

**The Role of Relational Healing in Psychedelics: A Comparative Study**

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## ABSTRACT

Psychedelics, acting primarily through 5-HT<sub>2A</sub> receptor binding and modulation of networks such as the default mode network (DMN), can induce shifts in self-perception, cognition, and emotion by promoting neuroplasticity and altering entrenched thought patterns. The biomedical model, emphasizing measurable neurochemical processes, often attempts to extract these neuroplastic benefits while downplaying subjective experiences. This approach may neglect essential elements of mental health, as psychological well-being is tied closely to meaning, context, relational dynamics, spiritual well-being, and community support. Medical anthropology and social constructionist theories demonstrate that focusing solely on a pharmacological viewpoint reduces psychedelic therapy to a biochemical intervention, ignoring cultural, communal, and existential dimensions of healing. As well, standard methods fail to address how risk, suffering, and spiritual experiences factor into transformative therapeutic processes. A holistic approach that acknowledges both neurobiological mechanisms and lived realities is thus critical.

“Set and Setting” underscore the significance of mindset and environment in shaping outcomes, revealing that therapeutic benefits cannot be attributed solely to neurochemistry. This recognition challenges reductionist models and encourages an integrative understanding of healing, centered on subjective experience and relational factors. “Psychedelic Sociality” emphasizes the importance of non-pharmacological variables such as community support, cultural context, and shared meaning-making, in influencing therapeutic results. Because psychedelics operate within a biopsychosocial framework, it is vital to consider co-evolutionary processes, ritual elements, and synergistic “entourages.” While Indigenous traditions often view psychedelics as sacred, relational agents within community and ecology, Western approaches generally administer them strictly as pharmacological tools, overlooking broader relational, cultural, and spiritual dimensions.

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## INTRODUCTION: The Problem of an Overreliance on Pharmacology

In modern medicine, there is a long-standing assumption that medicines heal primarily through their pharmacological effects. This viewpoint, grounded in scientific reductionism, often frames healing as a direct outcome of drug-induced neurochemical interactions. Psychedelic science frames this by examining how psychedelics foster neuroplasticity. While clinical trials and controlled dosages are essential for evaluating safety and efficacy, they are not designed to engage with the Indigenous roots of many psychedelic substances, nor with the relational, ritual, and symbolic dimensions that often shape their healing. As a result, social, cultural, psychological, and spiritual dimensions are frequently sidelined, despite mounting evidence that these dimensions play a vital role in the success and integration of psychedelic experiences.

This thesis invites a reconsideration of the non-pharmacological dimensions of psychedelic healing, particularly the relational and psychosocial contexts in which these experiences unfold. Holistic perspectives suggest that cultural, interpersonal, and ritual factors may be just as influential, if not more so, than the pharmacological properties of the substances themselves. Core to this view is the concept of *set and setting*: the psychological mindset, expectations, physical environment, and social conditions that shape not only the quality of the experience, but also its long-term impact (Hartogsohn, 2018, 2020, 2021, 2022).

To explore this, the thesis focuses on three interconnected themes:

1. **Pharmacological vs. Holistic Models:** Modern Western clinical frameworks emphasize measurable biochemical changes and symptom reduction. In contrast, holistic approaches recognize that psychedelics may work most effectively when pharmacological action is harmonized with relational, ritual, and ecological dimensions of healing.

2. **Set and Setting:** Healing is influenced not only by the substance itself but by the context in which it is taken. Emerging clinical models, such as psychedelic-assisted therapy (PAT), are increasingly incorporating attention to mindset, space, and cultural meaning, thereby echoing practices long embedded in Indigenous traditions.
  
3. **Relational and Communal Healing:** Many Indigenous and traditional societies view healing as a collective endeavor, rooted in family, ancestral connection, and relationship to land. Recent research on psychedelic sociality (Roseman et al., 2022) and communal frameworks (Dupuis, 2021) highlights how psychedelics can deepen social bonds and amplify shared meaning.

## **Methodology**

To evaluate these three themes, I draw on anthropology, psychology, religious studies, and Indigenous studies. My research will primarily be guided by the principles of grounded theory, to construct this thesis through a comparative lens. And when doing so, I will apply the concept of “two-eyed seeing” (Etuaptmumk), introduced by Mi’kmaw Elder Albert Marshall (2012). This project adopts this Mi’kmaw concept that bridges biomedical and Indigenous ways of knowing as both its ethical orientation and research approach. One eye honours the strengths of Western science that are empirical, measurable, and analytic, while the other honours Indigenous and experiential knowledges that are relational, communal, and ecological. Rather than comparing these systems, the thesis aims for a synthetic and dialogical conversation about healing, viewing them as complementary rather than oppositional. This stance shapes every stage of the work: literature selection integrates both scientific and Indigenous sources; analysis engages pharmacological, psychological, and relational worldviews; and ethics are best intentioned to be grounded in relational accountability. Overall, this thesis is written to reflect a commitment to epistemological pluralism, recognizing that more than one valid way of knowing exists. I offer my thesis as an interpretive synthesis that invites ongoing, collaborative research.

**Research Question:**

How can “Western” psychedelic research, often rooted in pharmacological explanations, benefit from a more holistic perspective that recognizes the relational, cultural, and ritual dimensions of healing?

**Thesis Statement**

This thesis argues that while biochemical mechanisms play an important role in therapeutic outcomes, non-pharmacological factors such as relationships, ritual practices, cultural meaning, and communal support, are central to a deeper and more enduring model of psychedelic healing. By comparing dominant clinical models with Indigenous and relational approaches, this work calls for an expanded framework that embraces the full complexity of human transformation.

This thesis posits that while biochemical mechanisms play a role in therapeutic outcomes, non-pharmacological factors connected to meaningful relationships, communities, and cultural traditions are central to a deeper understanding of psychedelic healing.

By comparing clinical perspectives with cultural and communal models, this thesis highlights the relational dimensions long recognized as central to psychedelic healing. These factors, such as meaning-making, sociality, set and setting, and ritual, are not newly discovered; instead, they have often been excluded from biomedical discourse because they challenge its emphasis on standardization, individualism, and pharmacological causality. Many Indigenous traditions, for example, do not see psychedelics as "tools" but as sentient, relational beings that guide healing. This is a view incompatible with dominant clinical paradigms, but essential to understanding the full range of therapeutic meaning.

## THE PHARMALOGICAL MODEL

### The Biological Mechanisms of Psychedelics

Psychedelics create profound changes in consciousness by interacting with the brain's neural networks. Firstly, their primary target is the 5-HT<sub>2A</sub> serotonin receptor, noted as densely expressed in the cerebral cortex and critical for perception, cognition, and mood regulation (Preller & Vollenweider, 2019). Upon binding to these 5-HT<sub>2A</sub> receptors, psychedelics activate increased neuron activity which leads to altered sensory perception and cognition. For instance, this activation also stimulates downstream pathways such as BDNF (brain-derived neurotrophic factor) and mTOR, which are considered essential for neuroplasticity, synaptic growth, and dendritic branching (Ly et al., 2018).

As such, psychedelics significantly affect brain network dynamics and in particular what has come to be called the Default Mode Network (DMN). First characterized by Marcus Raichle in 2001, the DMN refers to a network of interacting brain regions that are highly active when the brain is at rest and less active during focused tasks. The DMN, responsible for self-referential thinking and mind-wandering, exhibits decreased connectivity and activity under psychedelics, leading to ego dissolution and enhanced inter-network communication (Carhart-Harris 2018, 2019, 2021, 2022). Neuroimaging studies reveal that psychedelics disrupt hierarchical brain organization, allowing typically segregated regions to interact freely. To understand this reorganization is to understand the expanded cognition, altered self-awareness, and increased emotional processing seen in psychedelic experiences (Mason et al., 2023).<sup>1</sup>

Neuroscientist Robin Carhart-Harris has described the DMN as the brain's "orchestra conductor or capital city," playing a key role in self-orientation and cognitive stability (Ghosh, 2016). The DMN is viewed as a crucial neural system that plays a role in both mental well-being

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<sup>1</sup> In human research, such processes cannot be directly observed, so claims of structural plasticity rely on indirect markers. For example, neuroimaging and electrophysiological data that demonstrate increased functional connectivity and temporary reorganization of brain networks following psychedelic administration (Carhart-Harris et al., 2016; Vollenweider, 2001). These findings indicate that psychedelics may facilitate new patterns of perception, emotion, and cognition, but translation from cellular to experiential healing remains inferred rather than proven. In summary, psychedelics appear to foster temporary neural and psychological flexibility that may enable new relational and emotional learning. Yet, these neurobiological models remain provisional frameworks, still to be discovered how we can integrate them with experiential and relational understandings of healing.

and pathology: for example, biological reductionist medicine links its neural and metabolic activity patterns to conditions such as depression and anxiety. This is seen when the DMN becomes overactive, it is associated with maladaptive thought patterns, necessitating therapeutic interventions to restore balance. For instance, hyperactivity correlates with excessive rumination and maladaptive self-focus; hyperactive DMN connectivity is associated with depression, anxiety, and OCD (Chou, 2023). As a result, pharmacological interventions targeting the DMN have become a critical focus in neuroscience, particularly in understanding mental health disorders and therapeutic mechanisms.

What is most exciting for psychedelic pharmacological researchers is that the DMN is highly sensitive to serotonergic modulation, particularly through 5-HT<sub>2A</sub> receptor agonists such as psilocybin, LSD, and DMT (Carhart-Harris et al., 2015, 2018, 2019). When these psychedelics bind to 5-HT<sub>2A</sub> receptors, they induce a temporary downregulation of DMN connectivity, which is associated with ego dissolution and increased neural entropy. This disruption in hierarchical brain organization appears to enhance cognitive flexibility, making the DMN a promising pharmacological target for treating disorders characterized by rigid thought patterns, including depression and PTSD (Roseman et al., 2018). For example, NMDA receptor antagonists, notably ketamine, provides rapid antidepressant effects by modulating DMN connectivity and increasing synaptic plasticity (Duman et al., 2019; personal communication ATMA CENA 2024). In contrast, selective serotonin reuptake inhibitors (SSRIs) influence DMN activity by gradually modulating serotonin levels rather than inducing acute receptor agonism. Most precisely, psychedelic science can be tailored to modulate the DMN to the specific pathophysiology of psychiatric disorders, critical for developing targeted biological treatments.<sup>2</sup>

While the default mode network (DMN) remains a dominant explanatory framework in contemporary psychedelic neuroscience (Carhart-Harris et al., 2014), human evidence for its role

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<sup>2</sup> This discussion of SSRIs and the default mode network (DMN) is meant to illustrate patterns within biological psychiatry, not to portray the field as uniform or reductive. Research shows that antidepressants can produce modest DMN changes that unfold gradually over several weeks, and that findings of hyper- or hypoactivity across disorders such as depression, anxiety, and OCD vary across subregions and samples. These should therefore be understood as associative tendencies, not fixed neural signatures. This critique addresses a broader epistemic imbalance within Western psychiatry, that biochemical explanations often take precedence over relational, contextual, and meaning-based understandings of healing. This is not to deny the diversity within the field; medical professionals do integrate biological, psychodynamic, and trauma-informed perspectives, noted subsequently in my thesis. This broadens the frame, positioning neurobiological insights within a pluralistic, Two-Eyed Seeing approach, that values both empirical data and lived experience as complementary, interdependent ways of knowing rather than secondary or derivative phenomenon.

is indirect and should be interpreted with caution. The DMN represents only one among several candidate models still under development. Other explanatory strands such as thalamic gating and cortico-striato-thalamo-cortical (CSTC) circuit models (Vollenweider & Geyer, 2001), predictive-processing and REBUS/free-energy frameworks (Carhart-Harris & Friston, 2019), and global-connectivity or large-scale network-desegregation theories, offer complementary perspectives that broaden the neurobiological picture. At a cellular level, activation of 5-HT<sub>2A</sub> receptors on layer V pyramidal neurons is thought to modulate cortical gain, supporting a distributed and dynamic systems view rather than one confined to a single network locus (Carhart-Harris & Friston, 2019; Preller & Vollenweider, 2018; Vollenweider & Geyer, 2001).<sup>3</sup>

One insight is that these models function less as definitive truths and more as explanatory strands, with each illuminating aspects of an evolving whole. Thus, neuroplasticity, DMN modulation, REBUS, and future models may be understood both as mechanisms and as metaphors for flexibility, openness, and integration. This resonates with the psychological and relational dimensions of healing, where transformation emerges through dynamic interaction rather than isolated processes. In keeping with a Two-Eyed Seeing stance, measurable neural changes and lived transformation can be seen as distinct yet mutually informing expressions of a single relational process of healing.

### **Modern Medicine and the Pharmacological Model for Psychedelics**

Modern Western medicine emphasizes this pharmacological model for psychedelics primarily because it aligns with the biomedical framework that dominates psychiatric and neurological treatment approaches. Disease is defined as an objective biological entity with identifiable pathologies, making pharmacological interventions the primary means of treatment. Biological psychiatry exemplifies this approach by framing mental disorders as neural dysfunctions treatable through neurochemical modifications (Kleinman, 1978). In other words,

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<sup>3</sup> In June 2018, neuroscientists Gregory Scott and Robin Carhart-Harris presented emerging findings at the Royal Hospital for Neuro-disability in London, illustrating evidence that psychedelics can temporarily increase the complexity of brain activity beyond levels typically observed in normal waking consciousness (Bainbridge, 2018). Subsequent neuroimaging analyses confirmed these effects, demonstrating increased signal diversity and entropy under LSD, psilocybin, and ketamine (Schartner et al., 2017). These findings challenged long-standing assumptions that waking consciousness represents the peak of neural organization, suggesting instead that psychedelics may enhance the brain's informational richness. Nevertheless, the precise mechanisms linking receptor-level events to such global transformations in consciousness remain uncertain.

biological psychiatry is a paradigm that posits the etiology of mental illness as being organic in nature. It then follows that the treatments should be material, ie. pharmacological, rather than other models of treatment such as talk or physical therapy because it is assumed that mental illnesses are diseases of the brain.

In the context of psychedelics, this approach to healing is often understood as a pharmacodynamic process with psychedelics as catalysts for neural rewiring. Here, consciousness and complex mental phenomena are entirely reducible to physical brain functions where psychiatric disorders can be effectively treated with psychedelics (Letheby, 2021; Cameron et al., 2023). For instance, it has been demonstrated that psychedelics can reverse neuronal atrophy associated with stress and depression by promoting synaptogenesis and neurogenesis, facilitating long-term structural changes in the brain (Ly et al, 2018). Contemporary psychedelic therapy often centers on these neurobiological processes, emphasizing dendritic growth and structural brain changes as the primary mechanisms of healing, rather than focusing on the subjective, experiential dimensions of the psychedelic state (Letheby, 2021). This biological model has also influenced the development of psychedelic-assisted therapies, where healing is often attributed to measurable changes in brain structures rather than subjective experiences.<sup>4</sup>

One reason cited for this is that the pharmacological model allows for rigorous scientific study of psychedelics under clinical trial conditions, ensuring dose control, safety monitoring, and standardized treatment protocols (Carhart-Harris & Goodwin, 2017). For instance, regulatory agencies such as the FDA, EMA, Health Canada and other regulatory bodies regulate psychedelics to fit within these existing pharmaceutical frameworks.<sup>5</sup> This is essential for legal integration into clinical practice: control distribution, prevent misuse, and facilitate patentability

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<sup>4</sup> “In summary, “psychedelic-assisted psychotherapy” does not capture the true mechanism of change facilitated by psychedelic experience. The effects observed thus far in the best controlled studies of psychedelic treatment must be attributed to the drug itself and not to psychotherapy. In the case of psilocybin, for example, let us say simply “psilocybin treatment.” To continue to use the “PAT” phrase at this stage risks confusing and impeding the development of serotonergic agonists as medications at psychedelic doses. We can think more clearly without it.” (Goodwin, 2024)

<sup>5</sup> This was evident in the FDA’s 2024 rejection of MDMA-assisted therapy for PTSD due to challenges in standardizing patient experiences (Van Elk & Fried, 2023; Psychedelic Community Reacts, 2024). The pharmaceutical industry, which plays a central role in healthcare, operates primarily within the pharmacological model. Companies developing psychedelics aim to create drugs that are approved by regulatory bodies so that can be prescribed and reimbursed by insurance, rather than promoting traditional or Indigenous psychedelic practices. This commercial model is essential for large-scale adoption within Western healthcare systems, thereby reinforcing the dominance of the pharmacological approach in modern psychedelic medicine.

and commercialization (Vollenweider & Preller, 2020). It is therefore reasonable to state that their primary incentive is to follow this model of prescription-based psychedelic-assisted therapy rather than advocating for subjective uses outside of the pharmacological model. This means that non-ordinary states of consciousness triggered by psychedelics are not clinically valuable; moreover, they are also more problematic because they are often understood as being ‘unwanted’ side effects of treatments. Therefore, the aim is to stabilize neurotransmitters and reduce adverse experiences such as distress without requiring patients to confront these challenging emotions. All drugs however can produce side effects ranging from mild to severe. In response, standard practice involves prescribing additional medications to counteract these effects, adjusting dosages to minimize their impact, or transitioning to alternative treatments.

This perspective has spurred the attempt to develop psychedelic-based drugs that preserve their neurochemical advantages while eliminating “hallucinogenic” effects<sup>6</sup>. For instance, synthetic psychedelics, often described as “brain fertilizers,” highlight this role in fostering neural growth (Bains, 2023). The industry is further refining treatments through non-hallucinogenic “psychoplastogens,” harnessing therapeutic benefits without the altered state (Olson, 2018). For example, psilocybin-containing mushrooms can require up to eight hours of immersive experience and significant time for reflection (Carhart-Harris & Friston, 2019). In response, Beckley Psytech (2025) has pursued more “time-efficient” alternatives by delivering psilocin intravenously, thereby streamlining the treatment process. This approach aligns with biological reductionism by minimizing the resource-intensive requirements of “set and setting” such as specialized therapists, dedicated facilities, and extended patient sessions. It also integrates seamlessly into standard clinic workflows, paralleling the existing models for ketamine and esketamine (Spravato). Similarly, Swiss researchers have developed “pharmahuasca,” a pharmaceutical formulation that replaces traditional ayahuasca with more predictable dosing and reduced side effects (Ott, 2012; Mueller et al., 2025).<sup>7</sup> By administering

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<sup>6</sup> While ‘hallucinogen’ defines altered perception and cognition, “entheogens” specifically highlight that nonpharmacological factors need to be considered (Ruck, C. A. P., Wasson, R. G., Hofmann, A., & Staples, J., 1978). This focus extends across history and diverse religious traditions. For instance, “celestial botany” and “divine botany” concepts that link plants to cosmic or divine forces, the roles of “plant intelligence” and “plant signaling” in shamanic healing contexts, the interpretations of biblical, Qur’anic, Hermetic-alchemical narratives reinforcing the idea that plants hold transcendent and cosmological significance.(Freke & Gandy, 1997, Jain & Kapoor, 2007, Dannaway et al., 2007).

<sup>7</sup> Significance Statement: “Traditional ayahuasca, which contains these compounds, has shown potential therapeutic effects but is often accompanied by significant adverse reactions and intense experiences. In this study, we tested a new formulation of intranasal DMT and buccal harmine in healthy participants, using a repeated-intermittent dosing approach to achieve sustained drug release. Our findings demonstrated

DMT via nasal spray and harmine sublingually, they achieved enhanced pharmacokinetics, diminished nausea, and improved overall convenience, effectively tackling many challenges associated with traditional ayahuasca consumption. Therefore, the argument of the pharmacological model is that if psychedelics confer healing purely through biochemical processes, the subjective experience becomes superfluous.

This aligns with the neurobiological disorder of ‘addiction’<sup>8</sup>, being attributed to compulsive behavior shaped by genetic predispositions and substance-induced neural adaptations; rather than to an “illness of meaning” embedded within socially constructed realities (Kleinman et al., 1978; Helman, 1981). Correcting these dysfunctions through pharmaceutical means reinforces the belief that the right pharmacological solution can effectively serve as a cure. In line with this, the DSM-5 defines the adverse experiences of psychedelic use primarily through diagnostic disorders like Hallucinogen Persisting Perception Disorder or hallucinogen-induced mood disturbances, largely excluding psychological, developmental, and environmental factors (Gorman, Nielson, Molinar, Cassidy, & Sabbagh, 2021). By centering on biological mechanisms, this approach supports eliminating challenging aspects of the psychedelic experience to optimize therapeutic outcomes. By this reasoning, an altered state of consciousness or non-ordinary experience could be classified as a disease since disease is broadly defined as any condition that disrupts normal biological functioning; therefore, it is viewed as a neurobiological disorder arising from changes in brain chemistry. Thus, therapy in this context is not only a distraction from healing outcomes (the underlying drug-induced neural reconfiguration) but may also constitute a risk factor in its own right, especially given the profound personal impact of psychedelic experiences.

In summary, this perspective positions psychedelics as pharmaceutical agents whose therapeutic value lies in their ability to induce biochemical changes in the brain. This model prioritizes pharmacological methodologies over experiential, psychological, or cultural dimensions of healing. While this approach strengthens the scientific credibility of psychedelic

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favorable PK/PD profiles, with good tolerability and few side effects. This study represents a step forward in developing safe, controllable psychedelic therapies for individualized mental health care.”

<sup>8</sup> This is known as substance use disorder (SUD) in the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders

medicine, it also fails to be curious whether reducing mental health treatment to neurochemical manipulation fully captures the complexity of human consciousness and psychological well-being.

## **Limitations of the pharmacological approach**

The pharmacological model constrains our understanding by reducing both illness and healing to overly narrow definitions within the realm of psychedelic therapy. While it unquestionably contributes to the renewed acceptance of psychedelic treatments in modern medicine, its emphasis on brain chemistry over subjective experiences and relational contexts introduces significant constraints. In this section, I draw on perspectives from medical anthropology, social constructionist theory, and contemporary psychedelic research.

Firstly, the pharmacological model neglects “lived experiences” and “meaning”. This can be seen in the emphasis on “disease” over “illness”. For example, medical anthropology suggests that modern medicine, often noted as “Western Medicine”, guided by Cartesian dualism, often treats mind and body as separate (Wade, 2017, Kleinman, 1983). In doing so, it privileges measurable pathologies under the category of “disease” while marginalizing the lived experience of “illness” (Helman, 1981; Carel, 2013)<sup>9</sup>. This dualistic thinking has also shaped religious and spiritual interpretations, often privileging Christian-centric experiences or rationalist interpretations while marginalizing Indigenous and mystical traditions (Hannegraaf, 2012) that emphasize holistic healing and relationality.

Another reason why lived experiences and meaning are neglected in the pharmacological model is that evidence-based medicine (EBM) particularly through randomized controlled trials (RCTs), prioritizes standardized and quantifiable outcomes. While this approach is well-suited for pharmaceutical validation, it tends to sideline the subjective, relational, and contextual dimensions of healing. For instance, RCTs, designed for pharmaceutical validation, prioritize

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<sup>9</sup> One example is Oppositional Defiant Disorder (ODD), which is recognized as a clinical disorder in Western medicine but may be understood differently in non-Western cultures, where childhood behaviors are managed relationally rather than through medical intervention (Baydala, 2006; Boersma & Das, 2008).

quantifiable data while disregarding the complex social and relational dimensions of healing. RCTs serve modern pharmacological healthcare models rather than patient well-being, as they reinforce individualistic, biomedical approaches while ignoring structural and systemic inequalities and socio-relational dimensions (Dumit & Sanabria, 2023). This perpetuates the marginalization of non-biological perspectives and overlooks how relationships, cultural narratives, and communal support shape therapeutic outcomes (Tupper, 2002; Blainey, 2021). For instance, research studies are confirming that consistent integration support, strong therapeutic alliances, and community networks significantly enhance the durability of psychedelic-assisted therapy results (Hartogsohn 2018, 2020, 2021, 2022). By neglecting these elements, the pharmacological approach essentially cuts off healing factors because a healing process depends on human connection and holistic well-being (Chun & Lee, 2008; Flückiger, C., Del Re, Wampold, & Horvath, 2018). Psychedelics, however, challenge this model by demonstrating the importance of contextual factors, ex. “set and setting”.

Subjective spiritual experiences also remain largely excluded from modern medical paradigms due to their incompatibility with reductionist frameworks. For instance, mystical or altered states of consciousness are treated as epiphenomena of biochemical processes (Letheby et al., 2024).<sup>10</sup> This inadvertently sidelines the transformative potential of these experiences, which often involve shifts in emotional processing and personal meaning that cannot be captured solely by quantitative measures (Roseman et al., 2022). It is reasonable to state that such standardization is ill-suited for substances that inherently produce diverse and personally meaningful shifts in consciousness. As a result, patients could be under-served by rigid frameworks that do not accommodate their unique psychological and social complexities. A purely pharmacological model, which treats psychedelics like conventional medicine, fails to account for these qualitative aspects of healing.

Letheby (2021) introduces a novel understanding to how we can integrate both neurobiological processes and the subjective dimensions that underpin therapeutic change. Specifically, he maintains that while psychedelics may not always cure an underlying disease

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<sup>10</sup> Indigenous perspectives posit that consciousness, and mystical states are not merely epiphenomena but interconnected with ancestry, land, and spiritual beings.

(the goal of biological reductionism), they can influence one's experience while ill thereby alleviating psychological suffering. Letheby (2021) thus affirms the value of meaning in "set", and to a lesser extent 'setting', as legitimate data for psychedelic research especially for understanding "mystical" or other highly meaningful states. Furthermore, by acknowledging subjective phenomena as clinically significant, this increases our capacity to understand "mystical" or highly meaningful states while balancing reductionist perspectives. For example, psychometric tools like the Mystical Experience Questionnaire (MEQ) facilitate empirical investigations. However, they cannot alone resolve the tension between subjective experiences and broader ontological interpretations (Letheby et al., 2021).

This underlying need to address subjective experience over biology presents a fundamental tension: biological pharmacology endeavors to manage and regulate psychedelic practices, yet the meaning-laden, often transgressive nature of these experiences also reveals certain "risks." These risks are not limited to potential adverse reactions, but include the psychological, existential, and cultural challenges that arise when individuals confront deeply personal insights and seek to integrate transformative meanings. It is precisely this process of discovering and integrating meaning that can catalyze profound growth, prompting us to question whether strict controls may stifle or support the full potential of psychedelic interventions. Scholars have examined the function of liminality and danger in rites of passage, demonstrating that transformation often depends on the power of such experiences to destabilize and challenge participants. In some traditional ceremonial rites, extreme pain and life-threatening circumstances are intentionally included because these elements are believed crucial for fostering deeper insights, facilitating profound personal change, and ultimately illuminating the transformative role of meaning itself.<sup>11</sup>

These experiences have psychological and therapeutic worth regardless if their mystical elements are not objectively verified. These experiences are meaning-full. Therefore, it is

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<sup>11</sup> This perspective aligns with anthropological theories on the necessity of "liminal spaces," which disrupt ordinary structures to facilitate profound change. This concept of liminal spaces suggests that controlled risks are necessary for transformation (Turner, 1967). The citation Van Gennep, 1909/1960 typically refers to the original publication and later translation of Arnold van Gennep's seminal work, *Les Rites de Passage*. The original French edition was published in 1909, and the influential English translation by Monika B. Vizedom and Gabrielle L. Caffee was published in 1960. (van Gennep, 1909/1960). Apostle Paul writes, "We also glory in our sufferings, because we know that suffering produces perseverance; perseverance, character; and character, hope", the theological implications of suffering, perseverance, character, and hope within the context of Paul's letter. (Romans 5:3-4: Longenecker, 2016)

reasonable to state that many practices, including ‘spiritual’ practices, involve inherent risks, such as psychological distress or even psychotic breaks. And these risks are considered significant to the journey and cannot be eliminated without diluting its power. In other words, meaningful growth, including ‘spiritual growth’, cannot occur without being vulnerable to the risk potential factors which are inherent in the transformative potential of psychedelics. As such, the role of risk in psychedelic practices directly asks whether we can get psychedelic benefits without it. Most importantly, part of the risk profile may also be seminal to the health profile, that the agreement to enter in the psychedelic spaces is to take a fundamental “risk” that may also be a fundamental factor for healing.

The challenge then is how to navigate psychedelics so to ensure that those practices remain meaningful without causing harm. Recent research has expanded the understanding of challenging psychedelic experiences, moving beyond previous limitations to encompass a broader range of characteristics as well as highlighting subjective experiential tensions between suffering, transformation, and risk (Romeo, 2025)<sup>12</sup> Mainstream reductionist approaches seek to eliminate distress<sup>13</sup>, yet Evans (2023), Turner (1995), and Mathai (2024)<sup>14</sup> argue that suffering itself plays a role in healing. Studies on psychedelic experiences confirm that social support and adaptive coping strategies improve outcomes particularly when recovering from trauma (Maté, 2011; Levine, 2005; Robinson, 2024; Van der Kolk 2014) while Indigenous and spiritual traditions embrace suffering as integral to healing (Blainey, 2021; Ahenakew & Asapass, 2016).<sup>15</sup> Furthermore, the common phrases of “good trips” and “bad trips” often used in discussions of psychedelic use may represent an overly reductive framework because they obscure the complexity and multifaceted nature of psychedelic encounters. For example, psilocybin journeys, like most psychedelics, frequently encompass a broad emotional range that

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<sup>12</sup> Highlights: Intensity of the psychedelic experience was associated with clinical improvement (Romeo, 2025)

<sup>13</sup> “Interest in psychedelic substances as medicines is rising. Identifying the neural circuits that mediate the benefits of psychedelics could pave the way for long-lasting anxiety treatments without the short-term sensory disturbances.” (Knox and Quan, 2025)

<sup>14</sup> This study of 679 psilocybin users found that about 70% experienced some degree of shame or guilt during their trip, with an average duration of 10 minutes to an hour. Individuals who were able to work through these difficult emotions showed higher levels of well-being two to four weeks later with better outcomes than those who did not feel shame or guilt at all. This suggests that engaging with challenging emotional content under the influence of psilocybin may boost its therapeutic potential. However, roughly 30% saw an increase in day-to-day shame, emphasizing the importance of proper psychological support before, during, and after a psilocybin session. Overall, the findings highlight how confronting and processing uncomfortable feelings can be pivotal for long-term mental health benefits.

<sup>15</sup> Hart (2021) highlights self-medication as a coping strategy that can provide relief or lead to harm, depending on context. The stigma surrounding improper psychedelic use stems from biological reductionist biases.

unfolds in identifiable phases. Recent empirical findings illustrate this phenomenon through the qualitative mapping of psilocybin experiences derived from hundreds of trip reports (Brouwer, 2025).<sup>16</sup> As well, traditional ayahuasca ceremonies that involve group settings, guidance from experienced shamans, music, and ritual practices that shape and direct the experience, may also be ‘stressful’ (Tupper & Labate, 2015; Labate & Cavnar, 2018). In summary, these elements enhance psychological insight, emotional catharsis, and communal bonding which are vital for healing trauma and mental health conditions. The medicalized approach to psychedelics often removes these dimensions, prescribing substances in clinical or laboratory settings without incorporating meaningful subjective experiences of engagement alongside journeys of distress.

There are holistic approaches that integrate cultural, relational, and existential dimensions. These approaches move medicine toward more inclusive, patient-centered care by acknowledging that recovery includes meaningful social and/or spiritual engagements. For example, scholars emphasize social support and self-determination as crucial to improving patient outcomes (Chun & Lee, 2008; Flückiger, C., Del Re; Wampold, & Horvath, 2018; Tynan, 2021). Likewise, research indicates that a positive mindset and strong therapeutic rapport significantly enhance the therapeutic benefits of psychedelic experiences (Leary, 1963; Osborn & Haijen, 2024; Levin, 2024). Furthermore, many global and Indigenous healing traditions provide an alternative perspective, situating health within communal, spiritual, and ecological dimensions (Metzner, 2013; Tynan, 2021). Likewise, psychedelic spiritual practices place a central emphasis on relational healing as a fundamental aspect of this holistic approach (Rojas, 2021; Hannegraaf, 2012; Ahenakew & Asapass, 2016).<sup>17</sup> When medicine reduces psychedelics to purely pharmacological tools, it severs them from the communal support, ceremonial rituals, and ancestral knowledge that have historically shaped their meaning (Labate & Cavnar, 2014). Consequently, a narrow focus on neurochemistry or personal introspection fails to capture the

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<sup>16</sup> Participants reported a distinct emotional trajectory that began with an *Angsty Ascent*, characterized by anxiety (28%), nausea (34%), restlessness (21%), and confusion (17%), which researchers linked to the uncertainty of the onset phase. This was followed by a *Stillness Phase*, during which sensations such as energy rushes (19%), tingling (15%), coldness (9%), and heaviness (9%) induced a quieter, more introspective state. As the acute effects subsided, participants described a *Blissful Return*, marked by pleasantness (34%), peacefulness (22%), reflection (17%), and sociability (16%). Finally, a *Clarity Window* emerged, where the reduction of confusion gave way to sharpened mental acuity, heightened “flow states,” and a renewed appreciation for everyday experiences.

<sup>17</sup> Alternative healing traditions incorporate relational frameworks beyond conventional psychology. Orisa healing practices blend biological, psychological, social, and spiritual dimensions (Abímbólá, 2021). These traditions critique medical labeling, which reduces individuals to diagnostic categories, neglects strengths, and fosters social exclusion. Ubuntu philosophy, rooted in collective healing, emphasizes communal well-being (Mugumbate, 2013).

full breadth of these holistic practices by framing Indigenous insights as nothing more than “data” for pharmaceutical research. By respecting the relational communities and spiritual foundations at the core of many healing traditions, healthcare can expand beyond reductionist models that honour both the biochemical and the lived dimensions of human experiences.

The tension between these two perspectives becomes most evident when exploring cultural and experiential understandings of healing in relationships. This contrast underpins how individuals construct meaning around illness, often shaped by communal beliefs, relational support, and personal narratives. Consequently, many medical anthropologists, phenomenologists, and clinicians argue that focusing solely on disease indicators neglects the cultural contexts and lived experiences that shape how people heal in relationships (Carel, 2013; Kleinman, 1978; Schooler & Schreiber, 1991). Overall, therapy is inherently relational, aligning with psychodynamic perspectives that emphasize how relationships, particularly in childhood, shape personality and mental health (Maté, 2011). Advocates argue for expanding psychological interventions beyond behavior therapy (BT) and cognitive-behavior therapy (CBT) to include psychodynamic approaches<sup>18</sup>, particularly in psychedelic-assisted therapy, where relational meaning-making plays a crucial role (Zamaria, 2025). Historically, psychotherapy has been shaped by relational thinkers. Freud (1916-1917) explored unconscious mental processes and defense mechanisms, while neo-Freudians like Jung (1965) introduced the collective unconscious, and Adler (1927) emphasized belonging. Also, existential, and meaning, based psychotherapies, as seen in Frankl’s (1962, 1986) Logotherapy, centers on the search for meaning in adversity. Yalom (1980) demonstrated that group therapy fosters meaning through relationships. Other researchers such as Moerman (2022) highlights the "meaning response," showing how personal and cultural belief, and therapeutic settings, influence healing, while Mitchell & Greenberg (1983) integrates drive-based and relational models of psychological development in object relations theory. All in all, healing is fundamentally a relational process, created through connections rather than in isolation (Binder, 2022).<sup>19</sup>

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<sup>18</sup> For example, a group of researchers wrote a letter on behalf of numerous signatories to the same letter addressing the World Health Organization’s Psychological Interventions implementation manual. In it, they stated that the WHO guidelines on psychological interventions should include a broader range of therapies, including psychodynamic therapy, rather than predominantly endorsing behavior therapy (BT) and cognitive-behavior therapy (CBT).

<sup>19</sup> If we integrated object relations theory with Indigenous psychedelic traditions, it would expand understandings that humans do invest non-human entities with emotional significance and that the same relational mechanisms can apply. Such a perspective recognizes and highlights the

A relational approach highlights the importance of interconnectedness in health and healing. Moving beyond purely medicalized models allows for more inclusive and culturally responsive therapeutic practices, embracing holistic and spiritual dimensions of care.

## **SET AND SETTING**

While ‘set’ (mindset, expectations, intentions, traits, preparation) is recognized as an important factor, it is in the second factor, “setting”, as illustrated by research on “set and setting,” which highlights how non-pharmacological variables (such as environment, mindset, and social context) shape and modulate psychedelic experiences. These findings suggest that context may be as important as the substance itself, thereby calling into question a second assumption in reductionist research, namely, that set and setting merely “enhance” or are secondary to the drug’s pharmacology. Emerging evidence shows that contextual influences can independently drive positive outcomes, even where the psychoactive effects are minimal<sup>20</sup> (See Appendix B).

Thirdly, in light of the first two factors highlighting the prominence of non-pharmacological influences, it follows that another pivotal implied factor in healing could be ‘relationships. By “relationships,” we refer to the ongoing, supportive bonds established among individuals, including therapeutic alliances, peer connections, and community networks. Such connections create a space for empathy, trust, and shared understanding, which collectively enhance the integration of the psychedelic experience and foster deeper healing. As Hartogsohn (2018, 2020, 2021, 2022) points out, consistent integration support, strong therapeutic alliances, and communal networks (ancestral knowledge, ritual structures, meaningful connections), all exist in non-psychedelic contexts and do similarly promote profound transformation. In settings

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complexity of human–non-human relationships as an extension rather than a core principle of classical object relations. Expanding perspectives beyond human-centered models allows for a broader understanding of interactions between human and non-human entities, emphasizing the complexity of relationships.

<sup>20</sup> This interpretation is plausible within certain experimental designs such as microdosing or placebo-controlled trials where participants report therapeutic benefits despite minimal or absent psychoactive effects. However, such findings require tight citation and boundary conditions as expectancy, context, and participant belief can significantly influence outcomes.

where these non-pharmacological factors primarily drive positive outcomes, it could be speculated that any “power” attributed to the psychedelic substance could instead be replicated by other approaches that invoke similar relational and meaning-making processes. Psychedelic research explores this idea through the concept of “set and setting.”

What is fundamentally clear is that set and setting research has broadened research beyond the limitations of biology alone, overseeing causation and healing into the fullness of biopsychosocial factors. Research is robust showing the importance of these factors outside of the psychedelic factor itself (Klerman & Dimascio 1960; Devenot, 2023; Dimascio and Rinkel 1963; Feigenbaum & Feldman 1963; Leary et al. 1963, Carhart-Harris et al. 2018; Hartogsohn 2018, 2020, 2021, 2022; Kramer, 2022; Krabbe, 2024; Metzner, 1967); within Indigenous communities (Brabec 2011; Braun 2010; Hartogsohn 2022; Helman 2001; Metzner, 2013), in the Brazilian Ayahuasca churches that use Ayahuasca as the sacrament (Hartogsohn, 2017, 2021; Labate, 2018; Blainey 2021); as well as in the Native American church that uses peyote as the sacrament (Hartogsohn 2022). Most critically, this research continues to show the meaning components that are enhancing drug effects missing in mainstream medicine clinical trials, such as the application of cultural and spiritual ways acting as set and setting factors (Dyck, 2012, Smith and Snake, 1998)<sup>21</sup> (See Appendix A). For example, meaning components such as within shamanic or neo-shamanic ceremonies; therapy usages; the structure of a circle, with an altar or fire; presence of an experienced elder or guide, done in semi-darkness, using drumming, rattling, or singing; and using the four directions to cultivate space, are all meaning-full (Mezner, 2013). Winkleman (2019) states clearly what the entheogenic knowledge<sup>22</sup> teaches us: it brings mythic beliefs and the supernatural into our experience; gives our spirit access into the supernatural world; activates powers within us and outside of us; allows direct relationship with animals; transforms us through ego-death and rebirth; informs us with knowledgeable visions; heals us emotionally; and finally, integrates our social group with time tested approaches.

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<sup>21</sup> For instance, Hartogsohn (2022) examines non-positive set and setting variables with MDMA as well as other nonpsychedelic areas such as mindfulness research. Another example is the cultural examinations of “mental health challenges” alongside spiritual factors and pharmacological agents (Thompson 2022, Wallace 1959).

<sup>22</sup> Entheogenic knowledge refers to ways of knowing, understanding, and relating that arise through the intentional use of psychoactive plants or substances in spiritual, ceremonial, or healing contexts: this distinguishes these sacred and/or consciousness expanding uses from both recreational and pathological framings of drug use.

Eisner (1997) adds ‘matrix’ to set and setting theory, considering all environmental elements such as the full contextual background of users, the present context of users, and the everyday living environment after using psychedelics. Hartogsohn (2017) introduces the term “collective set and setting” to acknowledge that broader social environments encompassing cultural beliefs, group attitudes, and community norms, do significantly shape the nature and impact of psychedelic experiences. Going beyond ‘set and ‘setting’, this view emphasizes how communal narratives, historical precedents, and shared expectations interact with and influence both the process and outcome of psychedelic encounters. Petranker et al (cited by Hartogsohn 2022) points out that set and setting research is also limited outside of macro-dosing discussions, yet it is in these other areas where set and setting may explain research gaps. One example is microclimates, in which Hartogsohn (2022) proposes the “concept of psychedelic modality to describe how distinct sociocultural microclimates lead to thematic aggregates in which distinct types of expectations, intentions as well as physical, social, and cultural environments all tend to cluster, producing characteristic outcomes and results” (p. 579). Going further into spiritual modalities, one can examine corresponding sub modalities of the psychedelic churches. For instance, the ways in which the Native American Church uses peyote, or the Santo Daime’s use of ayahuasca (Daime), in conjunction with Christianity, leads to unique spiritual outcomes (Hartogsohn 2022, Blainey 2021). Also, “psychological common factors” theory suggests that common setting factors significantly influence the therapeutic outcomes of psychological therapy (Gukasyan and Nayak, 2022).<sup>23</sup>

## **Psychedelic Sociality: How Community and Relationships Shape Healing**

Researchers and the broader psychedelic community are increasingly acknowledging the crucial role of social factors by commonly using the term “community” to describe the vital role of relationships in fostering well-being during psychedelic experiences.<sup>24</sup> By “community,”

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<sup>23</sup> For example, ritual proves effective by offering individuals a familiar framework to navigate unfamiliar experiences, thereby increasing their sense of mastery and self-confidence. While rituals vary across cultures, the underlying mechanisms are few and are highly consistent, and are often leveraged for community cohesion (Turner, 1995).

<sup>24</sup> The entire school of Object-oriented Ontologies expands claims around relationships and relationality.

this refers to the network of relationships and supportive connections that individuals consciously maintain such as connected peers, family members, and broader social groups. These interconnected bonds help shape collective attitudes, shared beliefs, and mutual trust, all of which contribute to a nurturing environment that profoundly influences individual experiences and outcomes.

This understanding has become so central that the concept of "psychedelic sociality" was recently examined across twenty-one multidisciplinary research papers (Roseman et al, 2022). What is not recent, however, is the understanding that is central to many traditional societies, that healing is inherently communal. It encompasses not only the individual, but also their relationships with family, ancestors, and, by extension, the land and animals, healing is inherently communal. Healing is seen as a collective process, emphasizing relationships rather than focusing solely on the individual (Winkleman, 2021). Research consistently demonstrates that psychedelics influence interpersonal outcomes, fostering increased empathy, trust, and connection, which in turn enhances their therapeutic potential (Roseman, 2022).

First, to understand how interactions among psychedelics, people, and communities might shape particular outcomes, researchers in psychedelic sociality look beyond isolated pharmacological mechanisms to the "extra-pharmacological" influences on meaning-making. For example, they consider how the wider influence of psychedelics likely involves a complex network of receptors that affects brain circuitry, mental health, and the "meaning" individuals assign to their experiences.<sup>25</sup> A purely pharmacological lens that reduces "meaning" to neural processes, however, overlooks how social and cultural contexts crucially co-create the significance of these encounters. By integrating neurobiological insights with an appreciation of communal bonds and cultural frameworks, psychedelic sociality foregrounds how experiences emerge through relational processes rather than through neural pathways alone.

Crucially, their examination of the concept of "psychedelic sociality" highlights how shared psychedelic experiences can foster empathy, social closeness, and group synchrony

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<sup>25</sup> While they acknowledge psychedelics act on receptors like 5-HT<sub>2A</sub>, 5-HT<sub>2C</sub>, and 5-HT<sub>1A</sub>, and classic psychedelics (LSD, psilocybin, and DMT) primarily target 5-HT<sub>2A</sub>, recent evidence points to the importance of other receptors like TrkB or 5-HT<sub>1A</sub> for therapeutic effects (Cameron, 2023) working with broader entourage social effects, meaning pharmacology alone overlooks communal significance.

(Roseman, 2022; Langlitz 2021; Vizeli, 2024). This social dimension can broaden psychedelic therapy into a bio-psycho-social model by acknowledging that both positive changes (ex. shifts in personality traits, improved interpersonal bonds) and adverse outcomes (e.g., paranoia or isolation) are an interplay between receptor activation and cultural practices, collective rituals, and supportive networks. Research demonstrates that certain receptor functions amplify personal narratives, beliefs, and symbols, thereby intensifying how individuals relate to one another and to the world (Preller et al., 2019, 2020). By illustrating how social bonds, cultural practices, collective rituals, and supportive networks shape both beneficial and adverse outcomes, the concept of “psychedelic sociality” expands our understanding of psychedelic therapy beyond mere receptor activation. This perspective demonstrates that fostering empathy, social closeness, and group synchrony involves more than just neurological events; it also depends on the meaningful context in which these substances are consumed and integrated. Consequently, rather than attributing prosocial effects solely to pharmacology, we see those non-pharmacological elements being relationships, shared beliefs, and communal structures, as critical in mediating how individuals experience, interpret, and ultimately benefit from psychedelics.

Psychedelic Sociality research further suggests that psychedelics may have shaped human social behavior and cultural development through a process of coevolution (Roseman, 2022). They did this by using rituals to tap into ancient brain circuits in the limbic–striatal–thalamocortical and salience/attentional networks, potentially enhancing core social and cognitive processes.<sup>26</sup> By interacting with receptors such as 5-HT<sub>2A</sub>, these substances appear to heighten openness and enhance shared experiences like music, symbolic communication, and relational beliefs (Henrich, Boyd, & Richerson, 2008). One example is that 5-HT<sub>2A</sub> receptor activation can either induce anxiety in low-trust settings or foster bonding in supportive environments, indicating that psychedelics’ effects are highly dependent on social context. So, building on the coevolution hypothesis, psychedelics supported human social and cognitive flexibility, influencing mate selection, conflict resolution, and group collaboration (Winkelman, 2019, 2021). Also, early humans occasionally ingested substances like psilocybin, eventually

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<sup>26</sup> Winkelman (2021) also draws parallels between shamanic guidance and Vygotsky’s scaffolding theory, highlighting how skilled practitioners can foster a “zone of proximal development” for participants (Malik, 2017). By guiding individuals through preparation, structured ceremonies, and post-integration, shamanic practitioners may help participants gradually internalize the psychological, social, and cultural benefits of psychedelic experiences. This framework suggests that modern PAT could benefit from merging shamanic insights with biomedical methods to expand our clinical understanding beyond mere pharmacology.

integrating them into communal ceremonies: this process may have bolstered cooperative behaviors in what may be our “socio-cognitive niche” (Rodríguez and Winkelman, 2021). From an evolutionary psychology standpoint, shamanic rituals likely harnessed these effects by combining psychedelics with specific “set and setting” factors, such as dance, drumming, or spirit-focused practices.

Psychedelic Sociality research also explores “entourage effects,” the idea that many compounds work synergistically to produce therapeutic outcomes. For instance, traditional “plant-based” medicines,<sup>27</sup> which includes fungal-origin medicines, often involve complex chemical profiles that surpass the sum of their individual components (Ribeiro, 2018). As an example, aeruginascin alongside psilocybin may contribute to the overall efficacy of certain mushroom species (Chue, 2022). Cannabis research similarly reveals that combining THC with other phyto-cannabinoids yields more robust results than using THC alone (Sanchez-Ramos, 2015; Russo, 2019). Piercey’s (2024) study of festival-goers who paired cannabis with psychedelics corroborates this synergistic perspective: nearly half the participants reported calmer, more balanced experiences, while some encountered greater confusion or anxiety. These findings also suggest that synergy is not confined solely to pharmacological interactions among compounds. By expanding the concept of the “entourage effect” to include extra-pharmacological practices such as communal support, cultural traditions, and ritual frameworks, we see how social and contextual factors can likewise shape therapeutic outcomes. This broader understanding highlights that an individual’s experience and integration of psychedelics emerge from an interplay of biological, psychological, and cultural influences, rather than from molecular action alone.<sup>28</sup>

Psychedelic sociality research, in summary, makes clear that multiple active compounds work in tandem, but it also highlights how these pharmacological interactions alone

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<sup>27</sup> The phrase “plant-based medicines” functions more as a relational or spiritual term than a biological one.

<sup>28</sup> While I have not discovered this perspective in psychedelic research, “assemblage theory” highlights how relationships, cultural narratives, and broader contexts can be just as important as the substances themselves. Ex. a theory could be explored that therapeutic outcomes emerge from a web of interactions (noted as ‘synergy’) rather than from ‘a drug’ alone because a shift in any part of this assemblage can shape the overall experience. Why? This approach “decenters” the psychoactive substance because its impact is always situated within an interconnected network of actors, contexts, and relationships. This implies future research could look at this ‘synergy’ between trusted guides, a supportive environment, ritual aspects, etc., as well as ‘borrowing’ from aspects of assemblages (DeLanda, 2016).

are insufficient to fully account for psychedelic healing. Even though biochemical mechanisms, such as 5-HT<sub>2A</sub> receptor activations, contribute to therapeutic outcomes, these findings reveal that meaningful relationships, communal practices, and cultural traditions are equally integral in shaping and sustaining transformative experiences. By adopting this broader perspective, we can see healing as a process rooted in biopsychosocial inputs: an overall “**relational entourage**” composed of cultural practices, environmental contexts, and interpersonal connections.<sup>29</sup> Recognizing this interplay not only clarifies how psychedelics can facilitate profound change, rather it also underscores the importance of integrating extra-pharmacological elements for a more nuanced, effective approach to psychedelic therapy.

### **Indigenous vs. Western Approaches to Psychedelic Use**

To meaningfully compare Indigenous and Western approaches to psychedelics, it is essential to begin with their underlying purposes. In many Indigenous traditions, psychoactive plants are revered as sacred medicines, deeply embedded within spiritual, ecological, and communal worldviews. For example, Indigenous Traditions tend to revere plants as sacred medicines deeply integrated into spiritual, ecological, and communal frameworks. Healing extends beyond individual symptoms, emphasizing reciprocal relationships with plants, ancestors, and the land (Taita Alonso-Muisca Nation, personal communication, 2023, Dev, 2018, 2020). Such ceremonial use is not merely therapeutic but fundamental to cultural identity, communal bonding, and spiritual continuity.

In Indigenous contexts, set and setting are not external parameters to be controlled, but are embedded in ceremonial practices involving communal participation, music, perfumes, fasting, and dietas (Dupuis, 2021; Shanon, 2002; O’Shaughnessy, 2021). The entire

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<sup>29</sup> This belief resonates with anecdotal and historical findings about the ‘healing’ process, such as from citizen science where large, diverse communities offer a “bottom-up” informational reservoir that can complement formal research (Fadiman, 2021). Holistic psychiatrist Florian Birkmayer (2021, 2022, 2024) highlights the therapeutic role of aromas in psychedelic-assisted therapy. He points out that sacred herbs and incense (ex. sage, cedar, palo santo, black pepper essential oil) have long been integral to ceremonial practices. This notes a historical track record of safety and efficacy. Birkmayer also reminds us that dopamine and serotonin, while integral to human neurobiology, are themselves part of an ancient biochemical heritage derived from plants that once co-evolved with pollinators. These observations reinforce the notion that psychedelic therapy may benefit from embracing a broader ecological and evolutionary framework.

ceremony/ritual constitutes ‘set and setting’ intentionally designed to accommodate individual and communal challenges. It is all part of longstanding cultural traditions. For example, continuous singing (icaros) or strategic silences may be integral to connecting participants with ancestral knowledge and the “spirit” or “family” of the plant. These elements are not mere therapeutic tools but part of a larger relational network that shapes the experience. A deeper relational responsibility underpins these elements: shamans or healers co-create ritual space in which every sensory input is meaningful. Rather than simply “optimizing” outcomes, these rituals reinforce communal bonds and demonstrate respect for plant intelligence.<sup>30</sup>

What is fundamentally different is how we decipher these relationships. Many Indigenous groups regard “psychedelics” like ayahuasca as sentient, plant humans, and are guiding forces that co-direct the healing journey (personal communication, Ronin Nai Shipibo maestro, 2022). They may or may not give knowledge as relations are established with them and connected to more-than-human beings (Viveiros de Castro, 2012). Engaging with these plants involves long-term commitments, such as “dietas.” More than simply a set of restrictions, dietas fundamentally recalibrate relational fields, temporarily suspending ordinary human social interactions (and everyday ways of eating) to foster new connections with plant teachers. This relational aspect places dietas within a broader notion of “psychedelic sociality,” emphasizing how dietary and behavioural practices become a means of coexisting and communicating with more-than-human others. Through ethical responsibilities, fasting, and behavioral discipline, participants build relationships that go beyond the human sphere, highlighting how plants and other beings co-create the healing process (Gearin, 2018; O’Shaughnessy, 2021). The plant is treated as family and its “intelligence” guides the healing process which, in Indigenous frameworks, is deeply holistic and dimensional: psychological, communal, ecological, and spiritual (Dev, 2018, 2020).

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<sup>30</sup> By way of contrast, biomedical protocols regard set and setting as external variables to be controlled or standardized in order to minimize unpredictability (Golden et al., 2022). Ritual is reframed into specific clinical activities such as music therapy, mindfulness techniques, or curated environment that aim to enhance safety and therapeutic results, rather than preserving cultural traditions (Fotiu, 2020). For instance, measures are controlled to optimize therapeutic outcomes (Kaelen, 2018; Gloekler, 2024). So, although patient preparation and integration are acknowledged, these elements typically lack the profound cultural or spiritual depth of Indigenous ceremonies. In some Western clinical trials, music is referred to as a “hidden therapist,” while silence used in ceremonial contexts remains underexplored (Kaelen, 2018, Gloekler, 2024). While the overarching goal is safety and outcome consistency, there is no exploration of cultural reasons for usage of silence vs music.

In such traditional cultures, the entire healing practice is embedded in spiritual obligations, communal teachings, and ecological reciprocity (Labate & Cavnar, 2014; Sanabria, 2023).<sup>31</sup>

During ceremonies, music, chanting, and other multisensory elements are considered part of an “entourage” that interacts with the plant’s agency (Dupuis, 2021; Shanon, 2002, 2010; Narby 2013). Communal support is central, and the healing process can evolve spontaneously based on shared insights and the plant’s perceived guidance. These traditions do not categorize set and setting as merely techniques; rather, they are integral aspects of an entire way of life.<sup>32</sup> By contrast, in biomedical approaches factors such as communal bonding or spiritual accountability are optional components rather than structural cornerstones.<sup>33</sup>

Indigenous healing is grounded in a collective commitment to healing, where transformation is understood as a communal, not merely individual, process. It involves the assignment of participatory roles that engage each person actively in ceremony or ritual, emphasizing relational and spiritual involvement. Central to this model are Elders, Knowledge Keepers, and community leaders who offer teachings, prayers, and songs, grounding the process in tradition and cultural continuity. Healing begins with intention-setting and concludes with communal integration, framed within a narrative and moral context rather than a clinical one. Cultural and spiritual transmission occurs through designated “helpers” who carry and share ancestral wisdom, making healing inseparable from the stories, songs, and rituals of the people. The practitioner’s role is thus reimaged as a mediator: someone who facilitates a relationship

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<sup>31</sup> This ‘place’ of practice is not merely a geographical location, but a dynamic entity intertwined with identity, history, and spirituality. It acts as a living record of ancestral narratives, cultural practices, and ecological knowledge (Keepness, 2023). This is ‘land-based’ relationality.

<sup>32</sup> It is important to avoid framing Indigenous and Western approaches as binary opposites (ie. Indigenous as relational or sacred and Western as reductionist or clinical) since contemporary psychedelic-assisted therapy (PAT) sometimes integrates, in practice, relational and contextual elements such as preparation, music, therapeutic dyads, and integration as structural features of treatment (Carhart-Harris et al., 2014; Carhart-Harris & Friston, 2019). The distinction lies not in their practice but in their rationale: biomedical frameworks justify these practices through psychological safety, neuroplasticity, and therapeutic alliance, whereas Indigenous or ceremonial traditions understand them within cosmological and relational ontologies. Recognizing this overlap prevents reductive comparison and allows for dialogue grounded in Two-Eyed seeing : references to “plant intelligence” can be read not as empirical claims about cognition, but as expressions of an Indigenous relational ontology that attributes agency and wisdom to living systems rather than isolating consciousness within the human mind (de Castro, 2004; Kohn, 2013; Kimmerer, 2013).

<sup>33</sup> In modern day approaches, psychedelics are generally treated as pharmacological agents administered under controlled conditions for specific pathologies. While therapists may encourage meaningful reflection during and after sessions, the substance itself is not viewed as a teacher or living entity. The focus rests on pharmacological actions influencing responses. There is no discussion about ongoing relational or spiritual bonds with the medicine. While post-session integration may explore subjective insights, the overarching model remains rooted in medical diagnostics and individual well-being (Dumit, & Sanabria 2022).

not only between participants and plant medicines but also with the broader community and spiritual world. A stark contrast emerges.

This relational, ceremonial approach reflects how Indigenous ceremonies weave psychoactive substances into communal rituals, spiritual obligations, and ecological knowledge, treating plants as relational agents rather than mere “drugs.” In contrast, Western practitioners tend to emphasize standardized protocols, symptom alleviation, and data-driven outcomes in clinical or research-based contexts. Moving forward, a two-eyed approach can combine rigorous Western scientific methods with the relational depth characteristic of Indigenous traditions, which could align with aspects of psychedelic sociality (Roseman, 2022). Such a synthesis would not only broaden the therapeutic potential of psychedelics but also safeguard and respect the ancestral wisdom that has shaped these sacred medicines for generations.

This synthesis could take different forms. Some practitioners and organizations may pursue intensive, reciprocal collaborations with Indigenous healers (see Appendix E), grounded in shared ceremony, co-designed protocols, and community involvement. Others may draw on Indigenous wisdom more indirectly, allowing their work to be ethically shaped by core insights without claiming direct participation. In both cases, what matters is a sustained commitment to respect, humility, and responsibility: recognizing that Indigenous traditions are not toolkits to be extracted from, but living systems of knowledge embedded in culture, land, and relationship. Whether through close partnership or reflective influence, the goal is not merely to incorporate Indigenous elements, but to allow their relational ethics to reshape how healing is imagined and practiced in psychedelic-assisted therapy.

Appendix C offers a proposed framework for Two-Eyed Seeing, designed to support respectful and sustained collaboration with Indigenous healers. It outlines guiding principles such as shared decision-making, mutual respect, and relational accountability, that can inform deep partnerships. At the same time, the framework may serve as an ethical compass for those engaging with Indigenous traditions from a greater distance, helping ensure that such engagements remain transparent, non-extractive, and grounded in ongoing reflection on positionality, privilege, and responsibility.

## **Framing Indigenous and Western Ontologies of Healing**

This project seeks to hold Indigenous and Western approaches to psychedelic healing in dialogue, rather than in opposition. My comparison between ceremonial, relational healing practices and protocolized Western clinical models is meant to expose their differing ontological orientations, not to portray them as mutually exclusive or hierarchically ordered. While Western psychedelic-assisted therapy (PAT) increasingly includes relational dimensions such as preparation, music, and integration, these are typically justified within a biomedical rationale. As such, they are used as variables that enhance safety or treatment adherence rather than as sacred or cosmological relations. By contrast, Indigenous and animist traditions embed healing within a network of reciprocal relations-relational entourage, among humans, land, ancestors, and other-than-human beings. The distinction, therefore, is one of ontological grounding rather than moral or scientific superiority.

A key example concerns the idea of “plant intelligence.” In mainstream biology, plant responsiveness through signaling, phototropism, and chemical communication is described as adaptive behavior, not as evidence of consciousness or intention (Letheby, 2021). Within Indigenous and relational ontologies, however, intelligence is ongoing and revolving as a process of relational participation, grounded in the belief that plants and ecosystems possess agency and awareness. It is reasonable to assert that this means that thought and agency emerge through relationships rather than residing solely within the human mind. It is therefore reciprocal and thus happens because of the relationships. Viveiros de Castro (1998) describes this as “perspectivism”, a worldview in which humans, animals, and plants share a common field of subjectivity, each capable of perception and intention from its own standpoint. Kohn (2013) extends this insight to the forest, arguing that communication and meaning are not human monopolies but properties of living systems that “think” through interdependence. These perspectives suggest that intelligence is relationally created and thus “extended”, co-created through participation, ceremony, and responsiveness rather than abstract reasoning. In the context of psychedelic healing, this view resonates with Tupper et al. (2015), that therapeutic insight arises not only from neurochemical processes but from relational, contextual, and

ecological engagement. It is a pluralistic understanding of mind and healing that honours cognition as both embodied and relational.

Therefore, to say that “plants think” in this context is not to assert a testable hypothesis but to affirm relational connections. My use of the term therefore follows Indigenous epistemologies that treat knowledge as relational, acknowledging that what counts as “intelligence” depends on one’s agency as well as cosmological lens. This is in contrast to some discussions that draw a binary between “Western = reductionist” and “Indigenous = holistic.” Instead, curiosity between knowledge systems that understand healing through different yet complementary logics means that Western neuroscience can contribute valuable insights into mechanisms of change around neuroplasticity, network dynamics, and predictive processing; simultaneously, Indigenous traditions remind us that these processes unfold within relationships that we may understand because of positionality within new worldviews. Framing these perspectives together under a Two-Eyed Seeing stance allows both the empirical and the relational, recognizing that each offers partial yet vital truths about what healing means.

### **Implications for the Future of Psychedelic Therapy**

An expanded understanding of psychedelic-assisted therapy (PAT) is possible by integrating relational, spiritual, and communal dimensions alongside its biological underpinnings (See Appendix D). Such an approach moves beyond symptom reduction to engage broader existential, social, and ecological aspects of healing. It calls for collaborative research that includes both quantitative clinical outcomes and qualitative metrics of communal well-being. Central to this vision is the transformative potential of mystical or transcendent experiences. Healing, in this expanded view, is not solely an individual or biochemical process but a relational and ecological one—fostering deep connection with oneself, with community, and with transcendent realities.

The expansion of psychedelic-assisted therapy to include spiritual, relational, and communal elements raises the critical question of whether, and how, these dimensions can be integrated into models that have traditionally focused on biological and psychological

mechanisms. Such a model would seek to honor the complexity of human experiences, embracing multiple epistemologies and ethical frameworks, particularly those rooted in Indigenous and communal traditions. Thus, if we do not include these perspectives, we are perpetuating an extractive model by negating the cultural and spiritual roots in which they exist.

### **Emphasizing a Holistic Biological Foundation**

Firstly, a future biopsychosocial relational model could still use robust biological and neuroscientific foundations. For example, understanding how serotonin receptor sites promote neuroplasticity not only helps in managing clinical risk, but also provides evidence that can reassure regulatory bodies and the broader medical establishment about the safety, efficacy, and reproducibility of psychedelic therapies. This is in alignment with emerging neuroplasticity research that alludes to the validity of these outcomes. Clinical trial data likewise could provide opportunities to incorporate qualitative metrics such as relational well-being, spiritual development, or community engagement alongside standard symptom assessments. Research could support projects examining these richer dimensions, helping push the field beyond a narrow biomedical scope. In a framework that is fully biopsychosocial and relational, this biological foundation would be coupled with a recognition that measurable changes in the brain are only part of the story. Neurochemistry can include subjective accounts where people undergo life-changing epiphanies or spiritual awakenings, as well as communal accounts that capture the social resonance of healing as it reverberates through families and communities. The biological aspect thus becomes one layer in a multi-layered approach. This may lead us to more significant explanations of psychedelic healing.

An area we can see emerging examples of this is in psychedelic sociality which is incorporating insights from the emerging “neuroscience of religion,” which examines how religious and spiritual beliefs shape human behavior at the neural level, an area previously overlooked in neuroscience (McNamara et al., 2024; Newberg 2000). For example, from 2005 onward, only 0.009% of titles and 0.09% of abstracts among 2.5 million NIH proposals included religion-related terms, and just 0.006% of titles and 0.05% of abstracts mentioned spirituality.

They also highlight recent brain imaging studies showing that psychedelic substances modulate brain regions associated with religious or spiritual experience and social cognition, further linking neurobiological and relational dimensions of meaning-making (Roseman et al., 2018). This integration reflects a growing recognition that the experiential, social, and neural aspects of spirituality are interconnected, a domain long neglected in neuroscience despite its significance for understanding human consciousness and culture (McNamara et al., 2024). In addition, tools like the Mystical Experience Questionnaire (MEQ) are helping researchers categorize practices as “religious” or “spiritual.” Further illustrating the scope of this work, anthropologist George Murdock (1957, 1967) documented supernatural agents and shamanic beliefs in 168 cultures, demonstrating a rich cross-cultural foundation for study. The authors argue that expanding the neuroscience of religion and spirituality will require more specialized researchers and the application of recent technologies such as AI, language models, and virtual reality to glean deeper, more comprehensive insights (Krakauer, 2020).<sup>34</sup>

## **Psychological Insights and Therapeutic Contexts**

Psychedelic therapy in Western clinical research already incorporates psychological components, often drawing on modalities like Cognitive Behavioral Therapy (CBT), Acceptance and Commitment Therapy (ACT), and psychodynamic approaches oriented towards the individual, focusing on personal symptomatology. A new biopsychosocial model would deepen psychological exploration by recognizing the centrality of relationships.

Interestingly, some pre-prohibition psychedelic research highlights the importance of contextual and clinician-related factors (Kishon et al., 2024). Researchers recognized early on that traditional psychoanalytic frameworks were inadequate for the psychedelic state. Classic psychoanalytic therapy is structured around long-term, verbal exploration of unconscious material, often with minimal intervention from the therapist. However, psychedelic states can be overwhelming, non-verbal, symbolic, and even mystical, thus requiring more active guidance,

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<sup>34</sup> Some in the broader medical field call for a more expansive framework that accounts for lifestyle and top-down approaches, rather than pursuing single-cause solutions. Krakauer (2020) critiques Western medicine’s tendency to treat chronic, non-communicable diseases with a one-pathway, one-drug strategy. He argues that COVID-19 revealed our inability to manage the complex interplay between infectious diseases and chronic lifestyle factors, urging a multifaceted perspective that acknowledges broader dimensions of health.

emotional containment, and contextual grounding than the psychoanalytic frame typically provides.<sup>35</sup> It is salient to note that this notion of “active guidance” also reflects an Indigenous and relational ontology in which plants and other non-human beings are regarded as sentient participants in the healing process, capable of communication and intentional influence. Within such traditions, guidance is not metaphorical but describes an interactive relationship of learning, reciprocity, and transformation. This differs from Western biomedical interpretations, where such effects are typically explained in terms of psychological projection or neurochemical mediation. Yet, even within psychodynamic therapy, which positions itself as non-directive, a comparable process of active guidance occurs. Therapeutic interventions such as interpretations, silences, and attuned responses all shape the field of awareness and direct psychic movement. The therapist’s presence, timing, and framing participate in a co-created dynamic that influences what becomes conscious and how meaning is formed. In this sense, psychodynamic practice also enacts a form of relational guidance that operates through inter-subjective attunement rather than cosmological participation. Seen through ‘Two-Eyes’, both perspectives challenge the idea of neutrality and affirm that guidance is always relational, whether conceived as the reciprocal agency of human and more-than-human beings, or as the mutual responsiveness of therapist and client within the analytic field. As a result, early therapists began to adapt their approaches, emphasizing set and setting, the therapeutic alliance, and the broader ceremonial or relational environment, thus laying early groundwork for the relational and contextual models being explored today.

Building on these observations, some PAT proponents argue for further inquiry into adjunct psychological interventions and modulation of non-pharmacological factors to ensure consistent patient benefits (Kishon et al., 2024). This broader biopsychosocial perspective involves expanding beyond conventional clinical research.<sup>36</sup> This could include cultural-

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<sup>35</sup> From a Two-Eyed perspective, what many contemporary psychedelic protocols describe as “non-directive supportive presence” could more accurately be understood as a contained form of active guidance. Even when therapists claim neutrality, the work of “holding” and/or “grounding” for example, inevitably shapes the emotional field and influences how the experience is metabolized. The clinician’s **tone, breath, timing, and embodied calm function** not in “absence” but often direct to establish what is often called “safety”. What is sometimes called “containment” risks overlooking the *mutual regulation* that occurs between facilitator and participant. In this sense, “non-directive” support is itself a relational intervention, one that guides through presence rather than instruction. This distinction is often minimized in institutional models such as Johns Hopkins or MAPS, where *safety* is emphasized more than *relationship*.

<sup>36</sup> In a reported case of adverse effects following MDMA therapy, energy medicine successfully resolved the patient’s physical and psychological symptoms where Western medical approaches had fallen short. By viewing these disparate symptoms as manifestations of a single

controlled trials that evaluate how diverse cultural backgrounds affect results or examining biological mechanisms alongside interpersonal factors in couples or group therapy (Pilecki 2021; Tarrant, 2022; Roseman et al., 2022). These approaches illustrate how psychedelics can enhance social connectedness, empathy, and prosocial effects, while also underscoring that therapeutic efficacy is heavily shaped by cultural context, suggestibility, and social environment.

Another crucial step involves extending integration frameworks so that follow-up sessions or support groups extend well beyond the initial treatment (Hart, 2021). In doing so, patients can process and anchor their insights over weeks or months in group settings. A compelling historical example is Osmond's 1950s LSD-based treatment program for alcoholism, which contrasts sharply with today's more individual-focused, clinician-monitored approaches (Dyck, 2006). At the Earle Alcoholic Unit, it was emphasized communal sharing, where participants served as both patients and supporters, a model that echoes certain First Nations therapeutic traditions emphasizing **relational reciprocity**. The group structure fostered mutual learning and extended the healing process into interpersonal dynamics. Reported outcomes included reduced rates of severe alcoholism and enhanced relational insights from spouses of participants. Most importantly, Osmond's integration of familial and social perspectives, along with participant self-reports, offered a holistic understanding of therapeutic impacts often sidelined in modern clinical frameworks.<sup>37</sup>

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energetic principle, acupuncture, which is grounded in centuries of clinical practice, helped restore energetic balance through carefully placed needles, leading to full recovery (Kronman, 2025).

<sup>37</sup> Alcoholics Anonymous (AA) also uses a communal, ritualized model to foster healing and connection, which is similar to how ceremonial psychedelic practices bring people together in a shared framework of mutual support and spiritual or cultural significance. In AA, the meetings follow a familiar structure (readings, sharing, prayer or meditation), which can feel ceremonial and collective, and members keep each other accountable by maintaining and investing in relationships. This correlates with the two-week, 8-man cohort format used at the Earle Alcoholic Unit, in which only two participants received LSD on a given dosing day while the remaining six acted as sober companions—an approach that framed every patient simultaneously as a healer and a recipient of care—similar to First Nations approach of **relational reciprocal care**. In other words, a communal peer support model of treatment, is a treatment.

## Conclusion: Honouring Spiritual and Existential Dimensions

One of the defining attributes of psychedelic-assisted therapy (PAT) is its ability to provide a supportive framework around mystical or transcendental states.<sup>38</sup> Rather than dismissing these experiences as superficial “hallucinations,” a relational approach recognizes them as meaningful catalysts for growth. In practice, this can involve incorporating guided meditations, breathwork, or other spiritually resonant elements into PAT protocol. Clinicians could further collaborate with spiritual counselors, chaplains, or Indigenous healers to co-create a culturally sensitive “sacred container” for the psychedelic journey. This framework invites PAT to engage more directly with religious studies and spiritual care, advocating for the inclusion of entheogen research within broader conversations on the spiritual dimensions of psychology<sup>39</sup>(Roberts & Hruby, 2002).

Ritualized or ceremonial structures could offer meaningful anchors for these spiritual dimensions, especially when co-developed in alignment with participants’ personal or cultural worldviews.<sup>40</sup> This could promote existential exploration, granting clients the space to interpret experiences from their own spiritual or philosophical agency. Rather than reducing such experiences to mere “hallucinations”, PAT could fully regard them as valid drivers of personal transformation.<sup>41</sup> Lastly, PAT can welcome structuring environments that foster spiritual

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<sup>38</sup> A large-scale study on people who inhaled DMT suggests that many felt they encountered an “autonomous entity” (Davis AK, Clifton JM, Weaver EG, Hurwitz ES, Johnson MW, Griffiths, 2020). 69% said they received a “message,” and 19% reported a “prediction.” Only 21% intended to have such an encounter yet 69% said the entity initiated first contact, described as a guide, spirit, alien, or helper. They propose that these subjective experiences could have therapeutic benefits. Like Jung, the belief is that entities may stem from our “micro” or “macro” personalities, autonomous entities acting as aggregators of “socially modified” personalities of the ‘collective unconscious’, and exploration into them could have benefits. (Mckenna, 2022; Heuser 2006)

<sup>39</sup> Historical investigations suggest that entheogenic plants (e.g., Amanita muscaria and Syrian rue) have influenced religious traditions across Persian, Greek, Jewish, Islamic, and Sufi lineages, often referred to as “celestial botany.” In various faiths, such as from Moses’s burning bush to the Garden of Eden and Qur’anic paradise, plants carry symbolic or spiritual significance. Alchemical and Hermetic perspectives further emphasize nature’s divine reflections, underscoring the idea that certain plants may hold transformative or healing properties. Contemporary scholars and practitioners extend this view to potential therapeutic benefits, exploring frameworks like “plant intelligence” and “plant signaling” to better understand how entheogens could inform both religious studies and mental health treatment. (Doyle, 2011, 2012)

<sup>40</sup> This belief that this is all in the brain tweaking with our nervous system is best echoed by Dr. Matthew Johnson (2023) in the Plant Medicine Podcast hosted by Dr. Lynn Marie Morski: *My bet is that if people believe that there’s some sort of reality to these disincarnated entities—that it’s not just in their mind—there are certain people that can hold that experience in a positive way that might benefit them... and probably some of these over 2,000 folks, there’s probably some people that—again, aside from whether we know it’s true or not—believing in things that no one else can prove are there is probably a bad thing.* (12:38)

<sup>41</sup> After a large search, it is worth questioning why there may be no “professional” PAT program that dives into the nuances of non-human intelligences encountered during these experiences. Instead of solely focusing on the existence of entities, these programs could explore the diverse ways non-humans interact with humans while also examining the proper protocols for engaging with these forces. This is part of the training of every psychedelic “maestro” as well as most shamans. Incorporating such discussions would not only add an intriguing and potentially

reflection. This could include nature-based aesthetics, a central altar that echoes communal Indigenous practices and/or psychedelic churches. The purpose is to validate mystical and spiritual insights as an integral part of the healing journey.

Meaningful progress requires systemic changes in PAT, meaning practitioners need continued training in cultural humility, social justice, and spiritual care, as well as in areas in which changes are not yet realized such as broader integration into public systems, discussions around equitable access, as well as the ethics of ecological responsibility and protection for the indigenous peoples who live within these ecologies (Lum, 2018, White 2007).<sup>42</sup> For example, academic and professional programs could include courses on Indigenous epistemologies and the ethical integration of alternative healing practices. Policymakers, in turn, could collaborate with advocacy organizations to develop safeguards around ceremonial plant use, protect Indigenous communities, promote ecological responsibility, and remove barriers to equitable treatment access. If fully realized, a biopsychosocial relational framework for psychedelic therapy promises a substantial shift in mental health care. Rather than merely reducing symptoms, this perspective treats healing as a process of reconnection with oneself, with the wider community, with nature, and with transcendent realities. Biological, psychological, spiritual, and social elements all function as interwoven threads in the fabric of well-being.

Recognizing psychedelics as all these elements, as psychic phenomenon (i.e., directly interacting with consciousness) and social phenomenon (i.e., shaped by culture) are essential to understanding their full therapeutic potential. Psychedelic experiences do more than alter the inner world of the individual; they unfold within and are profoundly shaped by broader relational, cultural, and communal contexts. When we only view psychedelics as personal, biochemical events, we ignore how cultural beliefs, communal practices, and social settings

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transformative module to psychedelic training but also challenge participants to consider that even if these perspectives are ultimately speculative, they might still offer valuable frameworks for understanding complex experiential phenomena. As Narby (1998) argues, the interconnection of consciousness could be rooted in our shared DNA, suggesting that all humans are inherently related. This view implies that our learning and healing processes extend beyond neuropsychological mechanisms to include broader relational dynamics. Thus, exploring the nature and roles of 'all our relations' within psychedelic experiences is not merely an academic curiosity. It is integral to appreciating how deeply interconnected relationships, both human and non-human, contribute to indigenous healing.

<sup>42</sup> In therapy, Michael White (2007) adapted Myerhoff's concept to facilitate "remembering" conversations, connecting clients with sources of support and solidarity. This deliberate "re-aggregation of members" of one's life story shows how it can be used therapeutically to connect clients with sustaining relationships, employing "dis-memberment" to signify the process of othering and exclusion and "re-membering" to describe the emergence of post-emergence thought.

guide how these substances are used, interpreted, and integrated into daily life. Conversely, focusing solely on their cultural significance risks overlooking the powerful individual transformations that can occur at a deep psychological or spiritual level.

By recognizing both dimensions, we gain a more complete picture of how psychedelics work and what promotes healing, personal growth, or even spiritual insight. We also see how “set and setting”, which includes expectations, relationships, cultural rituals, and physical environments, all fundamentally shape one’s experience. This dual understanding is at the heart of ‘psychedelic sociality’. What is woven throughout is its quest to lead us to be more inclusive, ethical, and effective in our therapy and research approaches, so that individual well-being is supported while respecting the collective values and traditions that surround these substances.

The future of psychedelic therapy stands at a threshold: it can either continue down a path of reductionistic biomedical framing, or it can evolve. The proposed emerging relational model that interweaves biological science, psychological processes, spiritual insight, and social solidarity holds the promise of broader, deeper healing. By embracing shared leadership with Indigenous communities, honoring spiritual experiences as essential to well-being, and embedding therapy in communal and ecological contexts, this emerging paradigm could redefine mental health care for generations to come: that true healing does not happen in isolation but in thriving relationship to all that surrounds us.

## APPENDIX A

### Meaning in lived experiences

What is also challenging for psychedelic pharmacology is to label these phenomena because no agreed-upon definition exists to differentiate the distinction between subjective events and potential supernatural interpretations. As a result, biological perspectives fail to acknowledge possible clinical value in these experiences because to do so means accepting supernatural claims. For instance, the “comforting delusion objection” raises concerns that psychedelic therapy can foster illusory, but emotionally reassuring beliefs about universal consciousness and/or divine or higher power presences (Letheby, 2021). While these experiences often feel real, it can be argued that they are cognitive distortions rather than genuine insights. Challenging this view is the assertion that the therapeutic value of psychedelics does not rely on adopting metaphysical beliefs; instead, their benefits stem from psychological growth, increased mental flexibility, and deep emotional processing (Letheby, 2021). Crucially, the search for “meaning” in these experiences remains central, as it shapes how individuals integrate and interpret any insights gained. Recognizing this emphasis on meaning is vital for understanding how subjective perceptions—whether deemed illusory or authentic—profoundly influence therapeutic outcomes. Thus, the healing potential of psychedelics can be fully understood within their ability to help people, for instance, reframe their self-perception, ease existential distress, and enhance overall well-being.

This ongoing struggle to include meaning in subjective lived experiences is seen in our language of care, especially around the role of relationships. For example, words used by healthcare providers, “*patient pathway, medicine optimization, discharge*” inadvertently marginalize the lived experiences of those they aim to serve (Taylor, 2013). These terms can imply “doing to” patients rather than “being with” them, and this disables the formation of empathetic, reciprocal relationships. Speraw’s (2009) work on children and young adults with disabilities underscores how seldom these individuals’ perspectives are solicited. The results are care systems that prioritize clinical protocols over personal narratives and meaning making. Such

patterns resonate with the experiences of many marginalized communities, who find themselves treated as mere objects of care rather than active participants in their own healing (Kenny, 2009). Speraw (2009) proposes four broad reflections to shift from a purely technological or pharmacological orientation to one that values relational meaning-making<sup>43</sup>. She reveals how patient perspectives are often overlooked especially among marginalized, disabled communities. This further emphasizes the need for participatory engagement and relational lived experiences in how we frame psychedelic care.

Looking more broadly, these experiences create confusion for providers in clinical practices. Lum (2018) notes that physicians frequently encounter Medically Unexplained Symptoms (MUS), which create anxiety and drive over-diagnosis. The rigid medical framework struggles to address these cases, highlighting the need to include broader healing factors and stronger therapeutic relationships. Similarly, Krakauer (2020) critiques the reductionist approach to treating chronic diseases, advocating for broader frameworks like allostasis (Sterling, 2012) that integrate biopsychosocial factors. Social norms and medical labeling shape illness experiences, often reinforcing structural inequalities (El-Gilany, 2023; Durkheim, 1982).<sup>44</sup> Linguistic labels influence identity and healing trajectories, as seen in the language used in healthcare, which shifts focus from relationships to rigid diagnoses (Taylor, 2013).<sup>45</sup> In summary, we can differentiate from biological psychiatry because the therapeutic impact of psychedelics stems from the changes that happen, particularly in the subjective experience. This highlights the need to address lived experiences, not just biology.

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<sup>43</sup> 1. Respect for Individuality: Diminished capacities do not inherently reduce awareness; people with different abilities offer new insights. 2: Time and Relationship: Investing time to build authentic relationships benefits both provider and patient.3: Reciprocal Responsibility: Both parties contribute to creating meaningful interactions.4: Continuous Learning: Clinicians and patients alike must remain open to new understandings.

<sup>44</sup> Reframing substance use within a social constructionist framework challenges traditional views on addiction. Many substances, including psychedelics, have been used medicinally and ceremonially across cultures but were later criminalized through colonization and commodification. Hart (2021) highlights self-medication as a coping strategy that can provide relief or lead to harm, depending on context. The stigma reinforces the need to reassess the language and assumptions surrounding substance use.

<sup>45</sup> Health and illness are shaped by cultural and lived experiences, influencing how individuals attribute meaning to their conditions. Helman (1981) and Carel (2013) emphasize that illness extends beyond biological dysfunction, with phenomenology offering an alternative perspective that considers personal experiences. The medical model, by focusing solely on disease, often neglects the positive aspects of health within illness, particularly in chronic conditions

## APPENDIX B

### The Placebo Effect and Its Implications for Set and Setting

The placebo effect makes it difficult to isolate a drug's distinct therapeutic benefits.<sup>46</sup> Participating in a formal "therapeutic system" (structured environments, counseling-style support, interpersonal dynamics) creates measurable physiological and psychological changes. This poses a challenge when researchers attribute any observed improvement solely to the drug rather than to broader contextual factors. Consequently, studies often try to reduce non-biological influences by limiting therapeutic contact or excluding participants deemed "too responsive" (Sanabria, 2023). However, these measures can overlook valuable insights into how care and context work synergistically to enhance healing.

The placebo effect is often explained by identifiable biological and psychological mechanisms, such as expectation, learned conditioning, or shifts in neurotransmitter activity. Rather than focusing on social or contextual elements, reductionists concentrate on detecting and quantifying these processes by examining changes in brain function or the release of specific neurochemicals. In contrast, set and setting theory interprets the placebo phenomenon in terms of meaning, relationships, and social context. Within this framework, communal elements, culturally embedded rituals, and interpersonal rapport are seen as integral drivers of healing and not confounding variables to be removed.

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<sup>46</sup> Another issue is because psychedelics produce unmistakable effects, it is obvious who is on the real drug. This "functional unblinding" means everyone knows who received the actual substance, even though the study is technically blind. That awareness can bias perceptions and behaviours, making it harder to distinguish the "drug's" true impact from people's expectations. Avoiding this issue is crucial for reliable findings from a pharmacological perspective. However, from a **relational perspective**, functional unblinding is not just a "flaw" to eliminate; it highlights how important interactions and surrounding contexts are in shaping experiences. Once it is clear who is on the real psychedelic, then reactions, expectations, and shared understandings become part of the overall "psychedelic" process. So, rather than a bias, this shift can reveal ways that meaning-making, rapport, and social connections contribute to how people "experience" the psychedelic. This shows that healing or insight is not just about a chemical effect, but also about the relationships and context in which it unfolds.

For example, non-pharmacological factors have been shown to influence outcomes such as the relevance of ‘intention’ and ‘ritual’ factors that amplify and multiply the purported effects of psychedelics (Beyer, 2010: Chapter 3; Helman, 2001: Chapter 1, Hartogsohn, 2017, Metzner 2013). Also, Szigeti (2021, 2023) shows that in several psychological measures, such as well-being and life satisfaction, findings were not significantly different than those taking placebo. This suggests that capsule composition does not determine improvements but rather one’s beliefs about expected outcomes do. So, these findings can be interpreted as highlighting the importance of both placebo effects and the individual’s “set,” or mindset and expectations, which are integral to how one processes any treatment or experience. In other words, the data showing no significant differences from placebo suggests that the belief in therapeutic benefit can be just as impactful as the specific pharmacological action of the substance, indicating that placebo and “set” may substantially overlap in their influence on outcomes. One additional study found that every participant assumed their microdosing would have significant and a wide breadth of positive outcomes, yet the effects assumed were not connected to the “observed pattern of reported outcomes” (Polito and Stevenson, 2019). These results highlight how belief, motivation, and environment can produce meaningful changes irrespective of the drug’s biochemical action.

The placebo effect question has led Boris D. Heifets, a Stanford anesthesiologist, to investigate the nature of psychedelic experiences and their therapeutic effects at the Heifets Laboratory at Stanford University. He examines whether the therapeutic benefits of psychedelics are primarily due to the drug itself, the conscious experience of the trip, or other non-drug factors such as patient expectations and the environment in which the drug is taken (Heifets 2023; Hack 2024; Lii 2023). What is most crucial about these studies is that they suggest that non-drug experiential factors play a substantial role in the therapeutic effects of psychedelics, again challenging the notion that the biochemical drug alone is responsible for the benefits. He explains that while chemicals do interact with our brain chemistry, it does not mean that our conscious experiences and sensations are caused due to the biochemical effect. Rather, it could be due to psychedelic experiential effects. To explain, Heifets (2023) describes a framework to study psychedelics, dividing the effects into three categories: biochemical drug effects, conscious experiences, and non-drug factors (set and setting). In an experiment involving ketamine

administered under general anesthesia so participants would not have conscious experience of the drug, they found that patients improved from depression. This highlights the significant role of non-drug factors, such as ‘placebo’ effects being ‘set and setting’ effects (Lii et al, 2023). This clearly opens up the possibility that there may be nothing significantly special about a drug activating a receptor; one’s experience overall is what transforms us psychologically speaking. They plan to further explore the distinct components of psychedelic therapy, studying non-psychedelic drugs with similar biochemical effects to classical psychedelics but without inducing a trip, and investigate experiences that mimic psychedelic trips without using drugs such as replicating vivid dream states to replicate the therapeutic effects seen with psychedelics.

Dosing effects overall may be due to the “meaning response”, as Moerman (2022) defines it: “the physiologic or psychological effects of meaning in the origins or treatment of illness; meaning responses elicited after the use of inert or sham treatment can be called the “placebo effect” when they are desirable and the “nocebo effect” when they are undesirable.” (p. 472) Moerman adds two critical points: placebos in and of themselves are inert but their meaning can and does have impact; in addition, medicine is full of meaningful elements no matter how much practitioners have no intention of letting them be such. As an example, he notes what Margaret Lock calls “local biologies,” which increase life longevity simply because of meaning (Moerman, 2022). Furthermore, each individual’s experience often aligns with the social or cultural setting they inhabit, in particular during non-ordinary states of consciousness (Schleim, 2022).

Schleim (2022) proposes that our psychobiological unity within social environments implies that psychological processes fundamentally reflect underlying physiological states. Building on this premise, he introduces the ideas of “transcultural pharmacology” and “pharmanthropology” to highlight the vital role that meaning, and correspondingly, social context, plays in any discussion of the placebo effect. It is impossible to address placebo phenomena without incorporating the cultural and interpersonal dimensions that shape them (Hartogsohn, 2018).

Overall, “set and setting” spotlights the profound role of psychological expectancy and social context in shaping psychedelic outcomes. Rather than treating variables such as the placebo effect as factors to minimize, embracing its implications can deepen our understanding. For instance, how meaning, belief, and communal connections can amplify, resist, or avoid pharmacological actions.

## **APPENDIX C**

### **Framework for Ethical Collaboration with Indigenous Healers**

To ethically integrate Indigenous knowledge into Psychedelic-Assisted Therapy (PAT), we must move beyond cultural appropriation and recognize the relational, communal, and ecological foundations of Indigenous healing. While Western models often emphasize individual self-exploration and symptom reduction, Indigenous approaches focus on ceremonial context, community support, and restoring relational balance—with others, the environment, and the cosmos.

Simply borrowing Indigenous elements (e.g., songs, tobacco, ayahuasca) for private or clinical use without honoring their cultural roots leads to fragmentation and commodification. True ethical integration requires collaboration with Indigenous Knowledge Keepers, equitable benefit-sharing, and shared decision-making about how therapies are practiced. Ultimately, the promise of psychedelics lies not in isolated healing, but in co-creating relational models of care that reflect the deep wisdom of Indigenous traditions.

## APPENDIX D

### **Rethinking Psychedelic Therapy: Relational Insights from Indigenous Traditions**

Typically, psychedelic-assisted therapy (PAT) follows a structured biomedical and psychotherapeutic framework, centering on individual preparation, controlled dosing, and integration sessions (Phelps, 2017; Sloshower et al., 2020). This ensures safety, meets institutional review standards, and generates data-driven outcomes (Canady, 2022; Brennan & Belser, 2022). However, many Indigenous healing paradigms frame personal distress as part of a broader communal imbalance rather than focusing solely on pharmacological mechanisms (Weaver, 2002; Taita Alonso-Muisca Nation, personal communication, 2023; Keepness, 2023).<sup>47</sup>

Building on a relational perspective, these Indigenous approaches emphasize reciprocity with the land, ancestral teachings, and collective support (Keepness, 2023). In contrast, Western PAT tends to spotlight the individual within a therapist–patient dynamic (Rice, 2008; Sloshower et al., 2019). Yet exploring Indigenous insights on communal participation need not entail adopting entire ceremonies. Instead, PAT can integrate key relational dimensions such as assigning supportive roles, encouraging group reflection, and welcoming cultural knowledge keepers. These could deepen social connectivity and shared understanding (Angyus et al 2024; Letheby, 2021).

These relational elements align with existing Western frameworks that recognize the central role of meaningful relationships in therapy (ex. existential, psychodynamic, and family systems).<sup>48</sup> By broadening clinical practices to include intentional community engagement and

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<sup>47</sup> This aligns with a social constructionist lens, disease and illness labels are intertwined with socio-political forces (Rosenberg, 1989). The medical model asserts objective categorization, but cultural, moral, and historical contexts shape what is deemed pathological or normative (Baydala, 2006; Durkheim, 1982; El-Galany, 2023). Consequently, defining psychedelic usage such as why and how to use it as pathological or therapeutic depends on cultural norms, power imbalances, and political interests (Speraw, 2009; Taylor, 2013).

<sup>48</sup> In trauma therapy work, there is a common saying: “we are wounded in relationship, and we heal in relationship.” This relational connection piece is missing in isolated individual sessions of psychedelic work. This is also in resonance with traditional knowledge of the Americas, where one is a supporter in a shared experience of learning and growing with “diagnostic assessments” usually being completed by the other party before yourself, also exemplified by Speraw’s (2009) simple question of asking others what it is like to be them (Cohen, 2003, Keepness, 2023; Barry Ahenakew-Cree Nation, personal communication 2016).

land-based gatherings, PAT gains avenues to foster prosocial outcomes like empathy, trust, and intergenerational bonds (Roseman, 2022). Ultimately, weaving relational principles from Indigenous traditions into PAT can enrich its holistic scope, enhancing healing beyond symptom relief and honoring the broader social tapestry in which individuals exist.<sup>49</sup>

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<sup>49</sup> This is a phenomena in underground PAT, often aligning with neo-shamanism, where people adapt “set and setting” elements like ritual, altered states, and communal ceremonies to modern contexts. As Braun (2010) notes, neo-shamanism provides an “enchanted framework” for reconciling biomedical models with spiritual and experiential aspects of healing, while still differing from traditional shamanistic lineages (Dev, 2018, 2020; Viveiros de Castro, 2012). Further examination of these practices could allow PAT to also move closer to a holistic approach that values relational, spiritual, and cultural dimensions.

## APPENDIX E

### **Addressing Cultural Appropriation: Ethical Integration of Indigenous Knowledge**

To address cultural appropriation in PAT would be to appreciate what Indigenous knowledge systems can help PAT appreciate. For instance, research has indicated that the reexperiencing of challenging memories is shaped by ceremonial and relational contexts, communal participation, and the relational entourage of botanical compounds that comprise psychedelics. These findings underscore how factors beyond mere biochemistry can profoundly affect healing processes, paralleling insights that “set and setting” may function as “spiritual technologies” (McKillop, 2020; Ritchie, 2021). Specifically, they orchestrate ceremonies that foster relational healing, communal support, and deep ecological ties (Narby, 2013; Keepness, 2023).

While individual self-exploration can indeed foster personal growth and healing, prioritizing it exclusively within PAT risks a multilayered process of cultural appropriation. When these insights are used solely for private benefit rather than integrated into a broader cultural and communal framework practitioners may begin to commodify Indigenous symbols, songs, and substances such as tobacco or ayahuasca. This selective appropriation fragments the healing process by isolating individual experiences from the collective context that originally imbued these practices with meaning. Moreover, by focusing on individual privilege in psychedelic use, we risk reinforcing historical injustices and marginalizing the communities that have long maintained these traditions. Ultimately, while self-exploration is not inherently negative, when divorced from its cultural and communal roots it transforms a potentially rich, collective experience into a decontextualized, clinical exercise that undermines the integrity and transformative power of Indigenous practices.

What is important to note is that emerging areas of PAT and traditional shamanic practices share an emphasis on structured preparation and integration (Letheby 2021, Winkelman, 2000). However, the explanatory foundations differ when viewed through a

relational lens, whereby the fundamental aim is not solely symptom reduction or personal insight, but includes the revitalization of social, ecological, and cosmic relationships that have been disrupted. Consequently, ethical integration means to pay attention to this through collaboration with Indigenous Knowledge Keepers, equitable benefit-sharing, and culturally relevant outcome measures. In other words, the ethical path may be to recognize that healing is far beyond the individual mind and is a process that includes family, community, and the living environment. Indigenous knowledge may be showing us that the promise of ‘psychedelics’ is not about curing symptoms, but it is instead about designing a relational model of care.

The future of any biopsychosocial relational model hinges on these considerations. Historically, Western pharmacology has commodified Indigenous plant medicines without compensating or even acknowledging the communities that have stewarded these traditions. As the global demand for psychedelics grows, the risk of ecological harm and cultural exploitation becomes acute. Hence, a biopsychosocial relational model must include formal agreements where Indigenous or local healers and communities are recognized as equal collaborators and knowledge keepers. This involves shared decision-making on how ceremonies are conducted, how profits are distributed, and how cultural protocols are preserved. By fostering authentic collaborations, the model would demonstrate respect for the cultural origins of these healing modalities while also enhancing therapeutic outcomes for participants.

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