

The commonalities between ketamine and other psychedelic-assisted medicines are only now being mapped out by clinical trials. The significance of the conscious subjective experience (usually referred to as "dissociation") that patients report during the subanesthetic ketamine infusion regimen is still up for dispute.

Studies have suggested that conscious awareness and sensory processing are essential for ketamine's antidepressant impact and have connected the drug's dissociative effect to its antidepressant effectiveness However, some clinical evidence indicates that dissociation is neither sufficient nor necessary to explain ketamine's effectiveness. The newly popular technique of ketamine-assisted psychotherapy may be functionally and mechanistically different from ketamine antidepressant therapy in a medicalized setting.[39]

3. 3,4-METHYLENEDIOXYMETHAMPHETAMINE (MDMA)

There was an assumption that MDMA "secured the therapeutic alliance by inviting self-disclosure and enhancing trust" when it was first used clinically in the 1970s. Following this, several short, uncontrolled trials revealed that MDMA was a useful supplement to psychotherapy, particularly for individuals with anxiety. When MDMA was added to the DEA Schedule 1 list in 1985, research was put on hold, and it wasn't until the middle of the 1990s that scientists began evaluating the compound's potential for therapeutic Use.[40]

Shortly after, a Phase 1 dose-finding and safety research was carried out in patients who had previously used MDMA, which revealed that a range of dosages (0.25-1.0 mg/kg, p.o.) could be administered safely with few adverse effects. According to more recent data, MDMA frequently causes mild to moderate side effects that go away on their own without help and quickly after treatment, such as headache, tooth grinding, clenching of the jaw, nausea, fatigue, dizziness, and lack of appetite). (Psychological Effects of Methylenedioxymethamphetamine (MDMA) When Administered to Healthy Volunteers, 2020) More Phase 1 data are presently being gathered. Although MDMA's possibly harmful effects had previously raised concerns, the study that revealed widespread dopaminergic and serotoninrgic neurotoxicity in nonhuman primates was later retracted due to serious flaws.[41]

According to preliminary human research, MDMA may be especially helpful in promoting emotional processing and, consequently, healing in PTSD patients. According to the first randomized and controlled pilot trial, PTSD symptoms could be significantly and permanently reduced with two or three MDMA injections.Perhaps most intriguingly, MDMA's effects on PTSD symptoms were not only strong but also seemed to endure for at least a year following therapy.

There are currently about a dozen Phase 2 studies that use MDMA in populations with severe, treatment-resistant PTSD, and the outcomes are typically positive. The FDA granted MDMA Breakthrough Therapy status for treating PTSD thanks to pooled analysis from six of these Phase 2 clinical trials. This also made it easier to start a Phase 3 clinical trial (Multidisciplinary Association for Psychedelic Studies, 2018). For the treatment of severe PTSD, a Phase 3 randomized, double-blind, placebo-controlled trial of MDMA-assisted psychotherapy is presently underway (Multi-Site Phase 3 Trial of MDMA-Assisted Psychotherapy for PTSD, 2020). According to J. Mitchell's unpublished data, MDMA significantly and robustly reduces several of the classic symptoms of PTSD, according to the open-label lead-in data from this Phase 3 research.[42]

The early trial data indicates that MDMA, when combined with psychotherapy, may be a successful therapy for several complex treatment populations, though we still need to wait for final analyses and the publication of Phase 3 data. This supports the idea that psychedelic medications could be quick, long-lasting, innovative treatments for mental health conditions.

According to recent research, MDMA may also be helpful in other therapeutic populations, such as those with alcohol use disorder and autistic spectrum disorder. A Phase 2 clinical trial aimed at assessing changes in alcohol use disorder is presently in progress (Bristol Imperial MDMA in Alcoholism Study, 2020), and safety and tolerability findings from a pilot population have already been published. Even though it has been demonstrated that therapeutic facilitation has a significant impact on treatment outcomes, further study is still required to identify the most effective therapeutic interaction for various clinical groups. Additionally, despite the fact that context is recognized to have a significant role in the therapeutic effects of psychedelics, not much research has been done to far to fully understand the complex relationship between setting and MDMA therapy outcomes.[43]

SAFETY AND ETHICAL CONSIDERATIONS IN PSYCHEDELIC PSYCHIATRY

A revolution in mental health care has been spurred by the renewed interest in psychedelic-assisted psychotherapy. In clinical trials, drugs like psilocybin, ketamine, and MDMA are demonstrating encouraging outcomes for disorders like addiction, PTSD, and depression. These advancements, however, bring up significant ethical and safety issues that need to direct how they are included in mental health treatment.[44]

Clinical Potential and Emerging Use

Psilocybin, which comes from psychedelic mushrooms, has shown promise in the treatment of substance use disorders, major depressive disorder, and end-of-life anxiety.

Ketamine, which is already FDA-approved in its esketamine variant, gives quick relief from suicidal thoughts and depression that is resistant to treatment.

MDMA is on the verge of FDA approval and has demonstrated exceptional efficacy in treating PTSD when combined with psychotherapy.[45]

Safety Considerations

- **Psilocybin** may cause temporary anxiety, nausea, or perceptual disturbances.
- **Ketamine** has a higher risk profile, including **dissociation**, bladder toxicity, and **addictive potential** with unsupervised use.

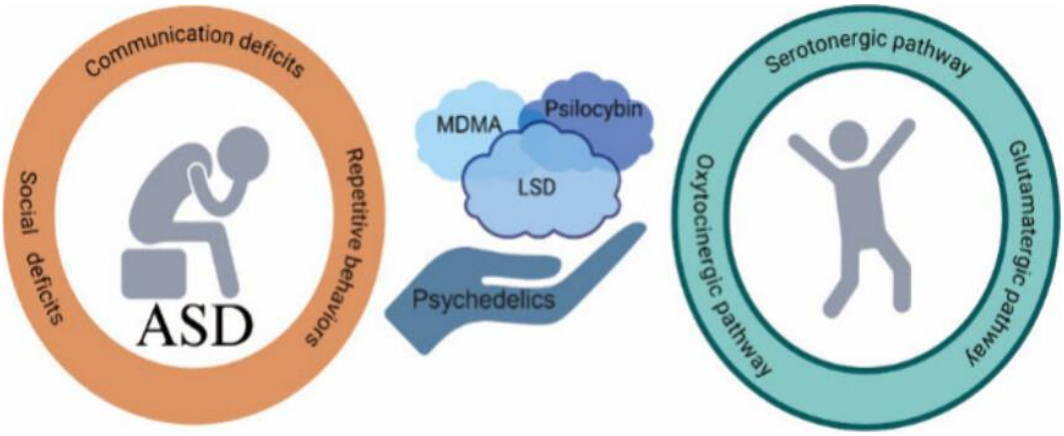
- **MDMA** is not adequately handled, it can lead to serotonin-related problems, emotional overload, and cardiovascular stress.

Additionally, all three substances can lead to **intense psychological experiences**, which, without adequate preparation and support, could worsen mental health symptoms in vulnerable individuals.[46]

Ethical Considerations

The ethical deployment of psychedelic therapy requires thoughtful attention to several key issues:

- **Informed Consent**: Patients must understand the nature of the experience, the experimental status of the treatments, and the potential for emotional discomfort or trauma resurfacing.
- **Therapist-Patient Boundaries**: Altered states can increase emotional vulnerability and suggestibility, creating risks for boundary violations. Proper therapist training and supervision are essential.
- **Equity and Access**: Psychedelic treatments are expensive and often not covered by insurance, raising concerns about health disparities. Efforts must ensure access for underrepresented and low-income populations.
- **Cultural Respect**: Psilocybin's traditional use in Indigenous communities must be acknowledged to avoid cultural appropriation. Ethical research and practice should involve collaboration with these communities.
- **Commercialization Risks**: The growing commercial interest may lead to overhyped expectations and insufficient safeguards in for-profit clinics.[47]



DOES MICRODOSING WORK?

When used at moderate to lower than typical dosages, psychedelics have been effectively used to treat anxiety and other mental health conditions, such as serious depression. With these smaller, sporadic dosages (also known as "microdosing"), users have reported a longer-lasting impact with minimal to no hallucinatory effects. Usually, one-tenth of the "full" active quantity is used in microdosing. Nevertheless, the effectiveness or duration of the therapeutic effects are not well supported by scientific research or clinical trials.

Animal models were used to investigate microdosing when low doses of DMT were administered for an extended period. Researchers found that following a single high dose of the psychedelic drug differed significantly from employing a regular low-dose schedule in terms of behavioral and cellular assay readouts. Based on these findings, the researchers concluded that microdosing DMT resulted in "enhanced fear extinction learning," an antidepressant-like effect that did not impact the animals' social interactions or working memory.[48]

FURTHER DIRECTION IN PSYCHEDELIC PSYCHIATRY

We can now treat mental health conditions in novel ways due to a fresh perspective on psychedelic substances.

Our prospects of creating novel medications to treat and possibly cure certain neuropsychiatric and neurodegenerative illnesses are increasing along with the number of psychedelic businesses, which are a result of the optimism generated by the initial wave of traditional psychedelic research.[49] Sylvia Plath, an American poet, famously said: "I was depressed by the silence." The quiet of silence wasn't it. I was the one who was silent. When barriers of quiet are shattered, the possibilities are limitless.[50]

CONCLUSION

Psychedelics offer a fresh and perhaps revolutionary way to help people with ASD behave more prosaically. Psychedelics like LSD, psilocybin, and MDMA may provide special advantages for improved social interaction, empathy, and emotional identification in people with ASD by modifying the serotonergic system, encouraging neuroplasticity, and boosting emotional connectivity.

But there are several obstacles in the way of clinical acceptance, such as safety hazards, ethical issues, and the requirement for individualized strategies. Future studies should concentrate on determining the neurobiological processes behind the effects of psychedelics, creating therapeutic regimens specific to the requirements of people with ASD, and proving the safety and effectiveness of these drugs through thorough clinical trials. If effective, psychedelic-assisted therapy may usher in a new era of ASD treatment that provides people with more emotional stability, social connectedness, and a higher standard of living.

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