

uniMIND Symposium 2025: Metamorphosis in Psychedelic Science

Problem-Based Learning (PBL)

Problem-Based Learning (PBL) is a dynamic method of education that focuses on critical thinking, dialogue, and collaborative inquiry. Rather than passively receiving information, participants engage with complex topics by analyzing curated material, discussing divergent perspectives, and developing informed positions together. This approach fosters deeper understanding, encourages intellectual openness, and strengthens the ability to engage with real-world challenges.

At the uniMIND Symposium 2025, PBL is the foundation for exploring the central theme: Metamorphosis in Psychedelic Science – spanning clinical, cultural, philosophical, and regulatory dimensions.

As a participant, you are assigned to one of five working groups, each focused on a distinct facet of the overall theme.

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How to take part in our PBL format

Before the symposium

Read the study material provided for your group topic in this document.

Reflect on the key ideas, questions, and arguments.

You are invited to study complementary materials, but that is not a must.

During the group session

Join your group for a focused discussion – this will be after the lunch break.

Your group will:

- Identify key insights from the text
- Exchange interpretations and perspectives
- Formulate a shared position or set of priorities

Group assignments

Each group has a facilitator, who:

- Keeps time and ensures inclusive participation
- Oversees note-taking and the selection of a group speaker
- Supports the preparation of a 30-second opening statement

The opening statement will be presented at the start of the panel discussion following the group work.

All participants are asked to follow the **step-up / step-down principle**:

If you tend to speak often, make space for others

If you tend to hold back, this is your chance to step forward

Panel Discussion:

At the end of the session, each group sends one speaker to the symposium panel.

The speaker presents the group's position and contributes to a collective discussion of the symposium's theme.

This document is your starting point. The texts are carefully written to stimulate thoughtful engagement – not to deliver consensus, but to challenge and inspire. As you read, ask yourself: What's at stake in this discussion? What position do I think our group should take? What perspective is missing – and how could we represent it?

Clinical implementation: Psychedelic-assisted therapy as disruptive treatment – from states to traits

Edited by: Caterina Bosa

Reviewed by: Dr. Marvin Däumichen

A growing – though still limited – body of evidence suggests that psychedelic substances and psychedelic-assisted therapy (PAT) may offer valuable contributions to psychotherapy and psychiatry (Barnett & Greer, 2021). Beginning in the 1950s and 1960s, compounds such as LSD and psilocybin attracted scientific interest for their therapeutic potential. However, this early momentum was curtailed by restrictive international policies, most notably the 1971 United Nations Convention on Psychotropic Substances, which led to a near-total cessation of clinical research for several decades. In recent years, a renewed wave of scientific inquiry has emerged, gradually elucidating the psychological and neurobiological mechanisms through which these substances exert their effects.

When combined with structured psychotherapeutic frameworks, psychedelics appear to induce profound experiential states that – under appropriate conditions – may facilitate lasting psychological and behavioral change. The state-to-trait transformation model (Kähönen, 2024) suggests that transient altered states of consciousness, when carefully integrated, can result in sustained improvements in mood, cognition, and behavior (Preller & Vollenweider, 2018). Psychedelic-assisted therapies may therefore function not only as symptom-relieving interventions but as potentially disease-modifying treatments (Cameron & Olson, 2022). This is particularly relevant in light of the global mental health crisis, where existing pharmacological strategies often fail to achieve full remission. Psychedelics could thus represent a disruptive innovation in psychiatric medicine – one that challenges existing paradigms and opens new therapeutic avenues for complex mental health conditions.

The effects of psychedelics involve a complex interplay of neurobiological and psychological mechanisms. Neurobiologically, these substances act primarily on the serotonergic system, particularly as agonists at the 5-HT_{2A} receptor. This interaction promotes increased neuroplasticity, heightened sensory perception, and altered states of consciousness, often characterized by vivid visual imagery, a sense of unity or connectedness, and changes in temporal and spatial perception (Cameron et al., 2023; Yaden & Griffiths, 2020).

Psychedelics also modulate large-scale brain network dynamics. Notably, they reduce functional connectivity within the Default Mode Network (DMN) – a system implicated in rumination, self-referential thinking, and identity formation, and frequently hyperactive in depressive disorders (Carhart-Harris et al., 2012). At the same time, they enhance

communication between regions that typically function independently, potentially facilitating cognitive flexibility and the emergence of novel insights. This pattern of disintegration and reintegration of neural networks may underlie the therapeutic effects observed in addiction, depression, and trauma-related conditions.

Psychologically, psychedelics influence emotion regulation, introspection, and self-related cognition. They can help individuals access previously avoided psychological material, supporting emotional breakthroughs and resolution. Users often report increased psychological flexibility – the capacity to shift perspective and adapt to new challenges – along with enhanced mindfulness and reduced cognitive rumination (Holas & Kaminska, 2023).

One of the most widely reported effects is a shift in self-perception. Psychedelics often catalyze reflection on identity, values, and life direction. These shifts are frequently accompanied by elevated mood and a heightened sense of connection to others or to existence more broadly. Mystical-type experiences, especially those induced by psilocybin, have been associated with long-lasting increases in openness – a personality trait linked to creativity, curiosity, and receptivity to novelty. While changes in other traits such as neuroticism, extraversion, or conscientiousness are generally more transient, they may still support meaningful changes in how individuals relate to themselves and others (MacLean et al., 2011).

Major depressive disorder has become a central focus of contemporary research on psychedelic-assisted therapy. Conventional antidepressants – such as selective serotonin reuptake inhibitors (SSRIs) – are designed to prevent relapse but typically do not aim for full recovery. They function within a pathogenetic framework and are largely symptomatic in their effects. In contrast, psilocybin – administered with psychological support – has been shown to produce rapid and lasting improvements in depressive symptoms, sometimes persisting for up to a year (Gukasyan et al., 2022). Psilocybin appears to induce neuroplastic changes more rapidly than SSRIs and may promote structural reorganization of brain circuits involved in emotion regulation (Husain et al., 2023; Shao et al., 2021).

This emerging evidence points toward a transdiagnostic, disease-modifying potential for psilocybin, offering not only symptom relief but deeper psychological change. Such a model aligns with the framework of salutogenesis, developed by Aaron Antonovsky, which emphasizes the origins of health, coherence, and resilience over the correction of pathology (Vinje et al., 2017). Instead of managing illness, salutogenic approaches aim to foster personal and social resources that promote well-being. Recent work by Spangemacher et al. (2024) applies this model to psychedelic therapy, arguing that it may not only support recovery but actively promote psychological growth and transformation.

A landmark randomized clinical trial conducted at Imperial College London in 2024 further demonstrated this potential. Participants received either two 25 mg doses of psilocybin or a six-week course of escitalopram, with both interventions supported by psychotherapy. While both groups showed similar reductions in depressive symptoms at six-month follow-up, secondary outcomes favored psilocybin: participants reported greater improvements in psychological connectedness, emotional resilience, and perceived meaning in life (Erritzoe et al., 2024). These findings suggest qualitative differences in how the two treatments affect mental health and subjective experience.

Supported by appropriate therapeutic frameworks, the psychedelic experience may enable individuals to recover what Antonovsky termed a “sense of coherence” – the belief that life is comprehensible, manageable, and meaningful. This reframing shifts the therapeutic aim from symptom reduction to personal growth, resilience building, and the actualization of human potential (Vossler, 2012).

The effectiveness of psychedelic therapy is not determined solely by the drug, but by the interplay of pharmacology, environment, and interpersonal process. A growing body of psychotherapy research has identified general change mechanisms – empirically supported processes that promote transformation across therapeutic modalities, to which psychedelic-assisted psychotherapy is no exception (Gassmann & Grawe, 2006; Wolff et al., 2024). These include the therapeutic alliance, resource activation, problem exploration, motivational clarification, and the development of mastery. Their success depends on the alignment between the patient’s mindset and the surrounding therapeutic context – what is commonly referred to as set and setting.

The therapeutic alliance, in particular, is recognized as a critical factor in treatment outcomes. A strong alliance establishes trust and emotional safety, allowing patients to engage deeply with their internal processes. However, the heightened vulnerability and suggestibility associated with psychedelic states may amplify relational dynamics, making boundary management essential. Ethical concerns arise when therapists – even unintentionally – project their own values, take on charismatic or directive roles, or violate professional norms. To safeguard against these risks, best practices emphasize transparency, adherence to ethical guidelines, and, where possible, the involvement of co-therapists to distribute relational influence (Johnson, 2020; Levin et al., 2014; Murphy et al., 2022).

Clinical risks also merit attention. While rare, psychedelics can induce adverse psychological responses, especially in individuals predisposed to psychotic or affective disorders. Documented complications include the onset or worsening of schizophrenia, depersonalization, derealization, affective instability, and hallucinogen persisting

perception disorder (HPPD) (Yildirim et al., 2024). Careful screening, informed consent, and structured integration are essential to minimize these risks.

Finally, significant regulatory challenges persist. The classification of psychedelics as Schedule I substances complicates clinical access and public health implementation. The U.S. Food and Drug Administration (FDA) continues to debate how to evaluate interventions that combine pharmacological and psychotherapeutic elements. A recent advisory committee vote against the approval of MDMA-assisted therapy for PTSD reflects both scientific caution and the methodological difficulties of maintaining placebo controls in trials where the psychoactive effects are unmistakable (Muthukumaraswamy et al., 2021).

Looking forward, the field must refine treatment protocols to ensure replicable outcomes, develop adaptive regulatory pathways, and build robust ethical frameworks to support safe practice. Equally important is a focus on integration strategies – the structures and supports that help patients sustain long-term psychological gains. Only through coordinated scientific, clinical, and institutional efforts can psychedelic therapies fulfill their promise as a transformative contribution to mental health care.

Discussion Questions

1. How could psychedelic-assisted therapy reshape clinical practice – and what unique benefits does it offer for treatment-resistant mental health conditions?
2. What regulatory and public health strategies are needed to safely integrate psychedelic-assisted therapy into mainstream clinical care?
3. How can psychedelic therapies support not just recovery, but personal growth – and what frameworks are needed to help individuals move beyond the patient role toward long-term flourishing?

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Neurobiology of psychedelics and translation into practice

Edited by: Marta Mihanovic

Reviewed by: Dr. Prateep Beed

Psychedelics primarily exert their effects by interacting with the serotonin (5-HT) system, specifically through the 5-HT_{2A} receptor (5-HT_{2AR}). These compounds are structurally similar to serotonin, allowing them to act as agonists at 5-HT_{2A} receptors, which are abundant in the neocortex and play a critical role in perception, cognition, and mood regulation (Banks et al., 2021). The role of 5-HT_{2A} receptor activation in neuroplasticity suggests that psychedelics may facilitate long-term changes in neural circuits, explaining their prolonged therapeutic effects even after a single dose.

The effects of psychedelics extend beyond serotonin receptors, influencing glutamate neurotransmission. The prefrontal cortex (PFC), a region included in mood regulation, exhibits increased extracellular glutamate levels following psychedelic administration. This leads to enhanced synaptic plasticity via ionotropic glutamate receptors (AMPA and NMDA) and metabotropic glutamate receptors (mGluRs). Furthermore, increased connectivity between the PFC and amygdala may explain the emotional breakthroughs observed during psychedelic experiences.

Neurophysiological research highlights several key effects of psychedelics on brain activity in various ways. Firstly, through increased brain excitability – heightened spontaneous neuronal firing correlates with sensory amplification and hallucinations (van Elk & Yaden, 2022). Secondly, psychedelics induce more unpredictable, diverse neural signals, correlating with the subjective intensity of psychedelic experiences (Aqil & Roseman, 2023) which presents enhanced brain signal complexity. Finally, psychedelics reduce default mode network (DMN) connectivity (Banks et al., 2021). DMN is linked to self-referential thoughts such as ego, identity and rumination, and when overactive, it is linked to depression and anxiety. Psychedelics disrupt DMN function which leads to loss of self-boundaries (ego-death) which could be part of the therapeutic process. This also adds on the point that psychedelics can simultaneously increase connectivity between certain parts of the brain (such as the PFC and amygdala) while decreasing connectivity in other regions (the DMN network), using different mechanisms and neural pathways.

Psychedelics promote structural changes at the neuronal level, enhancing learning, adaptation, and cognitive flexibility through increased dendritic spine density and neurite outgrowth which suggest long-term synaptic strengthening (Banks et al., 2021). Also, psychedelics affect the expression of Brain-Derived Neurotrophic Factor (BDNF), a key protein involved in synaptic plasticity and neuronal survival, even after one administration.

It leads to more dendritic complexity, which outlasts the acute effects of the psychedelic. Research showed that repeated administration of a psychedelic directly stimulated neurogenesis and increased BDNF mRNA levels up to a month after treatment (De Vos, Mason & Kuypers, 2021).

Changes in neuroplasticity may help explain some of the long-term effects of psychedelics. When used alongside psychotherapy, psychedelics have demonstrated clinical effectiveness in treating mood disorders and addiction, and even healthy individuals report improved mood following psychedelic use. One possible explanation for this is the enhanced dendritic and synaptic growth in neurons of the prefrontal cortex (PFC), which plays a crucial role in emotional regulation through its connections with the amygdala and other subcortical regions. Depression, in particular, is characterized by reduced cortical neuroplasticity and synaptic loss in the PFC. Furthermore, PTSD has been linked to fewer synaptic connections between the medial PFC and amygdala, impairing the PFC's ability to regulate fear responses (Calder & Hasler, 2023).

One more concept which needs to be mentioned is the Entropic Brain Hypothesis, used as a framework for understanding different states of consciousness. States of consciousness vary from waking awareness to dreaming and psychedelic states and differ from each other in levels of entropy. High entropy states (e.g., REM sleep, psychedelic states, early psychosis) resemble fluid, less constrained mental states which enable a broader range of thoughts and perceptions, while lower entropy states (e.g., waking consciousness) enable reality-testing, goal-directed behaviour, support self-awareness and demonstrate greater order.

Psilocybin studies using fMRI and MEG scans showed that psilocybin reduces Default Mode Network (DMN) activity, leading to disorganization and increased neural variability (Carhart-Harris et al., 2014). This aligns with the Entropic Brain Hypothesis, which suggests that psychedelics induce high-entropy brain states, promoting cognitive flexibility and emotional breakthroughs. These effects may help treat mental disorders like depression, PTSD, and addiction by allowing individuals to reframe experiences and emotions which can support psychedelic-assisted psychotherapy (Mason et al., 2021). It is also worth mentioning that, while high-entropy brain states can be beneficial in treating mental disorders, it can also have positive effect on mental health and well being. It allows breaking from conventional thought patterns, increasing innovation and creativity.

Connected with the entropic brain hypothesis is the REBUS (Relaxed Beliefs Under Psychedelics) model which explains how psychedelics affect brain function. Psychedelics reduce the rigidity of high-level priors (beliefs about the world), enabling new insights and experiences. By loosening fixed thought patterns, psychedelics facilitate personal growth,

self-reflection, and interconnectedness. Due to heightened suggestibility and dependence on the therapeutic setting ethical concerns arise, requiring strict guidelines, informed consent, and regulatory safeguards to prevent psychological harm (Villiger & Trachsel, 2023). As psychedelics move toward medical approval, establishing legal frameworks and standardized protocols is crucial for their safe and ethical use.

Finally, it is essential to note the challenges of moving from preclinical trials to clinical applications in the field of psychedelics. Mattu & Sullivan (2024) examined said challenges on using classic psychedelics for treating major depressive disorder (MDD) and treatment-resistant depression (TRD). Firstly, preclinical studies rely mostly on rodent models which have limited capacity in replicating subjective experiences in humans such as ego dissolution and emotional breakthroughs. Also, these studies use behavioral proxies to manifest depression and later psychedelic-induced cognitive shifts, but it is a question of how good of a reflection of human behavior those behaviors are. Another challenge lies in the lack of methodological standardization of human psychedelic research which limits reproducibility and interfere with drawing conclusions. Such problems are; dosing protocols – multiple low doses or single high dose, variations in metabolism of animals and humans, different brain responses after psychedelic administration. Because of these reasons it is encouraged to promote collaborative research, share findings across different disciplines, integrate knowledge from neuroscience, psychiatry, psychology in order to develop more holistic understanding of psychedelic effects. Also, it is recommended to establish uniformed protocols across preclinical and clinical research studies so the data extracted can be more easily compared.

Discussion Questions

1. What implications does reshaping of neural networks and changes in neuroplasticity following psychedelic administration have for healthy individuals and for long-term psychiatry treatment?
2. Following the entropic brain hypothesis how do the different states of consciousness (e.g., waking consciousness, REM sleep, psychedelic states) influence creativity, emotional processing, self-perception?
3. Since there is an imperative in ensuring safe and responsible psychedelic-assisted therapy for clinical use, what could be the guidelines on standardization of psychedelic dosing?

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Cultural Transformation and social renewal: Can there be an ethical culture of consciousness?

Edited by: Marta Mihanovic

Reviewed by: Dr. Marvin Däumichen

In the history of psychedelics, several traditions illustrate their importance for human culture and society. Dupuis (2021) emphasizes how psychedelic use in ritual contexts, particularly tribal initiations, facilitates social cohesion by inducing altered states of consciousness that participants interpret as encounters with symbolically significant entities. These experiences function as mechanisms of enculturation and belief transmission, aligning affective and behavioral patterns within the group. Similarly, the concept of “psychedelic communitas,” explored by Kettner et al. (2021), highlights the capacity of collective psychedelic experiences to foster unity and mutual understanding. Dupuis (2022) further demonstrates how culturally structured hallucinations reinforce group-specific worldviews, suggesting that psychedelics, when embedded in communal frameworks, contribute to the maintenance of shared cultural narratives.

In Western contexts, psychedelics gained substantial visibility during the mid-20th century, particularly through their influence on literature, music, and art (D’Angelo, 2019). Writers of the Beat Generation - such as Allen Ginsberg, Jack Kerouac, and William Burroughs - experimented with these substances as part of their critique of postwar conformity. This cultural trajectory continued into the 1960s, when psychedelics became emblematic of a broader countercultural movement that embraced consciousness expansion, civil disobedience, and alternatives to mainstream values. Often mischaracterized as a unified “hippie” movement, the counterculture in fact comprised politically diverse groups, including the New Left and the Black Panther Party, both of which sought forms of liberation and systemic change (Simić, 2023; Bach, 2020). Prominent figures such as Aldous Huxley and Timothy Leary popularized the idea of psychedelics as tools for personal and societal transformation, while Ken Kesey’s Acid Tests exemplified the search for community and altered consciousness (Smith, 2016).

Alongside their cultural symbolism, psychedelics have been viewed as catalysts for inner transformation. Sanchez Petrement (2023) notes that users often report mystical or religious awakenings marked by unity and interconnectedness. Tagliazucchi, Llobenes, and Gumiy (2022) support these observations, showing that such experiences can lead to emotional insight and cognitive reframing. These shifts may also extend to environmental values. Forstmann and Sagioglou (2017) found that psychedelic users often develop stronger identification with nature, while Paterniti, Bright, and Gringart (2022) link mystical-

type experiences to sustainable consumption behaviors. Timmermann et al. (2021) demonstrate that psychedelics can also shift metaphysical beliefs away from physicalism toward dualist or panpsychist orientations, suggesting potential implications for ethics, social behavior, and worldview revision.

While these transformations may foster values aligned with sustainability and cooperation, their impact is not automatic. Yaden et al. (2021) argue that while psychedelics do not resolve the “hard problem” of consciousness, they are valuable for studying the “easy problems”, such as perception, cognition, and emotional regulation, by temporarily altering conscious states. The entropic brain hypothesis and the REBUS model (Carhart-Harris et al., 2014; Carhart-Harris & Friston, 2019) suggest that psychedelics increase neural entropy and reduce the rigidity of high-level priors, enabling greater cognitive and emotional flexibility. These mechanisms may support transformative experiences but translating them into sustained cultural change requires ethical integration.

One challenge is the fragmentation of psychedelic cosmologies: the current landscape includes clinical research, underground retreats, Indigenous rituals, and personal experimentation, each grounded in divergent epistemologies and values. This pluralism can foster innovation, but it also complicates the development of shared ethical standards and integration frameworks. Without a coherent cultural-normative narrative, the risk of ideological confusion, spiritual bypassing, or commercialization increases. Hauskeller and Schwarz (2023) emphasize that insights from philosophy and anthropology are crucial to preventing exploitative or reductive uses of psychedelics. They warn against the unchecked medicalization of these substances, which may marginalize traditional and underground practices and lead to ethical concerns such as power imbalances, inadequate consent processes, and overpromising therapeutic outcomes.

The rise of psychedelic retreats illustrates these tensions. Neitzke-Spruill et al. (2024) document how participants often report life-changing insights and shifts in identity and values, yet heightened suggestibility during psychedelic states can raise concerns about autonomy and undue influence. Lutkajtis (2021), studying a legal retreat in the Netherlands, found that supportive structures, such as ethical guidelines, integration protocols, and safe environments, are key in fostering beneficial outcomes and avoiding harm. In contrast, a case study by Perna et al. (2025) describes how unregulated retreat settings can exacerbate psychiatric vulnerabilities. A participant with no prior history developed prolonged adverse effects following repeated high-dose psilocybin use, and facilitators failed to offer appropriate medical guidance. This example underscores the urgent need for professional oversight and enforceable ethical standards.

Dupuis (2022) and Hartogsohn (2017) both stress that psychedelic experiences are co-produced by a web of pharmacological, psychological, social, and cultural factors, commonly captured by the concepts of “set and setting.” Given this complexity, interdisciplinary approaches that draw on anthropology, neuroscience, and ethics are essential to understanding and guiding psychedelic use in a pluralistic society.

In envisioning a way forward, philosopher Thomas Metzinger proposes the concept of a *Bewusstseinskultur* - an ethical culture of consciousness. Fink (2018) outlines four key challenges to realizing such a culture: (1) establishing shared values linked to specific states of consciousness; (2) enabling prospective evaluation of these states; (3) identifying reliable causal pathways to induce them; and (4) ensuring these pathways are sufficiently controllable. Psychedelics challenge each of these criteria, given the subjective variability of their effects and their dependence on set and setting. Yet these difficulties do not preclude action. Emphasizing harm reduction, education, mutual care, and rigorous integration could be initial steps toward building an ethical infrastructure for their use.

Finally, Hartmut Rosa’s (2019) theory of resonance adds an important dimension to the discussion. He describes resonance as a mode of relating to the world marked by mutual responsiveness and transformation. Psychedelic experiences, especially those involving ego dissolution and affective depth, may foster precisely this kind of relational openness. Rosa’s companion concept of *Unverfügbarkeit* - the idea that some aspects of life must remain inherently uncontrollable - offers a cautionary counterpoint to attempts at full standardization or commercialization of psychedelic states. Rather than reducing these experiences to therapeutic tools or cognitive technologies, a resonance-based framework encourages a respectful attitude toward their unpredictability and existential depth.

Taken together, these perspectives suggest that psychedelics might be able to contribute to cultural transformation, if they are embedded within ethical, interdisciplinary, and culturally sensitive frameworks. What these frameworks will look like exactly and what worldviews are the most suitable to carry human societies into a better future remains under debate. Key directions need to support the development of more democratic, compassionate, and sustainable societies. And psychedelic experience might serve as a small piece of the puzzle.

Discussion Questions:

1. How can we avoid epistemological fragmentation and foster a shared cultural framework for making sense of psychedelic experiences?

2. In what ways could a psychedelic-informed culture of consciousness support more open, democratic, and sustainable societies?
3. What lessons from the past should guide today's public discourse and use of psychedelics—and what role should they play in societal change?

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Bridging the Western scientific worldview and indigenous traditions in the context of psychedelics

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Psychedelics are among the most culturally and epistemologically diverse phenomena in human history. They sit at the intersection of Indigenous traditions rooted in spiritual healing and ancestral knowledge, and Western scientific frameworks shaped by a biomedical paradigm. To some, they signal a profound opportunity for cultural collaboration and human flourishing; to others, they evoke concerns about esotericism, cultural appropriation, and ethical misuse. Bridging biomedical models – which emphasize neuroscience, psychopharmacology, and clinical efficacy – with Indigenous perspectives – which frame psychedelics as sacred medicines for spiritual and communal healing – may open pathways to more holistic and culturally respectful practices (Cirillo, 2025; George et al., 2020).

Peck (2021) traces the historical and symbolic importance of psychedelics in both Indigenous and Western contexts, arguing that integration of these perspectives can foster more inclusive therapeutic models. In many Indigenous traditions, entheogens (psychedelic substances used for spiritual purposes) have long been embedded in ritual contexts that address physical, psychological, and spiritual dimensions of health. For example, in Oaxaca, Mexico, Mazatec, Mixtec, and Zapotec communities use psilocybin mushrooms – known as *teonanacatl*, or “God’s Flesh” – in ceremonies led by shamans to communicate with spiritual beings and support healing (Díaz, 1977). Similarly, peyote, a mescaline-containing cactus, has been used by Native American communities in religious rites to promote spiritual insight and communal cohesion. Ayahuasca, a decoction of Amazonian plants, is revered by Indigenous and Mestizo groups as a “plant teacher” used in guided ceremonies for divination, healing, and communion with the spiritual realm (Tupper, 2011). In West Africa, the root bark of *Tabernanthe iboga* is used in initiation rites involving dream-like visions and intense introspection; its active alkaloid, ibogaine, is currently being explored for treating opioid addiction (Mash, 2023).

In contrast, Western engagement with psychedelics has largely followed a pharmacological and scientific trajectory. While the Eleusinian Mysteries of Ancient Greece are believed to have involved psychoactive brews like *kykeon*, modern research began in earnest following the synthesis of LSD by Albert Hofmann in 1938 (Hofmann, 1970). The 1950s and 60s saw early studies on LSD and psilocybin for psychiatric uses, including treatment of depression and addiction. However, as psychedelics became associated with countercultural rebellion (Smith, 2016), their use was criminalized, and scientific inquiry was halted for decades.

Today, the renewed interest in psychedelics is shaped predominantly by Western scientific institutions. Research focuses on standardization, clinical trials, and mechanistic explanation – often isolating these substances from the cultural and spiritual systems in which they originated. While this work has yielded promising outcomes for conditions such as PTSD, depression, and substance use disorders (Kyzar et al., 2017), it has also risked marginalizing Indigenous perspectives and knowledge systems (Fotiou, 2020). The Western scientific paradigm, with its emphasis on objectivity and quantifiability, often excludes cultural frameworks that do not conform to its epistemic norms, raising ethical concerns about appropriation and the erasure of originating communities.

Despite these distinctions, there are ongoing efforts to synthesize Indigenous and Western approaches in clinical settings. Metzner (2013; see also Efthimiou et al., 2024) describes contemporary “neo-shamanic” practices that integrate ritual elements such as low lighting, music, guiding figures, and intentional group settings – features drawn from Indigenous ceremonial contexts and repurposed in psychedelic-assisted psychotherapy. Integration practices common in clinical work – including sharing circles, meditation, journaling, and expressive arts – reflect similar functions in traditional healing settings: they help interpret and integrate altered state experiences in ways that support long-term psychological benefit (Aixalà, 2022; Gorman et al., 2021).

Fotiou (2020) proposes that psychedelics should not be approached solely as biomedical objects subject to clinical validation, but as components of ethnomedical systems – culturally embedded modalities with their own ontologies and therapeutic logic. This shift would encourage a more pluralistic model of care, grounded in intercultural respect rather than epistemic dominance. Collaborative approaches would also enable deeper engagement with Indigenous frameworks, not as symbolic gestures, but as coequal systems of knowledge relevant to contemporary therapy.

The contrast between Western and Indigenous paradigms reflects deeper philosophical differences. Western science emphasizes empirical observation, standardization, and methodological rigor to minimize subjectivity. In doing so, however, it often overlooks the cultural and ecological contexts in which psychedelic use is embedded. Indigenous systems, by contrast, approach healing as an integrated process that involves spiritual, communal, and environmental dimensions. Knowledge is transmitted through story, lineage, and ritual rather than empirical replication (Williams et al., 2022). Context, reciprocity, and relationship to the natural environment are essential – not optional – components of therapeutic efficacy.

A particular challenge for Western science is the difficulty of interpreting the spiritual and metaphysical content often reported in psychedelic experiences. Visions of deities,

ancestral presences, or revelations of cosmic order can serve powerful psychological functions – yet they resist straightforward neurobiological explanation (Dubini, 2023). Integrating Indigenous frameworks may offer more culturally coherent interpretations of these effects and, in turn, enrich therapeutic models for mental health (Dupuis, 2022).

As collaboration between Indigenous and Western models becomes more visible in psychedelic science, robust ethical frameworks are needed to ensure mutual respect and equitable inclusion. Celidwen et al. (2023) have outlined one such framework for integrating Indigenous healing traditions into biomedical settings. Their eight principles – reverence, respect, responsibility, relevance, regulation, reparation, restoration, and reconciliation – offer a roadmap for respectful engagement. These principles include protecting cultural knowledge through free, prior, and informed consent (FPIC), supporting Indigenous-led research, acknowledging sacred traditions, and ensuring benefit sharing in cases of commercialization. Authors such as Lutkajtis (2020) have further emphasized the importance of accountability and dialogue in addressing ongoing colonial legacies in psychedelic practice.

In addition to ethical frameworks, legal and commercial mechanisms are increasingly relevant to safeguarding Indigenous knowledge in the psychedelic space. Marks and Cohen (2021) outline specific tools for resisting unethical appropriation, such as challenging patent applications at the U.S. Patent Trial and Appeal Board (PTAB) when claims involve longstanding traditional uses. Initiatives like Porta Sophia aim to prevent corporate monopolization by documenting existing ceremonial and medicinal uses of psychoactive substances in open-access repositories, thereby making it harder for companies to claim exclusive ownership.

Beyond defensive strategies, some advocates have proposed a more radical approach: ensuring that both psychedelic compounds and associated ceremonial practices remain in the public domain. This would prevent the privatization of cultural heritage and promote equitable access to therapeutic innovation. While such proposals remain contentious – and raise complex questions about intellectual property, reparative justice, and epistemic sovereignty – they reflect growing recognition that legal structures must evolve alongside ethical ones to support truly inclusive and pluralistic psychedelic futures (Petranker et al., 2020).

At the same time, it is important to clarify the philosophical standpoint from which this inquiry proceeds. While this section highlights the significance of Indigenous knowledge and the need for ethical and collaborative engagement, it does so from the perspective of Western scientific rationality – one rooted in the Enlightenment tradition (*Aufklärung*), committed to methodological rigor, critical thinking, and universality. Indigenous

cosmologies and ceremonial traditions should be respected as culturally and historically meaningful frameworks, particularly in their therapeutic and community functions. However, this respect does not imply epistemological relativism. Not all knowledge systems are equivalent in scope, explanatory power, or universality. The task, therefore, is not to conflate worldviews but to engage across them responsibly – acknowledging asymmetries, avoiding appropriation, and striving for dialogue that is both ethically grounded and scientifically informed.

Discussion Questions:

1. In what ways can Indigenous knowledge of psychedelics inform Western research and therapy – without requiring epistemological equivalence or uncritical integration?
2. Should Western psychedelic science be ethically obligated to share benefits and decision-making power with Indigenous communities – and if so, how?
3. How can we responsibly integrate Indigenous traditions into clinical and research practice without reinforcing extractive patterns or compromising scientific integrity?

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Challenges in ethics and governance of psychedelic states across fields

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The renewed interest in psychedelics across clinical, cultural, and commercial domains has brought questions of ethics and governance to the forefront. As these substances move from countercultural margins into therapeutic clinics, scientific institutions, policy frameworks, and corporate boardrooms, the challenge is no longer simply one of efficacy or safety. It is about how psychedelic states, and the practices built around them, can be responsibly embedded in societies marked by pluralism, inequality, and evolving legal norms. This section explores the ethical and regulatory tensions that emerge across diverse fields of application, from clinical treatment protocols and informed consent to intellectual property disputes, cultural appropriation, and political manipulation. Given the aim to foster safe, evidence-based, and socially responsible psychedelic practice, we examine the risks and requirements for building trustworthy institutions and shared norms in the face of rapid and sometimes chaotic growth.

The clinical use of psychedelics in psychedelic-assisted therapy (PAT) holds considerable promise but presents a range of ethical challenges. While PAT may offer long-term therapeutic benefits — linked to mechanisms such as 5-HT_{2A} receptor agonism and enhanced neuroplasticity — its outcomes are highly sensitive to individual traits, psychological states, and contextual variables. Studies such as Aday et al. (2021) highlight how factors like age, prior psychedelic experience, trait openness, and psychological vulnerability shape therapeutic responses. This variability complicates clinical predictability and calls for a personalized, context-sensitive approach to preparation, dosing, and integration.

Informed consent becomes particularly complex in this setting. Increased suggestibility during and after psychedelic sessions can impair patients' capacity to fully comprehend potential outcomes, which may include acute perceptual distortions, persistent changes in

affect or worldview, and existential distress (Marks et al., 2024). A robust consent process must therefore go beyond formal documentation and involve ongoing dialogue, interactive tools, and staged opportunities to reaffirm or revise consent.

The therapeutic relationship itself raises further ethical concerns. Patients in altered states are especially susceptible to transference, projection, and emotional vulnerability. Even supportive gestures such as physical touch must be carefully regulated and explicitly consented to. To uphold patient safety and trust, therapists must be trained not only in trauma-informed care and psychedelic facilitation, but also in navigating altered states with clear ethical boundaries and transparent disclosure of their own experience and qualifications.

These ethical responsibilities extend beyond the clinic. Many elements now incorporated into PAT — such as the use of music to support emotional flow, memory access, and integration — originate in Indigenous and ceremonial contexts. Music, for instance, plays a central role in traditional shamanic and entheogenic practices, where it serves both therapeutic and spiritual functions (Efthimiou, Cardinale & Kepa, 2024). Yet these contributions are often overlooked or inadequately acknowledged in Western clinical discourse and practice. As Smith and Appelbaum (2022) and Pilecki et al. (2021) have argued, this oversight perpetuates historical patterns of epistemic marginalization and cultural appropriation.

Acknowledging the contributions of Indigenous and traditional knowledge systems requires more than symbolic recognition. It calls for material inclusion — such as engaging Indigenous scholars and practitioners in research and training, integrating plural epistemologies in protocol development, and ensuring equitable benefit sharing (McGuire et al., 2024). Ethical PAT must therefore be grounded not only in biomedical rigor, but also in intercultural respect and sociopolitical awareness.

Finally, as commercial interest in psychedelics accelerates, concerns about profit-driven motives overriding therapeutic integrity grow increasingly urgent (Neitzke-Spruill et al., 2024). Building trustworthy institutions for PAT requires clear regulatory standards,

safeguards against conflicts of interest, and a commitment to prioritizing patient welfare, public benefit, and cultural justice over proprietary control.

Beyond questions of individual safety and clinical ethics, the development of psychedelic therapies raises broader concerns about commercialization and cultural appropriation. Many contemporary practices in PAT, such as the use of music, ritual framing, or integration models, draw inspiration from Indigenous and non-Western traditions. Music, for instance, is a core element in traditional entheogenic ceremonies and is reputed to facilitate emotional processing and memory retrieval (Efthimiou, Cardinale & Kapa, 2024). These practices have informed modern therapeutic techniques, yet their origins are often unacknowledged or commodified. As Smith and Appelbaum (2022) argue, failing to credit these lineages perpetuates epistemic injustice and erasure.

This concern is not merely symbolic. Pilecki et al. (2021) emphasize that centuries of colonial extraction have shaped current global asymmetries in how psychedelic knowledge is produced, legitimized, and capitalized upon. Addressing these asymmetries requires not only citation and cultural sensitivity, but material inclusion – through the engagement of Indigenous and racialized communities in research, clinical practice, and governance. McGuire et al. (2024) further warn against the imposition of Western clinical standards onto ceremonial contexts, calling for reciprocal models of co-existence that respect cultural sovereignty and epistemic pluralism.

At the same time, the rapid growth of the psychedelic industry has sparked a wave of patent filings, with over 1,000 new applications in the 2020s alone (Vculek, Shiwcharan & Sterling, 2024). While patents can protect legitimate innovation, critics argue that many current applications – for aspects such as furniture layout, lighting, or the presence of a supportive therapist – risk enclosing elements that should remain in the public domain (Seidman, 2022). Such overreach can obstruct research, inflate costs, and consolidate market power. Marks and Cohen (2021) caution that when patents are granted for overly broad or culturally derivative claims, they may amount to a form of biopiracy, especially when rooted in traditional plant knowledge or healing practices. Ethical commercialization of psychedelics

must therefore be grounded in transparency, fair benefit sharing, and legal frameworks that prevent monopolization of communal or ancestral knowledge.

Compounding these challenges is a regulatory landscape still in flux. Cohen (2024) observes that regulatory bodies such as the FDA struggle to determine whether psychedelics should be treated as conventional pharmaceuticals or as components of complex psychotherapeutic interventions. The case of esketamine (Spravato) illustrates this ambiguity. Though chemically distinct from classic psychedelics, esketamine was approved under a Risk Evaluation and Mitigation Strategy (REMS), which mandates administration in certified clinical settings due to risks of dissociation and sedation (Jalloh, 2020; Fala, 2019). Its high cost, coupled with stringent monitoring requirements, has raised concerns about equitable access and health system integration. As psychedelic therapies move toward medical licensing, there is a growing need for regulatory models that can accommodate not only safety and efficacy, but also the unique relational, psychological, and cultural dimensions of these interventions.

Finally, the societal impact of psychedelics must be understood in political and ideological terms. While often assumed to foster liberal or progressive values, recent research suggests that psychedelics are “politically pluripotent” – capable of amplifying a wide range of beliefs depending on the user’s social and psychological context (Pace & Devenot, 2021). This underscores the centrality of set and setting: under conditions of heightened suggestibility, individuals may internalize prevailing norms, whether emancipatory or authoritarian. Lonergan (2021) adds that these shifts often occur only when group messages align with pre-existing beliefs, reinforcing rather than transforming ideological leanings. These findings call for careful reflection on the sociopolitical environments in which psychedelics are administered, and on the responsibilities of facilitators, researchers, and institutions in shaping those environments.

Taken together, these concerns point toward a broader challenge: building a shared normative and institutional framework that enables the ethical integration of psychedelic states into open, pluralistic societies. This requires more than clinical protocols or market

regulation. It demands sustained interdisciplinary collaboration, transparent governance, and cultural humility across all fields of application.

Discussion questions:

4. What ethical standards should guide psychedelic-assisted therapy – and how can they be designed to protect patients without over-restricting therapeutic potential?
5. How should psychedelics be regulated – as pharmaceuticals, psychotherapeutic tools, or something entirely new – and what risks come with each model?
6. What kind of societal values should guide the integration of psychedelics – and how do we prevent their use from reinforcing existing inequalities or ideological biases?

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