

What Can Critical Humanities Contribute to Psychedelic Research? A Naturalist Approach to Interdisciplinary Integration

*By Oliver Thorndike**

This paper explores the potential for interdisciplinary collaboration between science and the humanities, with a focus on recent advancements in psychedelic-assisted therapy. It provides an overview of key concepts in this emerging field and identifies research gaps that offer opportunities for interdisciplinary integration. Adopting a non-reductionist naturalist framework, the paper views psychological phenomena as emergent properties of underlying neuronal biochemical processes. The term “critical humanities” refers to integrating diverse perspectives—such as aesthetic, psychological, philosophical, spiritual, and recreational—with scientific inquiry. Within this framework, the paper argues that critical humanities can address metaphysical biases in language that hinder psychedelic research and public understanding. For instance, it can clarify antiquated dualisms, correct misconceptions about the nature of psychedelic experiences, and prevent premature psychological predictions lacking solid evidence. More precisely, the paper cautions against the notion that psychedelic experiences “cause” insights. Additionally, critical humanities can enhance therapeutic settings, such as the role of music in therapy sessions, and assist in designing comparative studies. Ultimately, it aims to foster a more coherent understanding regarding psychedelic experiences.

Keywords: *psychedelic-assisted therapy, altered states of consciousness, mystic experiences, humanities of psychedelics, philosophy, neuroplasticity, non-reductionist naturalism*

Introduction

This paper investigates the potential for interdisciplinary collaboration between science and the humanities, focusing on recent advancements in psychedelic-assisted therapy. Here, “psychedelics” will refer to classical psychedelic compounds including psilocybin, ayahuasca, peyote, LSD, mescaline, and DMT (N,N-dimethyltryptamine). The paper provides an overview of the key concepts underpinning this emerging field and identifies existing research gaps as opportunities for meaningful cross-pollination.

Historically, mystic experiences have been reported by both religious and secular thinkers as involving profound shifts in perception, mood, cognition, and personality. Traditionally, these experiences have been viewed through an entheogenic or metaphysical lens, which posits a transcendent layer of reality beyond normal consciousness. This perspective suggests that such experiences access a “deeper” or “more authentic” realm of being. In contrast, contemporary science approaches mystical experiences through naturalistic frameworks, including biochemistry,

*Associate Professor, Peabody Institute of the Johns Hopkins University, USA.

pharmacology, and neurophysiology. Research indicates that high dosages of psychedelics, such as psilocybin, can induce mystic experiences leading to sustained positive changes in mood and behavior within therapeutic settings. However, the effectiveness of these experiences is also influenced by psychological and environmental factors, such as “set and setting.” Current research questions include: How do psychedelics function biochemically and neurophysiologically? What role does subjective experience play in therapeutic contexts? Why isn’t psychedelic assisted therapy simply pharmacotherapy? And how do psychological and environmental factors, like music, enhance ego-dissolution?

A recent call for a “critical, psychedelic humanities” suggests that exploring metaphysical, ethical, and cultural dimensions of psychedelic experiences is crucial (Letcher 2023, p. 824). This perspective argues that science alone cannot fully capture the richness of psychedelic experiences, which are seen as “more than a set of defined molecules” (Hauskeller & Sjöstedt-Hughes 2022, p. 5). It advocates for integrating humanities perspectives to prevent science from “overextending” and potentially undermining the subjective mystic experience in its cultural, religious, or recreational significance (Devenot 2013). Such views reflect a long-standing tradition that contrasts the humanities with natural science, seeking to protect the unique and meaningful aspects of human experience from the impersonal laws of nature (Hacker 2002, von Wright 1993). The philosophical position that empirical science does not exhaust what exists, that there is a level of reality that cannot be translated into normal language—for example, what-it-feels-like experiences (*qualia*) or union with the divine—permeates the literature on psychedelics. This distinction hinges on the alleged dichotomy between normative and factual realms and their respective methods of hermeneutical comprehension and causal explanation.

I challenge the idea that scientific and humanities perspectives are inherently at odds. Instead, I align with those neuroscientists and philosophers who propose that mystical states can be understood as emergent properties of biochemical processes (e.g., Carhart-Harris & Friston 2019, Letheby 2021, Kwan et al. 2022). This naturalist approach enables a more integrated view that incorporates humanities perspectives without diminishing the importance of subjective experiences or their biochemical foundations. By viewing subjective experience as an emergent property, we can reconcile pharmacotherapeutic and psychotherapeutic approaches, rather than setting them at “loggerheads” (Lebedev et al. 2016, p. 3210). I use the term “critical humanities” to describe this inclusive domain, which integrates scientific exploration with diverse perspectives—encompassing aesthetic, psychological, sociological, anthropological, cultural, political, spiritual, and recreational viewpoints. A non-reductionist naturalist worldview, where multiple levels of explanation are valid as long as they are consistent with scientific principles (Carroll 2016), provides a legitimate space for the critical humanities to help identify and address research gaps, precisely because many of the numerous research gaps in this emerging field of psychedelic-assisted therapy lie at the intersection of biochemical mechanisms and subjective experience. For example, while it is generally agreed that psychedelics are serotonin 2A receptor agonists that can lead to profound perceptual, emotional, and cognitive changes—including lack of normal self-referential awareness (“ego-dissolution”)—there is also accumulating evidence that “set and setting” influence the

acute psychedelic experience and its long-term effects. However, exactly how and which aspects do so for whom has not yet been tied to specific biomarkers (Golden et al. 2022). A main task of current psychedelic-assisted therapy research is thus to tie the body of scientific knowledge on neuronal and network effects of psychedelics to perception, cognition, and long-term personality changes (Kwan et al. 2022).

There is a good scientific reason for the lack of testing “set and setting.” As one scientist puts it: “Integrating variables of set and setting into clinical drug research would entail great complications for a pharmaceutical industry bent on randomized controlled trials (RCTs) and with limited patience for injecting fuzzy social and cultural elements into its considerations” (as cited in Golden et al. 2022, p. 63). However, it lies in the very nature of the psychedelic experience that “fuzzy” intrapersonal and sociocultural contexts matter. After all, lived experience unfolds at the intrapersonal and sociocultural level, even if its mechanisms are biochemical.

By bridging the divide between science and the humanities, critical humanities of psychedelics can help advancing a coherent understanding of psychedelic-assisted therapy and is thus also relevant to policy debates about psychedelic therapy. More specifically, this paper focuses on three key areas where critical humanities can contribute to psychedelic research: clarifying linguistic frameworks, maintaining scientific boundaries, enhancing therapeutic settings and designing alternative control groups. These areas correspond to the paper’s main sections.

1. **Clarifying Linguistic Frameworks:** Removing metaphysical biases from our language to better understand and interpret psychedelic experiences. By highlighting antiquated dualisms critical humanities can bolster psychedelic research, which uses outdated language in its qualitative studies. Critical humanities can also aid in developing a more coherent public understanding and self-image by challenging the entheogenic perspective and cautioning against assuming that “insights” from psychedelic experiences are inherently trustworthy.
2. **Maintaining Scientific Boundaries:** Ensuring science does not make premature psychological predictions such as causally linking psychedelic use to material beliefs without solid evidence tied to biomarkers.
3. **Enhancing Therapeutic Settings:** Improving the design and impact of therapeutic settings, such as music, in psychedelic therapy. **Designing Comparator Studies:** By suggesting alternative control groups that could help isolate the effects of psychedelic compounds more effectively.

The Contingency of Language in Mystical and Psychedelic Contexts

Reports on mystic-type experiences permeate human history. Despite significant phenomenal overlap, these experiences vary widely subjectively and are described using vastly differing vocabulary across contexts such as religion, philosophy, art, personal development, and clinical research. When we ask “What is a mystic experience?” “What is a psychedelic state?” or “What is an entheogenic or hallucinogenic state?”—for, all these terms have some overlap as they share common phenomenal features—

the answer is: That depends on who you ask. The psychedelic experience involves subjective cognitive effects and behavioral dimensions that are not fully captured by current biomarkers (Siegel et al. 2024, Kwan et al. 2022). For lack of a better word, the Austrian 20th century intellectual, Musil, calls the mystic state simply “the other state” [*der andere Zustand*] indicating that what all first-person historical reports have in common—besides their “passionate imprecision” (Musil 1990, p. 199)—is that they understand the mystic state in *opposition* to everyday normal consciousness.

Despite the fact that subjective psychedelic experiences and their interpretations vary widely, as reports come from individuals with different backgrounds, interests, and cultural settings, common aspects in first-person reports of mystical experiences have been found to include

- perceptual distortions, including hallucinatory percepts and transcendence of time and space,
- a felt sense of sacredness,
- a sense of the experience of truth and reality at a fundamental level,
- a deeply felt positive mood,
- ego-dissolution, or the experience of profound unity or “oneness” with all that exists,
- and difficulty explaining the experience in words (Barrett et al. 2015).

Notably, the intensity of the mystic-type experience, specifically the phenomenon of ego-dissolution, where one loses one’s autobiographical narrative self while retaining a minimal sense of self, has been linked to the therapeutic success of psychedelic-assisted therapy (Lebedev et al. 2016, Carhart-Harris & Friston 2019, Letheby 2021, Siegel et al. 2024). However, it is far from clear what precisely is meant by “ego-dissolution,” as it is an unsettled philosophical and scientific question what “self” or “ego” refer to (if they are referring terms at all) (Hacker 2007, Lebedev et al. 2015, Millière 2017). Two complementary perspectives on ego-dissolution illustrate its complexity:

It became very important to distinguish between ‘I’ and ‘Me,’ the latter being an object defined by patterns and structures and responsibilities —*all of which had vanished*—and the former being the subject experiencing and feeling... Although I *lost all sense of ‘me-ness,’* the sense of ‘I-ness’ was intensified unbelievably. ... It was simply a sense of ‘is-ness’ or ‘am-ness.’ *I wasn’t anything* —I simply was. And at these moments of ecstatic clarity there was such a peace and rest and at the same time such exuberance and wildest joy (as cited in Letheby 2021, p. 53).

I was looking at my furniture, not as the utilitarian who has to sit on chairs ... but as the pure aesthete. ... I spent several minutes—or was it several centuries?—not merely gazing at those bamboo legs, but actually *being* them—or rather being myself in them; or, to be still more accurate (for “I” was not involved in the case, nor in a certain sense were “they”) being my Not-self in the Not-self which was the chair (Huxley 1954, pp. 21–22).

Most data on mystical experiences, including ego-dissolution, come from subjective reports like these, or questionnaires and other qualitative methods rather than analyses of neuronal and network effects of psychedelics. For example, the Mystical

Experience Questionnaire (MEQ) is a validated scientific tool used to assess mystical experiences in psychological and clinical research to quantify and analyze the nature and extent of mystical experiences (Barrett et al. 2015). It is often the basis for connecting subjective psychedelic experiences to brain changes (Siegel et al. 2024). However, the MEQ employs metaphysical and entheogenic language that is inherently at odds with naturalism. Consider statements such as: “Experience of unity with *ultimate* reality.” “Feeling that you experienced something profoundly *sacred and holy*.” “Feeling that the consciousness experienced during part of the session was *more real* than your normal awareness of everyday reality” (Griffiths et al. 2006; emphases added). Likewise, the Metaphysical Beliefs Questionnaire uses classical metaphysical positions to describe the mystical experience. Statements include: “There exists another separate realm or dimension beyond this physical world that can be experienced or visited. (Ontological transcendentalism).” “Visiting such immersive “realms” or “worlds” can sometimes depend on a supernatural/magical transition process or event. (Supernatural transcendentalism)” And “There are two separate realms of existence, the physical (body, brain and external world) and the mind, the latter being non-physical/non-material. (Dualism)” (Timmermann et al. 2021, p. 2).

Philosophically, these metaphysical interpretations of psychedelic experiences—whether historical or contemporary—presuppose an appearance-reality split. This dualist worldview assumes a transcendent level of self and world, a deeper layer of reality, that cannot be accessed by normal consciousness. The persistence of metaphysical dualisms in discussions of psychedelic states is not incidental but deeply ingrained in intellectual history. Briefly consider how this theme recurs across philosophy and cultural traditions: The Oracle at Delphi (8th–4th century BCE) invoked trance-like prophecy; the Eleusinian Mysteries (5th–4th century BCE) centered on altered states leading to profound insights. Plato (ca. 427–347 BCE) insisted that ultimate knowledge cannot be put into words but must be directly experienced “For this knowledge is not something that can be put into words like other sciences” (Letter VII, 341c). Spinoza (1632–1677) distinguished between empirical reasoning and *scientia intuitiva*, a direct grasp of essence. Kant (1724–1804) argued that moral feeling grants access to the noumenal realm, and Schopenhauer (1788–1860) held that music provides direct experience of the transcendent Will. Wittgenstein (1889–1951) maintained that “there are, indeed, things that cannot be put into words. They make themselves manifest. They are what is mystical” (1997, Proposition 6.522).

This long intellectual lineage underscores why the metaphysical interpretation of psychedelic states remains so compelling. Though such dichotomies are scientifically untenable, they remain deeply embedded in our language and ways of thinking. Even leading scientists on psychedelic-induced mystical states get caught up in this antiquated language. For example, in their landmark paper, Carhart-Harris and Friston suggest that “integrated properly, psychedelics have every chance of becoming a legitimate, if not lauded, tool of science and medicine—capable of awakening us to the *true depths* of our being” (Carhart-Harris & Friston 2019, p. 339, emphasis added) Or, in his Ted Talk, Fred Barrett, current director of the department of psychedelic research at Johns Hopkins University, speaks of psychedelics helping to overcome “disconnection from our *most authentic selves*”

(Barrett 2020, emphasis added). And Griffith, founder of the department, treats psychedelic therapy as something akin to the Oracle of Delphi:

So I did a session with a psychedelic and went into that explicitly asking a couple of questions. ... I asked a question directly of the cancer. I'm hesitant to talk about it because it's reifying the cancer as "other," and I don't hold that the cancer is some "other" with which I can have a dialogue. ...: "This process, is it going to kill me?" The answer was, "Yes, you will die, but everything is absolutely perfect; there's meaning and purpose to this that goes beyond your understanding, but how you're managing that is exactly how you should manage it (Marchese 2023).

Terms like "true depth," "authenticity," and "purpose beyond our understanding" have no place in science—and they should not in public discourse or in the context of psychedelic-assisted therapy either. Transformative psychological changes are realized in neurophysiological changes, and, for this reason, mystic states do not tap into a "truer" or "deeper" reality; rather they tap into the mind of the specific person having the mystic experience. The appearance-reality split that these expressions presuppose invites metaphysical speculation that empirical science does not exhaust what exists, that there is a level of reality that cannot, in principle, be translated into language—such as what-it-feels-like experiences (*qualia*). It also evokes false expectations in the public. Critical humanities of psychedelics can play a useful role debunking these views by removing metaphysical biases embedded in questionnaires that can hinder the integration of qualitative data with neurobiological findings:

- *Increased Conceptual Precision*—Terms like "authentic self" or "true reality" carry implicit philosophical assumptions that do not align with neuroscientific models, making it difficult to clearly define neural correlates or link subjective experiences to brain activity.
- *Avoiding Circular Reasoning*—Using metaphysical terms in subjective reports can lead to a feedback loop, where these terms are reified into scientific conclusions. These risks embedding unscientific assumptions into research models, such as interpreting "authentic self" as a specific neural signature.
- *Cultural and Interpretive Variability*—Metaphysical terms have different meanings across cultures, complicating the standardization of responses and the ability to correlate them with consistent neural patterns. The contrast between Huxley's (1954) and Letheby's (2021) examples of ego dissolution illustrates this challenge.

These concerns highlight the risks of treating metaphysical notions as scientific categories. More broadly, from a philosophical standpoint, there is no "true" self to be discovered, only contingent versions of oneself (Rorty 1989). For instance, one might connect with an earlier version of oneself that feels superior, such as during a mid-life crisis. While some versions of oneself might be healthier and preferable, they are not more "true" or "authentic." Historically, from antiquity to modernity, people spoke of a deeper self, but with contemporary understanding of natural causal mechanisms behind altered states, this perspective is less relevant. The dualisms that get the metaphysical perspective on mystical states off the ground and invite the idea

that other than linguistic means could be employed to access an alleged deeper layer of self and reality are part of a world view that is inconsistent with contemporary science. To be clear, it might feel during the acute drug experience—“acute” meaning while the psychedelic drug is pharmacologically active, which depending on drug and dosage can last for several hours—*as if* there exists another separate realm beyond this physical world that can be experienced. However, the use of metaphysical or abstract language creates severe obstacles to achieving a unified model of psychedelics that ties cognitive effects to neuronal and network effects. How can this problem be addressed?

Recent neuroscientific research regarding psychedelic-assisted therapy focuses on the biochemical mechanisms that disrupt neuronal networks and initiate neuroplasticity. The goal is to leverage these mechanisms to foster lasting changes in behavior, thought patterns, and emotional well-being (Ly et al. 2018, Shao et al. 2021, Vargas et al. 2023). One very promising unified model of psychedelic action is developed in Carhart-Harris and Friston’s landmark 2019 paper, “REBUS and the Anarchic Brain: Toward a Unified Model of the Brain Action of Psychedelics,” which links the subjective phenomenology of psychedelic experiences with their neurobiological underpinnings (Carhart-Harris & Friston 2019). The REBUS model—Relaxed Beliefs Under Psychedelics—aims to integrate three levels of describing human behavior: neuroscience, psychology, and everyday experience. A few key points are as follows:

Starting with the neuroscientific level, the biochemical mechanisms of psychedelics are not yet fully understood. It is known that psychoplastogens like psilocybin, the active compound in magic mushrooms, act as agonists at serotonin 5-HT_{2A} receptors, which are crucial for promoting generalized plasticity and cortical neuron growth (Vargas et al. 2023). Psilocybin induces rapid increases in dendritic spine density and enhances structural and functional connectivity, particularly in high-level cortical regions. Siegel et al. (2024) find that “psilocybin-driven functional connectivity changes were strongest in the default mode network, which is connected to the anterior hippocampus and is thought to create our sense of space, time and self.” (Siegel et al. 2024, p. 2) Accordingly, functional disintegration of these high-level networks has been linked to phenomenological features of transcendence of space and time, ego dissolution, and other cognitive and emotional changes under psychedelics (Lebedev et al. 2015, Vargas et al. 2023, Siegel et al. 2024). The key takeaway is that psychedelic-induced altered states are linked to specific functional connectivity changes induced by agonism of 5-HT_{2A} receptors.

Connecting these biochemical observations to psychological effects remains challenging, as the inter-individual variations in how people respond to the same dose of a psychedelic is also influenced by a person’s internal state and external environment. This means, set and setting influence the psychedelic-induced subjective experience. It is hypothesized that general neuronal plasticity underlies the rapid and sustained therapeutic effects of psilocybin, although the relevance of the hallucinogenic effects of psychedelics remains unclear (Kwan et al., 2022). Further, the integration of neuroplastic changes into long-term behavioral patterns involves extra-pharmacological factors such as supportive preparational psychotherapy, session facilitation, post-session integration meetings (Haijen et al. 2018, Carhart-Harris &

Friston 2019). This is one reason why the precise relationship between brain network changes and lasting effects of psychedelics remains unclear (Siegel et al. 2024). “Any theory of psychedelic meaning must therefore take into account that these [pharmacological] agents work on *encultured psyches*” (Letcher 2013, p.255).

A unified model of psychedelic action, such as REBUS, relies on Bayesian principles, which describe how the brain processes information by continuously adjusting its expectations based on prior knowledge and new sensory input. Prior expectations, shaped by past experiences, help filter perception and cognition, allowing the brain to make sense of the world efficiently (Feldman Barrett, 2018; Letheby, 2021). For instance, in the hollow mask illusion, prior knowledge about faces being convex overrides conflicting sensory evidence, demonstrating how deeply ingrained expectations shape perception. Beyond simple perception, high-level priors govern more abstract beliefs, such as one’s sense of self and understanding of reality.

Carhart-Harris and Friston (2019) propose that psychedelics temporarily weaken the influence of these high-level priors, making the brain less constrained by its usual assumptions. This idea, central to the REBUS model, suggests that psychedelics reduce the “precision” of these priors—meaning they become less rigid and dominant. In everyday terms, precision refers to how much confidence the brain places in a given expectation. When precision is high, the brain strongly favors prior beliefs over new sensory input. When precision is low, new information is more likely to reshape perception and cognition. Psychedelics are thought to lower the precision of high-level priors, allowing for greater flexibility in interpreting experiences.

Another key concept in this framework is “prediction error”—the difference between what the brain expects and what it actually perceives. Under normal conditions, strong priors help suppress minor mismatches between expectation and reality, maintaining a stable sense of the world. However, when high-level priors lose precision under psychedelics, prediction errors gain more influence, making the mind more open to revising deep-seated beliefs.

The predictive brain model can usefully be applied to various well-known psychological biases: for example, cognitive biases, where new data is squeezed to fit preconceptions; or confirmation biases, where the mind filters information that confirms beliefs it already has (Carroll 2016, Feldman Barrett 2018). Historically, the idea of prior expectations structuring our experience goes back at least to Kant, who famously said that intuitions without concepts are blind (Kant 1992, *Critique of Pure Reason*, A51/B75; A95-110)—meaning that without concepts the mind would not be able to structure sense data into useful units. This means, experience is not given; rather, it is made by the mind.

On this basis, integrating the neuroscientific and psychological perspectives, Carhart-Harris and Friston (2019) propose that certain psychopathologies such as depression or obsessive-compulsive disorder may be rooted in particularly rigid high-level priors or excessively dominant beliefs, thereby constraining an agent’s self-awareness and learning. Psychedelic-assisted therapy targets these rigid priors through two steps:

- (a) During the acute psychedelic state: relaxation of high-level priors via disruption of their neuronal substrates;
- (b) Post-acute relaxation of priors: fostering new forms of self-modeling (Letheby, 2021), as the acute brain conditions induced by psychedelics are ideal for revising high-level priors.

Although Carhart-Harris and Friston (2019) do not identify precise biomarkers for transformative changes following an acute mystical experience, they propose a neuro-pharmacological model to explain “the full gamut” (p. 339) of phenomena associated with psychedelics:

Our proposal is that psychedelics disrupt functioning at a level of the system ... that encodes ... priors, beliefs, or assumptions. At low doses, subjective effects may be felt most tangibly at the perceptual level..., but at higher doses, effects will become more profound as the functioning of higher levels of the global hierarchy become significantly disrupted, potentially accounting for phenomena such as the dissolution of ego boundaries and potential (long-term) revision of high-level priors (Carhart-Harris & Friston 2019, pp. 320–321).

A challenge arises when subjective reports of psychedelic experiences rely on abstract or dualistic language, such as “true self” or “accessing the divine.” These terms do not clearly map onto neural processes or mechanisms like changes in prior precision or sensitivity to prediction error. Without precise descriptions of how these experiences relate to shifts in perception and belief updating, it becomes difficult to connect subjective effects to their neural correlates. As a result, metaphysical language limits the ability to integrate first-person reports with neuroscientific findings, making it harder to understand how psychedelics influence the brain.

While 5-HT_{2A} activation is necessary for the acute psychedelic state, the precise pathways leading to mystical-type experiences and the mechanisms responsible for long-term therapeutic effects remain unknown. Future research must clarify whether hallucinatory effects are essential for therapeutic outcomes or if alternative mechanisms play a more direct role. Non-hallucinogenic 5-HT_{2A} agonists would offer a valuable test case (Kwan et al. 2022).

Among existing frameworks, REBUS couches the psychological effects of psychedelics, including increased cognitive flexibility, ego dissolution, and altered meaning attribution in terms of belief updating and predictive processing. Strengthening the connection of these cognitive processes to neuronal mechanisms will enhance the model’s explanatory power. Ultimately, while 5-HT_{2A} receptor activation is necessary for psychedelic effects, how this activation translates into subjective experiences and long-term therapeutic outcomes remains unresolved.

That said, if we accept the core idea of REBUS—that psychedelics disrupt high-level brain networks like the default mode network, increasing neural entropy and weakening deep-seated beliefs and expectations that usually shape perception and cognition—what does this imply about the reliability of insights gained during mystical experiences (Letheby 2016), and what can critical humanities contribute to this debate? The subjective experience of magic mushrooms remains “magical” despite a naturalistic explanation—and rightly so. This is similar to how the experiences

of beauty, the sublime, or free will remain valid at the subjective level, even when fully understood in terms of their physical, chemical, and biological determinants. From the first-person perspective, the mystic state is often described as ineffable or difficult to articulate. However, it's not entirely ineffable because people do talk about it. One challenge lies in that the experience falls outside normal narrative contexts, making it hard to express in conventional language. From a neuroscientific perspective, this "ineffability" arises because psychedelics profoundly affect the high-level narrative structure of experience (Carhart-Harris & Friston 2019). Psychedelics relax the constraints of prior knowledge by disrupting the neural correlates of predictive coding. Hence, the mystical state itself is neither strictly true nor false. For a statement to be true you need to give it a sense within a narrative framework—but for the mystic experience such a standard narrative framework is precisely missing from the first-person perspective. Thus, the individual impression that the experience is hard to put into words. Given the breakdown of the standard predictive model of self and world, there is thus the problem of how to "correctly" interpret a mystic experience that is essentially "ineffable" in terms of everyday language. This presents a challenge for those undergoing psychedelic-assisted therapy. The mystical state itself is neither true nor illusory but an experience shaped by radically altered perceptual and narrative frameworks, which can be integrated into ordinary experience in various ways.

While delusional beliefs induced by psychedelics are not objectively real, the first-person perspective, which varies based on individual factors, might still be experienced as spiritually enlightening and meaningful or disorienting and overwhelming. Carhart-Harris and Friston (2019) note that "it is popularly commented that Freudian-minded therapists saw Freudian contents in their patients' psychedelic experiences, whereas Jungians saw Jungian material" (p. 330). Emotional release during therapy, somatic changes, and the recapturing of autobiographical memories can be integrated into an individual's life, potentially altering entrenched negative thought patterns and behaviors. Granted that relaxation of priors allows for a fresh look at things, the mystical state itself cannot "signal" what that fresh look should be. The mystic state is not an oracle. Griffith appears to engage in an introspective dialogue with himself in the quote above (Marchese 2023), exploring his inner thoughts and feelings, as it were, but there is no non-contingent standpoint from which to interpret and unpack his mystic experience. The terms "correct" or "incorrect" interpretation are not applicable. Psychedelic states are a thing of nature that are experienced as extraordinary. They do not require deciphering and translation into propositional terms. Rather, they require, in one direction, a scientific explanation of how psychedelics impair normal consciousness, and, in the other direction, integration into one's personality and outlook on life. Whatever the intuitive insights are that one takes from "the other state," one has to reflect on them in normal language—be this in the language of everyday experience, science, or art. Outdated metaphysical language that seeks hidden truths in the mystical experience is non-sensical. The terms "true" or "not true" do not apply to the mystic state because it lacks the narrative framework within which we can meaningfully use these words. Describing psychedelics reaching "a deeper level" of the self, "most authentic sense of self," or "uncovering" truth is misleading metaphysical language. The home of understanding "truth" this way is the

Ancient Greek “*aletheia*” (ἀλήθεια), which means “unconcealment,” “un-hidden.” In Platonic thought, *aletheia* is associated with the ultimate reality beyond the physical world. Such language can mislead interpretations of psychedelic experiences.

Removing metaphysical biases embedded in our language may help individuals in the context of psychedelic assisted therapy dealing with the psychological uncertainty and unpredictability of the experience as well as promote understanding of psychedelics within the broader community. Carhart-Harris and Friston (2019) caution that an escalation in psychedelic use could lead individuals to cling to delusional beliefs if experiences are poorly integrated:

A strong psychedelic experience can cause such an ontological shock that the experiencer feels compelled to reach for some kind of explanation, however tenuous or fantastical, to close an epistemic gap that the experience has opened up for them. ...In experiencing such information overload, the psychedelic initiate may reach for bizarre beliefs or poorly understood platitudes, in an effort to explain away his/her felt uncertainty... Spiritual bypassing may be understood as an escapist defense, dressed up as a spiritual awakening (Carhart-Harris & Friston 2019, pp. 336–337).

The challenge of interpreting the ineffable mystical experience is a common issue in psychedelic therapy. Musil (1978) captures this dilemma by comparing mystical experiences to hearing a “whisper or merely a rustling, without being able to distinguish between the two” (p. 562). A whisper has meaning, but you need to listen very carefully. A rustling is a mere noise that lacks information. So, which one of the two is it? The answer is: neither. Psychedelic experiences are not signals pointing to a deeper layer of world and self. However, they are not mere noise either, because the relaxing of high-level priors can promote significant psychological insights after the acute experience and thus have therapeutic benefits if properly integrated into normal consciousness.

In conclusion, the exploration of mystical and psychedelic experiences reveals the influence of linguistic and cultural contingencies on our interpretations of these states. The language we use to describe mystical experiences—ranging from “ego-dissolution” to “divine encounters”—is deeply embedded in historical metaphysical dualisms, which often obscure rather than clarify the nature of these experiences. The REBUS model offers a way beyond this contingency by providing a neurobiological framework that aims to connect the subjective phenomenology of psychedelic experiences to their underlying biochemical mechanisms. While the language of metaphysics may continue to shape our perceptions, the REBUS model helps bridge the gap between the historically contingent experience of psychedelic states and the naturalistic explanations that can contextualize these experiences within contemporary science. This shift not only clarifies the nature of psychedelic experiences but also supports a more accurate and less biased interpretation, enhancing public understanding. Furthermore, by examining how metaphysical positions influence research and therapeutic practices—particularly in the use of qualitative questionnaires—critical humanities can enhance the accuracy of our understanding of psychedelic experiences. Hence, a key role of critical humanities is to bolster psychedelic research by examining historical and cultural contexts to clarify metaphysical assumptions and correct misconceptions rooted in outdated language.

Guarding Scientific Integrity: Challenging Causal Claims in Psychedelic Research

In clinical trials, psilocybin is administered in pill form. When has a pill ever caused a long-term material belief change —except, of course, the red pill in the movie *The Matrix*? Speaking of psychedelics “accounting” for lasting changes in beliefs (Carhart-Harris & Friston 2019, p. 321), or “causally” influencing long-term metaphysical beliefs (Timmermann et al. 2021, p. 1) is misleading. Why? Because it is generally acknowledged that it is not understood how “acute brain changes and associated mind states trigger the relevant long-term changes in beliefs” (Carhart-Harris & Friston 2019, p. 337). “It remains unclear how human brain network changes relate to subjective and lasting effects of psychedelics” (Siegel et al. 2024, p.1). While science has made great advances in understanding the biochemical mechanisms of the acute drug effect, such as neuroplastic effects of psilocybin on brain network function, these effects are not identical to psychological long-term belief and behavioral changes. For this reason, it would be better to speak of psychedelics as “mediating” belief revisions, as the latter depend on additional individual and environmental factors. “Psychedelic therapy depends on an interaction between a biological action of the drug and non-pharmacological contextual factors” (Timmermann et al. 2021). For this reason, the “insights” experienced by individuals differ vastly based on their personal context (Pace & Devenot 2021).

Distinguishing between the biological effects of psychedelics and the content of mystical experiences clarifies this point: Psychedelics promote neuronal plasticity via their agonist actions at the 5-HT_{2A} receptor. But this does not yet say anything about the content of the experience. As one author has eloquently put it: “to say that someone has taken LSD tells little more about the content and import of the experience than to say that he has had a dream” (as cited in Rowlandson 2013, p. 246). Insights denote some specific material content. Thus, psychedelics themselves cannot be said to “cause” insights. An insight is achieved or happens at the cognitive level—despite the naturalist assumption that cognitive insights are coarse-grained descriptions of underlying biochemical processes. It is important not to mix the neurophysiological level of describing human experience with the cognitive level of agency. This is so because post-acute transformative believe changes cannot be accounted for at the neuro-pharmacological level. If it could then psychedelic assisted therapy would be pure pharmacotherapy. But it isn’t. This point deserves more emphasis as it helps preventing systematic confusion of neurophysiological and cognitive levels of describing human experience. Research on psychedelic assisted therapy is interested in understanding how neuronal and network effects of psychedelics at the biochemical level may act as a catalyst for neuroplasticity at the cognitive level. For example, in a recent study, 54% of participants with treatment-resistant depression met the criteria for remission four weeks after psilocybin administration with psychological support (Davis et al. 2021). However, because neuronal plasticity cannot be directly mapped onto psychological plasticity, science should avoid equating biochemically observable neuronal plasticity with cognitive and behavioral changes, which lack clear biomarkers. Research should focus on the interplay between biochemical disruption and neuroplasticity, without overstepping

into unproven causal claims about long-term cognitive plasticity. While psychedelic's entropic effect on brain activity opens up the mind to psychological change, it does not "cause" that change by itself independently of "set and setting." Expectations that by understanding "the neural basis of psychedelic action, we hope to one day leverage the ability of these molecules to shape and heal minds" (Kwan et al. 2022, p. 1415) seem overstated.

It is crucial to recognize that while psychedelics alter the brain's predictive processing dynamics, they do not impose specific beliefs or meanings. Rather, they create a state of heightened plasticity in which individuals reinterpret their experiences through pre-existing cognitive and cultural frameworks. This means, psychedelics do not come with build-in material beliefs—be this on personality, politics, the environment, metaphysics, or any other topic that science is currently investigating. Beliefs are historically contingent products, constructed by an individual's past experiences. For this reason, there cannot be a context-independent core to mystical experiences. Proving that psychedelics cause material beliefs would contradict the predictive processing model of cognition, which posits that all experience is conceptually constructed. Scientists would undermine their own scientific paradigm if they could prove that psychedelics can cause universal material beliefs. Claiming that "psychedelic use may causally influence metaphysical beliefs" (Timmermann et al. 2021, p. 1) is particularly troublesome. If we were to prove scientifically that the brain causes beliefs that cannot be captured by science, this would mean to scientifically validate the existence of a material belief that, by definition, eludes scientific validation. Currently, research on whether psychedelics can cause material beliefs is ongoing. Studies linking psychedelic use to specific beliefs—whether related to personality, politics, or metaphysics—possibly involve participants already predisposed to such beliefs, as scientists have acknowledged this limitation of their studies (Lebedev et al. 2023, p. 11, Timmermann et al. 2021, p. 8, Barrett et al. 2020, p. 8).

The psychedelic experience is highly individual, despite its general biochemical underpinnings. Therefore, the long-term effects of the drug vary among individuals and are best described at the cognitive level. Material beliefs are held for contingent reasons, which are significantly more complex to describe at the biochemical level than measuring agonist actions at their cortical 5-HT_{2A} receptors. The importance of individual differences in the integration of psychedelic experiences recognizes the variability in human responses and the complexity of "translating" the specific neurobiological changes induced by 5-HT_{2A} antagonism into psychological outcomes. Fine-grained plasticity does not *entail* coarse-grained plasticity. This warning against an equivocation on "plasticity," suggesting that using the term across different levels of analysis (cellular and brain networks level vs. psychological level) without careful distinction can be misleading, emphasizes the need for clarity in scientific discourse, and provides an opportunity for critical humanities to assist research on psychedelics.

Enhancing the Therapeutic Setting: The Role of Critical Humanities in Shaping Psychedelic Music Environments and Designing Alternative Control Groups

Despite accumulating evidence that setting influences outcome, a robust understanding of the biochemical mechanisms underlying the effects of setting on psychedelic-assisted therapy is lacking (Golden et al. 2022). One area where this gap is evident is the role of music, which is central to the therapeutic process.

Music has been shown to enhance emotional and experiential aspects of psychedelic sessions, potentially promoting ego dissolution and increasing personality trait openness (Lebedev et al. 2016). However, the relationship between music and therapeutic outcomes is complex and highly individualized. Music, like psychedelics, does not cause emotional changes by itself but interacts with the “set and setting” of the participant. Studies have shown a diverse range of responses to music during therapy, with some participants finding it resonant and others experiencing it as dissonant or counterproductive (Kaelen et al. 2018, Davis 2021). This variability is not surprising, as music requires a cognitive framework to evoke emotions, which means that its effects are contingent on individual backgrounds (Kivy 1990). As music alone does not in itself contain emotionally evocative stimuli, there are many ways of listening to music. Some participants perceive music along a narrative structure, providing the sense of being on a journey to different psychological ‘places,’ while others do not (Kaelen et al. 2018), highlighting the importance of *extra-pharmaceutical* factors of the psychedelic music experience. “It is not merely the drug effect in isolation, but an interaction between the drug and the music on *subjective* experience that promotes positive therapeutic outcomes” (Kaelen et al. 2018, Section “Music experience predicts experience and therapy outcomes,” emphasis added).

That both music and psychedelics can evoke intense, personally meaningful emotionality, thoughts, and memories is an often-made observation: “Both unfold in duration; both are profoundly affectual and difficult to convey in words; and both only make sense in the light of cultural expectation” (Letcher 2013, p. 258). To better understand how music promotes emotionality in the context of psychedelic experience, we would need to know more about the exact relationship between the distinct neuronal effects of music and the relevant psychedelic pharmacodynamics. It is not clear how precisely music supports or modulates the emotional component of psychedelic experiences (or *vice versa*), because there is a gap between the qualitative body of data and its relevant neuronal underpinnings. Do the music lists used in trials affect any of the processes thought to be central to the biochemical workings of psychedelics? Or is the music experience independent of these neurobiological processes? While it is a neuroscientific claim that psychedelics temporarily dysregulate brain mechanisms that normally regulate emotion, it is not clear how this process is related to music enhancing “emotionality, thoughts, and memories that are most personally salient” (Kaelen et al. 2018, Section “Possible therapeutic mechanisms of music in psychedelic therapy”). This latter claim is based on qualitative data obtained from trials that lack control conditions. As Kaelen et al. (2018) acknowledge, “the data was acquired without a placebo condition, making causal inferences about the nature of the effects problematic” (Section “Limitations

and future directions”). Hence, questions remain about how music supports or modulates the emotional component of psychedelic experiences. Given the importance of individualized experiences, the project of creating general playlists for all participants may be misguided. As music’s impact is highly context-dependent, it is unlikely that research will find general “reliable indicators of positive (welcome/supportive) and negative (unwelcome/unsupportive) influences of music on the therapeutic processes during psychedelic therapy sessions” (Kaelen et al. 2018, Section “Implications for the use of music in psychedelic therapy”). A recent study found “no drawback to deviating from a standardized western art-music playlist and using a playlist primarily constructed over overtone music ... [which] does challenge the notion that western art music, or any particular playlist, holds a privileged place in terms of being able to support psychedelic experiences” (Golden et al. 2022, p. 60, Strickland et al. 2020). Critical humanities of psychedelics can provide the forum for this discussion, and play a key role in designing personalized music lists that resonate with specific individuals, thus enhancing therapeutic outcomes (Kaelen et al. 2018, Messell et al. 2022).

Music is just one component of the psychedelic setting. Similar considerations apply to social, ritual, ceremonial, and natural settings (Golden et al. 2022). Exploring these different environments could lead to more effective therapeutic settings and better-designed control groups in research. For example, a recent study found that natural settings are linked to the highest number of positive perceived changes, including greater connectedness to the world, introspection, positivity and increased happiness (Weiss et al. 2023). The same study also found that different psychedelic substances influence perceived personality changes differently—despite their neurobiological similarities and overlapping subjective effects. Currently, understanding how psychedelics shape personality remains limited, partly because these changes are highly variable and difficult to predict. One key reason for this uncertainty is that only 6.6% of relevant research has examined the effects of setting in relation to biomarkers (Golden et al. 2022). Developing alternative control groups could help researchers better isolate the specific impact of psychedelics. Critical humanities of psychedelics can support this endeavor as it has explored ego-dissolution and transformational personality changes in a broad variety of contexts and can thus suggest a variety of relevant comparators. Designing comparative studies, isolating components of the psychedelic experience, and tying these to biomarkers, would shed further light on why the intense subjective experience induced specifically by psychedelics has the transformative effect that is desired in therapeutic contexts.

In summary, a more nuanced understanding of the role of music and other environmental factors in psychedelic therapy, supported by quantitative measures, could improve the efficacy of therapeutic interventions and provide deeper insights into the complex interplay between biochemistry and consciousness.

Conclusion and Outlook

As psychedelics pharmacologically impair normal consciousness, acute psychedelic experiences cannot be phrased in ordinary language. Due to this experienced ineffability,

only a robust understanding of the biochemical mechanisms underlying the effects of psychedelic-assisted therapy can provide necessary granularity. However, integrating set and setting variables into clinical drug research is necessary, given the pharmacotherapeutic and psychotherapeutic aspects of psychedelic-assisted therapy. This integration presents numerous opportunities for researchers across disciplines to engage in meaningful dialogue, ultimately strengthening the connection between the neuronal and network effects of psychedelics and their psychological outcomes.

I use the term “critical humanities” to suggest that diverse perspectives—such as aesthetic, psychological, sociological, anthropological, cultural, political, spiritual, and recreational—are not separate from science but complementary to it. For those who see scientific perspectives on psychedelic experiences as a threat, it is worth emphasizing that understanding their individuality and meaning does not require exempting them from the laws of nature or invalidating traditional communal practices and first-person experiences.

While it is valid for individuals to find comfort in alternative beliefs or the ineffability of mystical experiences, we should remain epistemologically honest and avoid metaphysical misinterpretations. The psychedelic state is a state of nature, best understood in continuity with scientific language rather than as an autonomous alternative. This is an epistemological point. For this reason, I have argued that qualitative questionnaires should avoid metaphysical language. Whether interpreting mystical states through entheogenic or alternative frameworks poses a threat to individual or societal functioning is another matter. A significant byproduct of the critical humanities’ contribution to psychedelic research may be helping the public develop a more coherent worldview and self-image.

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