

**EDITORIAL:**

**IS PSYCHEDELIC TREATMENT OF MENTAL HEALTH DISORDERS READY FOR PRIME TIME?**

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**ABSTRACT**

Psychedelics, substances known to alter perception, mood, and consciousness, have been used across various cultures for centuries, often in religious ceremonies to facilitate spiritual experiences. Lysergic acid diethylamide (LSD) was used clinically from the 1950s until its ban in 1967. Recently, there has been a resurgence of interest in psychedelics for treating mental health disorders such as PTSD, anxiety, depression, and substance use disorders. The FDA has designated several psychedelic compounds as "breakthrough therapies," acknowledging their potential for safety and effectiveness. Psychedelics like Psilocybin, LSD, DMT/Ayahuasca, MDMA, Peyote, and Ketamine work through various mechanisms, including agonism at 5HT<sub>2A</sub> receptors and NMDA antagonism. These substances promote neuroplasticity and can disrupt pathological activity patterns in the brain's default mode network (DMN), facilitating new perspectives and emotional processing. Psychedelic-assisted therapy leverages these properties to help patients gain insight into repressed conflicts and reduce maladaptive defenses. The therapeutic process involves preparation, support during dosing, and integration phases. Safety concerns include hallucinogen persisting perception disorder (HPPD), serotonin toxicity, and potential boundary violations. Despite promising early results, comprehensive research is needed to fully understand the therapeutic potential and limitations of psychedelics. Psychedelic-assisted therapy could offer hope and transformation for millions suffering from mental illnesses if proven safe and effective.

**KEYWORDS**

Brain Consciousness; Default Mode Network; Neuronal Plasticity; N-Methyl-3,4-methylenedioxymphetamine; Psilocybin.

***Introduction***

Psychedelics are substances that alter perception, mood and consciousness. These compounds have been used for centuries across various cultures, and they continue to play a role in religious ceremonies to facilitate spiritual experiences or heightened states of awareness. Historical clinical use of Lysergic acid diethylamide (LSD) dates back from 1950s – 1960s till its ban in 1967 due to its perceived negative impact on cultural values.<sup>1,2</sup>

There has been a resurgence of interest in psychedelics for treatment of mental health disorders. Recent research has shown their potential to treat conditions like PTSD, other anxiety disorders, depression and substance use disorders. Unites States Food and Drug Administration (FDA) has designated several psychedelic compounds as, "breakthrough therapies," so their safety and effectiveness can be researched to support future studies and clinical applications.<sup>2</sup> This renewed interest is fueled by a growing recognition of the limitations of traditional pharmacotherapy and psychotherapy, particularly for treatment-resistant cases.

***Mechanism of Action of Psychedelics:***

Psychedelics or classical hallucinogens include Psilocybin, LSD, DMT/Ayahuasca, MDMA (Ecstasy), Peyote and Ketamine/Esketamine.

Psilocybin, LSD, Peyote and DMT work as agonists at the 5HT<sub>2A</sub> receptors. MDMA primarily inhibits the reuptake of monoamines and thus increases the concentration of norepinephrine, serotonin and dopamine in the synaptic clefts. Ketamine and Esketamine are both NMDA antagonists.<sup>3</sup>

The therapeutic benefits of psychedelics are believed to arise from their capacity to induce significant alterations in consciousness, resulting in enduring changes in perspective and behavior. These substances seem to facilitate the brain's ability to create new neural connections (neuroplasticity), which can be advantageous for individuals with inflexible thought patterns linked to various mental health conditions.<sup>4</sup> Furthermore, the mystical experiences triggered by psychedelics can offer patients a sense of connectedness and meaning, which can be transformative in their healing journey.

This can be further illustrated with the understanding of the default mode network (DMN) and the proposed mechanism of action of psilocybin on the DMN. DMN consists of widely distributed brain regions in the parietal, temporal, and frontal cortices. Increased DMN activity has been observed in depressed patients where its dysregulation can lead to excessive rumination and worry. Psilocybin and LSD may exert their long-lasting antidepressant effects by disrupting the pathological activity patterns within and between DMN regions. One such activity is decreasing the amplitude of alpha oscillations in the cortex, which is believed to promote emotion-based rather than knowledge-based modes of thinking. Thus, Psilocybin and other psychedelics allow the emergence of a new, potentially positive viewpoint by decreasing the influence of prior beliefs and expectations, reducing top-down inhibition and enhancing bottom-up information transmission.<sup>5,6</sup>

### ***Psychodynamic Perspective of Psychedelic-Assisted Therapies:***

Our psyche is governed by three agencies according to Freud's structural model of the mind: The id, the ego, and the superego. The function of the ego is to negotiate conflicts between id and the superego by utilizing defense mechanisms. These defense mechanisms lead to chronic and habitual patterns over time that ego employs to navigate daily challenges. Some of these chronic patterns become rigid and maladaptive for the individuals and contribute to anxiety and depression. Moreover, fundamental early life conflicts are shielded by the strong ego defenses of repression and are not easily available to the conscious memory of the patient. Psychedelics can induce regressed ego states, that are less shielded by the ego's defense mechanisms and thereby allow the early life conflicts to surface. This helps patients gain insight into repressed early life conflicts and facilitates recovery work.

Grof emphasized four major principles of psychedelic-assisted psychotherapy in his *psychodynamic realm* model.

- a) Cathartic abreaction - revisiting traumatic events in the setting of reduced ego defenses, allowing the release of unconscious material and the discharge of related emotional burdens.
- b) Understanding how past traumatic events and accompanying conflicts have persisted into adulthood, leading to the development of maladaptive, inflexible ego defenses that hinder emotional connection with others.
- c) Transference – the process where patient emotionally perceives or relates to the therapist as if the therapist were the person originally present during the traumatic event.
- d) A significant integration that combines past conflicts from early life events and incorporates their now neutralized emotional aspects into a more adaptable character structure.<sup>6</sup>

### **Setting:**

Psychedelics induce intense and often unpredictable experiences that require a comfortable, secure and visually appealing space to navigate these experiences. A familiar and supportive setting can significantly reduce anxiety and fear.

The right setting encourages patients to relax, close their eyes, and turn their attention inward, facilitating deeper introspection and emotional processing. Inward focus enables patients to explore their thoughts and feelings more profoundly resolving deep-seated trauma, gaining new perspectives, and achieving greater emotional resilience.

A secure environment in the presence of an empathetic and non-directive therapist helps build a strong therapeutic alliance, which is one of the essential elements of successful therapy outcome.

In summary, the setting in psychedelic treatment is a fundamental component that influences the patient's experience and therapeutic outcomes. It ensures safety, facilitates inner exploration without undue stress, provides support, reduces anxiety, and helps build a strong therapeutic alliance.<sup>7</sup>

### **Grounding Sessions:**

Grounding sessions in psychedelic therapy play a vital role in helping patients stabilize and integrate their experiences. They utilize various therapeutic modalities such as guided breathing exercises, mindfulness practices, physical grounding techniques, therapist support, reflective discussions, and creative expression. These sessions are essential for providing patients with a sense of safety and control, aiding in emotional regulation, and establishing a foundation for integrating psychedelic experiences into their daily lives, leading to enhanced therapeutic benefits and personal insights. Moreover, grounding sessions help patients maintain focus on therapeutic goals, equip them with tools for managing emotions in the future and build emotional resilience.

### **Administration of Psychedelics:**

The administration of classical psychedelics like psilocybin and LSD typically occurs in a supportive, comfortable setting involving extensive psychotherapeutic treatment with multiple preparatory sessions. Classical psychedelics have also been used in more interactive and group settings with small to moderate doses to lessen psychological defenses.

### **Phases of Psychedelic Assisted Therapy:**

There are several protocols for Psychedelic assisted therapy (PAP). They typically involve three main stages: preparation, support during the dosing session, and post-session integration.<sup>8</sup>

*Preparatory Phase:* This phase is conducted before the medication session. In this phase, therapist focuses on building a strong therapeutic rapport with the patient, collecting background information through comprehensive history taking, and providing education about the psychedelic experience. Patient is explained about the therapeutic process, the session duration, the dosing protocol, the safety protocol, participant's

active role in the session and acceptable boundaries of interaction between the therapist and the patient. This grounding session is critical for providing a safety net for patients to navigate and integrate their experiences constructively.

*Dosing Session Support Phase:* In this session, therapist generally provides emotional support and encourages the patient to engage with difficult thoughts and memories that may arise when the patient introspects during dosing sessions.

*Integration Phase:* This phase starts the day after the dosing session. During this phase, patients review their experience from the dosing session with the therapist. The therapist skillfully employs techniques to emphasize certain elements of the experience, fostering lasting positive thought and behavior patterns. This phase extends the therapeutic process that began in the preparation sessions and was intensified during the psychedelic experience. With the therapist's guidance, patients can strengthen their new mindset and begin making behavioral changes that aid in recovery.

### **Safety:**

While potentially beneficial, psychedelics have notable safety concerns and limitations beyond their acute psychoactive and dissociative effects.

1. **Hallucinogen persisting perception disorder (HPPD):** A condition characterized by the recurrence of perceptual disturbances that an individual previously experienced while using hallucinogenic substances, leading to significant distress or impairment.
2. **Serotonin Toxicity:** Clinicians should be vigilant about serotonin toxicity which can lead to life-threatening serotonin syndrome. They must exercise caution when prescribing other serotonergic medications alongside serotonergic psychedelics.
3. **Boundary Violations:** Trials of Psilocybin and MDMA have shown efficacy when delivered in a psychedelic-assisted psychotherapy setting. The primary concern here is safety, as these potent substances can trigger intense psychological experiences and have the potential to make patients vulnerable to sexual harassment and financial exploitation.

### **Conclusion:**

Although the early results are promising, comprehensive research is needed to fully understand the therapeutic scope, benefits, and limitations of these substances. Earlier this month, a panel of independent advisers to the U.S. Food and Drug Administration voted against recommending the approval of MDMA treatment, combined with therapy, for treating post-traumatic stress disorder (PTSD). FDA will make their final decision on the approval in August. If proven safe and effective, psychedelic-assisted therapy could offer hope to millions suffering from mental illnesses and holds the promise of healing and transformation for many.

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