

# Psychedelic Drugs as a Multidisciplinary Controversy

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## Psychedelic Drugs as a Multidisciplinary Controversy

Controversy surrounding psychedelic drugs is an interdisciplinary issue that spans across legal, medical, anthropological, and religious fields. Classical psychedelics such as psilocybin, lysergic acid diethylamide (LSD), and mescaline were heavily researched and used as psychiatric treatments. While there were many flaws in the research methodologies and practices at the time, clinical trial data supports theories of clinical efficacy demonstrated by these drugs until they were classified as schedule I substances under the Comprehensive Drug Abuse Prevention and Control Act of 1970 by the FDA [1,2]. The halt in psychiatric research on psychedelic drugs became collateral damage to legislative backlash against growing rates of illicit consumption. +/-3,4-methylenedioxymethamphetamine (MDMA), another drug producing similar side effects to psilocybin and LSD, was banned shortly after. Human psychedelic research was put on pause until the early 1990s, but has since seen massive advancements.

### Cultural Impact

Public opinion has seen similar trends as well. Psychedelics reached peak popularity during the mid-twentieth century, with more people than ever experimenting with their effects. They became a hallmark symbol of the counterculture movement that fostered a blend of eastern spirituality, Indigenous rituals, and particularly the use of psychedelics. As the “hippie movement” spread, especially in opposition to the unfolding of the Vietnam War, the use and infamy of psychedelics followed suit [3]. Even after legislative action was taken, outlawing their use, they continued to be a symbol of this anti-culture, anti-capitalist movement. The messages being

transmitted portrayed the use of psychedelics as deviant behaviors associated with high crime rates, violence, and poor quality of living [4]. Public opinion at the time, and even in modern times, was heavily influenced by the agendas of mass media outlets and served as the primary source of education concerning the issue.

It has not been until recently that the dialogue surrounding psychedelics has shifted, and conversations surrounding their use have become more common to talk about publicly. In an article “Holiday Gift Guide 2021: Gifts for the Psychedelic Explorer”, Siebert claimed that 2020 was the year psychedelics transitioned from covert, underground use to becoming mainstream [5]. As evident by an entire holiday gift guide devoted to psychedelic paraphernalia, it seems as though the pendulum of public opinion has swung. Financial analysts are even recommending switching investments to “shroom stocks,” as they are surpassing the medical marijuana industry in terms of profitability [6].

### Neurological and Behavioral Effects

These substances are primarily serotonergic agonists acting in the limbic and cortical regions of the brain. They affect the serotonin (5-HT<sub>2A</sub>) pathways in the pre-frontal cortex (PFC), which is responsible for high-level cognitive processing and self-monitoring behaviors [7]. They are also responsible for changes in perception, self-awareness, beliefs, visual and auditory disturbances, and related to mystical/profound experiences [8]. There is also significantly reduced activity in default-mode network structures, as shown by human neuroimaging studies [9]. However, much is still unknown about the mechanism of behavioral changes that occur as a result of psychedelic drugs.

While these psychedelic drugs are highly regulated due to their supposed high potential for abuse and adverse side effects, common media outlets and peer-reviewed studies alike have both present evidence supporting the incorporation of psychedelics into medicine and daily life because they do not have the same potential for abuse as other schedule I drugs, have historically functioned as a means of enlightenment and spiritual healing, and have shown success in therapeutic settings with treatment-resistant conditions.

### **Different Addiction Profile and Side Effects**

It is well known that psychedelic and hallucinogenic drugs lack the same addiction profile that other recreational drugs possess, specifically other Schedule I drugs, giving them a lower potential for abuse. Historically speaking, the definition of abuse potential has shifted as theories of addiction have developed. Potential for abuse was historically defined by the presence of physical dependence and withdrawal, but has since shifted to looking at the behavioral effects of substance use and repeated self-administration <sup>[10]</sup>. This paradigmatic shift, brought about by new information and research, questions the stringent regulation placed on these substances. Based on a review of medical psilocybin, Johnson and colleagues recommended reducing psilocybin to a schedule IV classification, thus lowering the barriers to obtaining adequate treatment.

Psychedelic drugs are also not considered addictive substances because they operate on serotonergic receptors. Andersen et al. found that psychedelics like psilocybin show high levels of activity at 5-HT<sub>2a</sub>, 5-HT<sub>2c</sub>, and 5-HT<sub>1a/b</sub> receptors <sup>[11]</sup>. Psilocybin also has a low affinity for dopamine D<sub>2</sub> receptors <sup>[10]</sup>. LSD shows activity at dopaminergic receptors, as well as 5-HT<sub>6</sub> and 5-HT<sub>7</sub> receptors. With the strong influence of serotonergically

controlled behaviors, rather than dopamine in the brain, the reinforcing effects that contribute to addictive behaviors are negligible. Additionally, the effect of psilocybin and LSD on serotonin has also been tested by administering a 5-HT<sub>2a</sub> antagonist, ketanserin, which inhibits the mood-boosting effects of psilocybin and LSD <sup>[12]</sup>. This proves that by inhibiting serotonin activity in the brain, psilocybin and LSD activity are also inhibited.

Acting as a defense mechanism to intense, repeated serotonin activation, 5-HT<sub>2a</sub> receptors are downregulated and desensitized. Additionally the receptors decrease their affinity for 5-HT<sub>2a</sub> in the synapse, leading to decreased binding. Buchborn et al. found that this process, known as tachyphylaxis, produces near tolerance within 2-3 days of administration at high doses <sup>[13]</sup>. Unlike classically addictive substances, which generate dopaminergic sensitization that reinforces and escalates compulsive use, psychedelic-induced 5-HT<sub>2a</sub> downregulation diminishes the effect of subsequent doses. This creates the characteristic self-limiting pharmacological profile.

Another factor when considering potential for abuse is the level of dependence and withdrawal. While dependence is not formed, tolerance is developed rapidly to psilocybin and LSD. There is also little evidence of withdrawal <sup>[10, 14]</sup>. Since there is no dependence and intense craving sensations associated with consumption, the risk for addiction is minimal. In therapeutic programs where it would be used, it does not include prolonged daily administration as part of the treatment plan, so there would be little to no concern about developing tolerance.

Cognitive processes also help explain the lower potential for abuse of psychedelics. First, it is important to recognize that there is unpredictability in the individual's reaction to the drug. When it comes to the subjective experience of taking psychedelics, someone's reaction may not be consistent <sup>[15]</sup>. This

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variability makes it hard for researchers to control, with cognitive and emotional state having such a significant impact on reaction [16]. When talking with a renowned psychedelic researcher at John Hopkins, Allen wrote that two people taking the same dose in the same setting can have two opposite reactions.

Although in behaviorist models of operant conditioning, the inconsistent and variable reinforcement promotes higher response rates, this kind of unpredictability is not what drives an addict's behavior. Regular heroin or methamphetamine users, they are motivated by the potent recall of a euphoric experience. This memory of previous experiences drives repeated administration, chasing the same experience [17]. Without this memory and reinforcement affecting behavior, addiction is not likely to form.

With respect to harm to self and others, psilocybin and LSD present the lowest rates of harm to self and others. When looking at physical, cognitive, and social harm to self, psilocybin ranked last, with other Schedule I drugs like methamphetamine and crack cocaine presenting the most harm to self [18, 19]. However, as with any medication or substance in the body, mild side effects have been reported, including headache, nausea, and vomiting. Since it is a serotonin agonist, there is a risk of serotonin syndrome and potential interactions with other psychoactive substances [20]. The more severe risks, such as prolonged hallucinations and psychosis, can be eliminated by using them in a safe and controlled environment, such as in a therapeutic setting.

Cultural shifts with the onset of the counterculture movement in the 1960s and 1970s played a large role in limiting research and public opinion for the next two decades. With the Controlled Substances Act of 1970, attitudes toward psychedelics shifted toward more negative beliefs, although they continued to be used in underground settings. The information surrounding side effects, both

positive and negative, comes largely from word of mouth. There are forums on the internet with boards offering advice for things like affirmations to recite before a psilocybin-induced trip. Most of the profoundly negative stories surrounding bad trips have become urban legends spread through the grapevine and community of users. Similarly, stories of the mind-expanding experiences motivate people to experiment with psychedelics. A major disclaimer that is not emphasized enough in the media and personal experiences is the variability of reactions people can have, which the lack of understanding and education surrounding the drugs can contribute to the dangerous and harmful side effects associated with psychedelics. There should be more media representation concerning safety for recreational use, given its rise in consumption, especially among young adults.

### **Historical means of enlightenment and spiritual healing**

Psychedelics have been used for spiritual purposes for centuries and continue to be used for such purposes today. They act as a gateway to transcendent experiences that expand one's sense of self and connect to spiritual forces in their environment [21]. In the last 10 years, there has been a shift from focusing on spirituality less in the context of organized religion to focusing on the individual spiritual journey and healing. Additionally, there is a greater priority placed on the self and searching for inner-human capacity, known to some as "the cult of the self" [22]. These have grown in popularity as holistic wellness has received more attention in the media.

Spiritual healing involves restoring an organism's energy and dates to Vedic times through practices such as unblocking chakras in the body. According to this theory, chakras are energy fields in the body that, when

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“blocked,” can cause somatic and psychological conditions. There are additional theories that relate different chakras in the body to endocrine glands, although none of these have been empirically proven [23]. Chakras can be healed through mindfulness meditation, yoga, and psychedelic use.

One of the hallmark traits of a psychedelic trip is the mystical experience and spiritual growth that come as a result. Participants in psychedelic research studies consistently rank these experiences as one of the top spiritual experiences and one of the most profound experiences of their lives [24]. Participants report increases in mood, deeper appreciation for the world around them, and improved relationships with themselves and others [25-29].

In addition to spiritual growth, there are societal benefits. Those who consistently use psychedelics, known as Psychonauts, possess spiritually influenced beliefs and attitudes about life that are strengthened as a result of their psychedelic trips. Ironically, it seems as though this functions, in some cases, as a protective measure against additional drug-seeking behaviors [30]. In addition to reduced drug-related problems, studies have shown that psychedelics are the drug least responsible for criminal activity in general [18, 31].

Many celebrities have become more open concerning their experiences with psychedelics, whether as a means of spiritual growth and healing or for recreational use. While the individual experiences vary, most report having enlightening and positive experiences. For example, country artist Kasey Musgraves reported that LSD has helped her find more meaning and a deeper appreciation for life [32]. Another actor and songwriter, Reggie Watts, shared that it opened his mind to a deeper understanding of the universe, and the changes he implemented as a result [33]. On the *Joe Rogan Experience* podcast, Miley Cyrus said that she experienced a major panic attack after taking psilocybin and marijuana

[34]. The conversation surrounding psychedelic use is becoming candid in a way that allows people to become educated about the drug, and, should they choose to use it either for recreation or spiritual growth, they can have an optimal experience.

### **Therapeutic Intervention for Treatment-Resistant Conditions**

Psychedelic research began studying the neurological correlates of schizophrenia and the basis of psychosis. This broadened to seeing how it impacted disorders like major depressive disorder (MDD), bipolar disorder, PTSD, obsessive-compulsive disorder (OCD), anxiety, and substance use disorders like alcoholism. While methodological practices for studies completed in the 1950s and 60s would not meet validity standards today, there was overwhelming data that supported psychedelic-assisted therapy. However, due to the equally overwhelming recreational use, it was banned, and research was effectively halted.

Not until recently, with updated research practices and technology, has research gained traction in medicine, but in the legal world as well. The state of Texas has begun investing funds and resources in MDMA treatment for veterans with PTSD [35]. Additionally, financial trend analysts predict that the psychedelic industry will surpass the medical marijuana market by monetizing both the production of the drugs and their therapeutic administration [6]. While ethically questionable, the psychedelic industry is indeed expanding in ways medical marijuana could not.

### **Psychedelics Altering Self and Social Processing**

Psychedelics also allow for a softening and alteration of staunchly held beliefs. Metaphysical beliefs surrounding health, religion, philosophy, and education are explored

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through experiences with psychedelic drugs. Some of these metaphysical beliefs can be harmful and maladaptive, and trigger psychiatric conditions such as depression and PTSD. Things like psychedelic-assisted therapy put patients in an impressionable state where they can explicitly discover these implicit beliefs [26]. It is this suggestibility that allows for confidence in these beliefs to be relaxed and for those beliefs to be changed. Not only can beliefs be changed, but behavioral changes can come as a result of psychedelic assisted therapy [36].

Another key alteration to self-processing is the dissolution of the ego. This produces a “decentering” effect that allows users to internalize a broader spectrum of beliefs and emotions. According to Vollenweider & Preller, this is thought to be especially helpful for someone with depression or PTSD who experiences intrusive thoughts and rumination [36]. These cognitive changes can translate to reduced levels of rejection sensitivity and empathy towards others [37]. It is these changes in self-processing that may cause changes in social cognition, both of which contribute to therapeutic success.

### **Psychedelics Altering Emotional Processing**

Psychedelic drugs cause a cascade of physiological changes in emotional processing. Kraehenmann et al. found that with psilocybin, there is a reduction in processing of negative stimuli in the amygdala and alterations in connectivity between structures in the limbic system [38]. This was shown by reduced response rates to faces with a frown or angry look. However, Bershad et al. reported a positive correlation between increased connectivity strength in the amygdala and middle frontal gyrus and positive mood with LSD [39]. Both studies suggest that emotional alterations occur within limbic circuits, although the exact mechanism remains unclear. From

a phenomenological standpoint, maladaptive beliefs can be deconstructed and changed by looking at them from an outside point of view, as users commonly report out-of-body-like experiences. However, additional studies are needed to investigate further the changes in emotional processing in other, more extreme, psychiatric disorders.

There is also evidence of neuroplasticity in the brain due to psychedelic use. This occurs because of enhanced AMPA activation, due to NMDA receptor blockages causing glutamate release by drugs like ketamine. Through the increase in presynaptic glutamate levels in the prefrontal-limbic circuits, it is possible that this is the location where the neuroplastic changes occur that are responsible for the therapeutic mechanism of drugs like psilocybin and ketamine [40]. By causing changes at the synaptic level, this supports the biological hypothesis underlying mood disorders.

### **Psychedelic-Assisted Psychotherapy**

When used in conjunction with psychotherapy, patients seem to experience marked decreases in psychiatric symptoms with psychedelic use. Positive therapeutic outcomes have been demonstrated in studies treating alcoholism and cigarette smoking, PTSD, OCD, and anxiety [11, 29, 35, 41-44]. Evidence shows that psychedelic-assisted psychotherapy is better at treating MDD than traditional pharmacological approaches and psychotherapy, and even when compared to medicine and psychotherapy combined [45, 46]. However, it is hard to control the individual experiences that people will have, which presents a limitation in generalizing conclusions about psychedelic research because it may vary on a case-by-case basis.

There are limitations to these studies, such as smaller sample sizes and the placebo effect of the drug itself. The mechanism of the behavioral effects of psychedelics

remains largely unknown. In conditions like alcoholism, the addiction to one substance is being overridden by the influences of another. It brings into question whether it is the drug itself causing changes to the behavior, or if the previously held beliefs and knowledge of the drug accounts for the positive experience and change. Participants in the studies typically were more open to trying experimental psychedelic therapy, so embracing the experience could play a larger role in predicting the outcome than is given credit. Conversely, someone who is staunchly against psychedelic experimentation could have a different experience because of their more rigid mindset.

Both common media outlets and peer-reviewed sources emphasized the importance of using psychedelics in a controlled environment, and if using in a therapeutic setting, under the guidance of someone who is trained to work with patients in altered states of consciousness [20]. If using recreationally or for ritual purposes, being in a safe physical environment will minimize the risk of any potential danger to yourself or others.

## Conclusion

With these drugs seeming to be a miracle “cure-all” for psychiatric conditions, there is a reason why experiments with them are extremely selective in the criteria for inclusion. They are still psychoactive substances that alter an individual’s state of consciousness. These results should be analyzed with caution, as limitations were present in each study, such as small sample sizes, limited to a narrow demographic or condition, and limited interaction with other medications. For practical implementation, responsibilities such as work and family, and the effects they have on other medications, need to be taken into consideration.

This also raises the question whether the well-intentioned, systematic regulations that

would allow for safe use in medicine would be consistently implemented at the individual level. Opioids were introduced to target severe pain, and they succeeded. So much so that despite stringent regulations and laws placed on their distribution, there remains an opioid epidemic in America. While psychedelics do not present the same potential for abuse and have been used for centuries in religious contexts without those same repercussions, there is the same risk of inconsistency and lax rule-following at an individual level between the clinician and patient. The potential for adverse effects is increased, and the optimal benefit of these controversial substances is minimized when they are not used in a controlled setting, under proper guidance.

## AUTHOR INFORMATION

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