Journal of Psychiatric Research 188 (2025) 117–125

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires

Therapeutic benefit versus epistemic risk: Need for empirical research in psychedelic epistemology

Lucas F. Borkel [a,b,1], Jaime Rojas-Hernández [a,b,c,1], Domingo J. Quintana-Hernández [b,d], Luis Alberto Henríquez-Hernández [b,e,*]

[a] Health Sciences Faculty, Universidad de Las Palmas de Gran Canaria, Spain
[b] Asociación Científica Psicodélica, Canary Islands, Spain
[c] Asociación Canaria para el Desarrollo de la Salud a través de la Atención, Spain
[d] Faculty of Psychology, Universidad del Atlántico Medio, Spain
[e] Toxicology Unit, Clinical Sciences Department, Universidad de Las Palmas de Gran Canaria, Spain

A B S T R A C T

This paper highlights the ethical and epistemic challenges posed by psychedelic therapy and vindicates the importance of epistemology in the clinical and psychotherapeutic setting. Despite their relative physiological and psychological safety, these substances can induce changes in the beliefs of those who use them, such as paranormal beliefs. To explain the changes in beliefs, we introduced the concept of epistemic criteria (i.e., the principles individuals use to validate and justify their beliefs) and hypothesized that psychedelics may alter beliefs by modifying epistemic criteria. Further research should be conducted to determine this potential and under-researched risk of psychedelic therapy.

1. Introduction

The beginning of the 21st century has seen a powerful comeback of psychedelics in the field of psychiatry and clinical psychology, which has been referred to as the "Psychedelic Renaissance" (Pollan, 2019). Psychedelics in the clinical setting have shown very promising results for the treatment of different pathologies such as treatment-resistant depression (Kamal et al., 2023), tobacco addiction (Johnson et al., 2014; Johnson, 2022), alcohol addiction (Bogenschutz et al., 2016; Morgan et al., 2017), anxiety disorders, and post-traumatic stress disorder (Luoma et al., 2020), cluster headaches, migraines and chronic pain (Castellanos et al., 2020; Flanagan and Nichols, 2018; Madsen et al., 2022; Nichols, 2016; Schindler et al., 2021) and eating disorders (Ragnhildstveit et al., 2022).

Psychedelics also seem to be relatively safe (Nichols, 2016; Van Amsterdam et al., 2011), especially when the use is in a controlled therapeutic environment (Borkel et al., 2024; Rojas-Hernández et al., 2024), due to its low toxicity and very low risk of addiction (Henríquez-Hernández et al., 2023). Psychologically, several other risks have been identified such as hallucinogen persisting perception disorder (Litjens et al., 2014) and psychosis (Wieβner et al., 2023).

Another risk associated with psychedelic consumption that has drawn some attention lately is epistemic risk (Letheby, 2016). Epistemic risk refers to an uncertainty or potential error in knowledge, which often arises in the context of decision-making or hypothesis testing. In science, it is closely related to the concept of inductive risk, which involves the risk of accepting a false hypothesis or wrongly rejecting a true one, especially in cases where the evidence is ambiguous or incomplete. This can occur due to various factors, such as the choice of methodology, the interpretation of evidence or the selection of statistical significance levels in the research. Therefore, epistemic risk is considered a threat to fundamental and defining aspects of knowledge about a topic. It encompasses the risk of intentional or unintentional distortion and mismanagement of knowledge. It has also been argued that therapeutic benefits outweigh epistemic risks and specific belief elicitation (Zeller, 2024).

Psychedelic substances have been the subject of study and a source of fascination across cultures and time, credited with the ability to offer profound insights about the self, consciousness and the world. Throughout history, these substances have also been prized for their potential to foster self-knowledge as well as for their "revelatory power". The relevance of this phenomenon for epistemology is indisputable and shows the need for a dialogue between this area of philosophy and empirical science. We argue that beliefs can change by modifying a

* Corresponding author. Paseo Blas Cabrera Felipe s/n, 35016, Las Palmas de Gran Canaria, Spain.
E-mail address: luis.henriquez@ulpgc.es (L.A. Henríquez-Hernández).
[1] These authors have contributed equally to this work and must be considered joint first authors.

https://doi.org/10.1016/j.jpsychires.2025.05.039
Received 19 September 2024; Received in revised form 13 March 2025; Accepted 22 May 2025
Available online 24 May 2025

deeper cognitive level called *epistemic criteria*.

2. Epistemic criteria as the underlying foundation of belief change by psychedelics

We define epistemic criteria as the standards or norms used to validate and justify beliefs. We postulate that epistemic criteria are subject to reprioritization through psychedelic use. Epistemic criteria include (but are not limited to) evidence, reason, authority, revelation, or faith (Table 1).

Evidence-based criteria involve the use of empirical data and observable phenomena to validate beliefs. Evidence can be broadly understood to include empirical observations, personal experiences, and corroborative testimony. This criterion ensures that beliefs are supported by data from various sources, whether from scientific experiments, personal experiences, or reliable testimonies (Kuhn and Weinstock, 2012). However, personal experiences during psychedelic states can be so vivid and feel so real that individuals may mistake these subjective experiences for empirical evidence of the ontological status of God, entities, other planes of existence, the soul, the ultimate nature of reality, etc. For example, a person may have a profound visionary experience and interpret it as strong and direct evidence of a metaphysical truth, despite the lack of external verification, reproducibility or falsifiability.

Table 1
Definitions and examples of epistemic criteria.

Epistemic Criterion	Definition	Example
Evidence-based	Validation of beliefs based on empirical data, observable phenomena, personal experiences, or testimony. This includes:	
(a) Empirical-scientific	Validation of beliefs based on objective, measurable, replicable, and falsifiable evidence obtained through scientific methodologies.	Accepting that a specific medication is effective based on results from randomized clinical trials.
(b) Personal experience	Validation of beliefs based on subjective perceptual experiences, even if they are non-replicable.	Believing that a certain food causes discomfort based solely on one's repeated experiences after consuming it.
(c) Testimonial or anecdotal	Validation of beliefs based on credible or multiple independent testimonies or anecdotal reports.	Believing that a restaurant is excellent because several friends independently recommend it.
Reason-based	Validation of beliefs based on logical coherence, consistency, and adherence to logical inference.	If John committed the crime, he must have been at the crime scene. John was in another country at the time of the crime. Therefore, John did not commit the crime.
Authority-based	Validation based on the perceived credibility, competence, expertise, or trustworthiness of a source.	Accepting beliefs suggested by experts, scientists, therapists, religious/spiritual leaders.
Revelation-based	Validation of beliefs based on experiences interpreted explicitly as communications, insights, or truths revealed by paranormal, supernatural or divine entities or forces.	The conviction that one's life's purpose has been divinely revealed.
Faith-based	Validation of beliefs based on personal conviction, emotional resonance, or trust without empirical or logical validation.	Holding religious beliefs based purely on personal conviction and trust in sacred texts or a religious tradition.
Intuition-based	Validation of beliefs based on immediate insights or gut feelings perceived as self-evident, without explicit analytical reasoning or empirical justification.	Having a hunch that one cannot trust another person.
Emotion-based	Validation of beliefs guided primarily by emotional responses, feelings, or affective states.	Believing that something is dangerous because one experiences anxiety or fear.

Note. This table provides definitions and illustrative examples of various epistemic criteria individuals may use to validate and justify their beliefs. The epistemic criteria include, but are not limited to, evidence-based (subdivided into empirical observation, personal experience, and testimony), reason-based, authority-based, intuition-based, emotion-based, revelation-based, and faith-based criteria.

Reason-based criteria involve the use of logical consistency and coherence in argumentation. Beliefs validated by reason must adhere to principles of logical inference, ensuring coherence and non-contradiction (Evans, 2002). Under the influence of psychedelics, individuals might experience altered states of consciousness where usual logical structures (e.g., non-contradiction principle) are perceived differently, leading to the formulation of beliefs that seem rational within the psychedelic state but do not hold up under traditional logical scrutiny (e.g., experience of oneness may be interpreted as implying that separation and mutually exclusive ontological categories are illusory and all is one or deeply interconnected). Additionally, psychedelic use may increase connections between concepts, normally unrelated under ordinary consciousness. These new connections might appear coherent or incoherent in an ordinary state of consciousness. This may be related to the entropic brain model (Carhart-Harris et al., 2014).

Authority-based criteria rely on the credibility and expertise of a source. These criteria often play a significant role in contexts requiring specialized knowledge, where individuals depend on experts for validated information (Zagzebski, 2012). Psychedelic experiences may involve encountering "higher beings" (e.g., dead people, aliens, interdimensional entities, God) (Michael et al., 2021) or gaining special insights through a therapist, a shaman or a spiritual guide. These experiences can be so compelling that individuals may grant undue authority to the perceived sources of these insights, potentially leading to the acceptance of beliefs without critical evaluation. Therapists and shamans, as guides of psychedelic experiences, should be considered as potential authorities imposing their worldviews and interpretations on the patient, who is in a particularly vulnerable state of suggestibility.

Revelation-based criteria involve the acceptance of beliefs based on spiritual or mystical experiences. This criterion is particularly prominent in religious contexts where divine insight or spiritual awakening is considered a profound source of knowledge (Hood et al., 2009). However, such experiences can be misinterpreted as empirical evidence, leading to epistemic challenges. Revelation and evidence, while both sources of knowledge, operate differently. Evidence involves empirical data and observable phenomena that can be independently verified and tested. Revelation, on the other hand, is deeply personal and often resistant to counter evidence and counter-arguments. The subjective nature of revelatory experiences can lead individuals to perceive them as equivalent to empirical evidence, especially when the experiences are profound and life-changing. The potential misinterpretation of revelation as evidence highlights the need for further research into how individuals undergoing psychedelic experiences differentiate between these epistemic criteria.

It is important to distinguish clearly between personal experiences as evidence-based criteria and revelation-based criteria. Although both rely on subjective experiences, they differ fundamentally in how they are interpreted and validated. Personal experience criteria involve subjective but direct sensory or cognitive perceptions that, although not scientifically replicable, are generally phenomenological and do not inherently invoke a transcendent source. Revelation-based criteria explicitly involve interpreting experiences as communications, insights, or knowledge revealed by supernatural or metaphysical entities or

realms. Thus, the key distinction is that revelation-based criteria explicitly reference a transcendental or metaphysical source, whereas personal experience criteria rely solely on subjective experiential content. Faith-based criteria involve accepting beliefs grounded in trust and conviction rather than empirical evidence or logical proof (Ichikawa, 2020). Psychedelic experiences can evoke deep feelings of connectedness and certainty, potentially leading individuals to adopt beliefs based on faith that are resistant to empirical scrutiny or logical reasoning.

Psychedelic experiences often blur the lines between subjective insights and objective validation, making it crucial to understand the implications for belief formation and modification. This distinction is vital for assessing the epistemic risks associated with psychedelic therapy and ensuring that the therapeutic benefits do not come at the cost of promoting unfounded beliefs. The role of psychedelic phenomenology, set and setting, and psychological variables (e.g., personality) could play a significant role in these changes. Psychedelic experiences often lead to profound shifts in perception and understanding, potentially elevating revelation as a source of knowledge and possibly affecting the balance with empirical evidence or reason. Understanding the reprioritization of epistemic criteria through psychedelic use is crucial for assessing the epistemic risks associated with psychedelic therapy. Further empirical research is needed to explore how these criteria are modified and the potential implications for individuals undergoing this kind of therapy.

At this point it is important for us to clarify our epistemic stance explicitly. We do not categorically dismiss other ways of knowing, such as revelation, faith, or subjective insights, as inherently invalid or inferior. Instead, our concern primarily stems from three interrelated points.

Firstly, individuals might be unaware of psychedelic-induced changes in their epistemic criteria. Such changes may not be subject to reflection or critical evaluation at the moment they occur, making the process largely unconscious and potentially problematic.

Secondly, alterations in epistemic criteria induced by psychedelics could be the mechanism leading to long-term modifications in fundamental beliefs (e.g. metaphysical, paranormal, or political) and personality persisting beyond the immediate pharmacological effects of these substances.

And finally, changes in epistemic criteria and beliefs can lead to epistemic isolation. Individuals may find their new perspectives incompatible with the norms, values, and beliefs of their immediate social groups, including family, friends, or their broader cultural context, which could result in interpersonal conflicts, social disconnection, and increased vulnerability to manipulation or exploitation.

Fig. 1 illustrates the temporal progression of potential harm within the context of psychedelic therapy. This raises the question of determining the specific point at which harm has occurred. Within this sequence, did harm manifest exclusively in a physical form, specifically at t_4? Furthermore, in addition to the physical and social harm at t_4, is there evidence of epistemic harm at earlier stages, such as t_2 or t_3? Finally, in the absence of physical harm at the conclusion of the sequence, is there a basis for identifying epistemic harm? Our call for empirical research into psychedelic epistemology is motivated by these pragmatic considerations, aiming to understand, anticipate, and mitigate such epistemic risks, rather than categorically dismissing non-scientific ways of knowing.

3. The psychedelic problem: an extraordinary phenomenology

The transformative power of psychedelics for healthy individuals and societies (Scheidegger, 2021; Wolfson, 2014) seems to be attributable to the phenomenology of psychedelic substance-induced experience itself, which, depending on the historical and social context (scientific, religious, traditional, recreational, etc.) has been conceptualized in different ways. There is a great deal of discussion surrounding the concepts of hallucinatory, mystical/religious, psychotic, dreamlike or introspective states, among others. Hence, these substances have been respectively called hallucinogenic, entheogenic, psychotomimetic or psychodysleptic, oniric or psychedelic substances. And it is precisely the variety of experiences induced by these substances that has made their proper classification difficult.

Recent studies with N, N-dimethyltryptamine (Lawrence et al., 2022) have found that mystical and ego-dissolving experiences were frequent. And that, in general, the experiences included a mixture of rewarding emotional responses and challenging aspects. Furthermore, the most common physical effects included somesthesias (37.5 % of participants) and auditory ringing (15.4 %), visual effects consisted predominantly of fractals, shapes, patterns (32.6 %) and vivid colours (25.2 %), including common architectural features such as alternate dimensions (25.2 %), rooms and tunnels. Additionally, 45.5 % of participants in these studies often report “encounters with benevolent entities”. Similar results could be observed in other studies (Michael et al., 2021) showing that 94 % of experiences with this substance produced encounters with “sentient

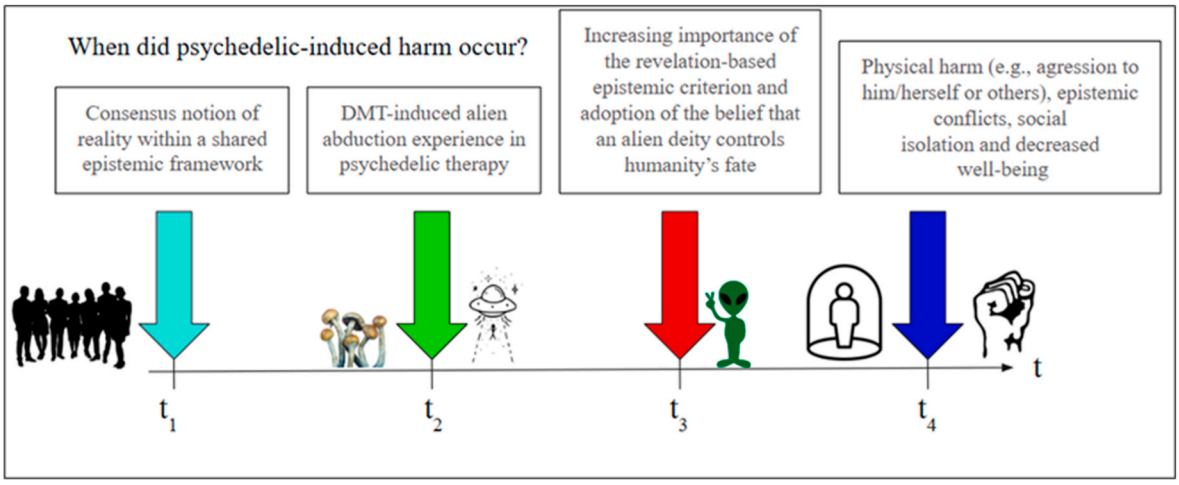

Fig. 1. Epistemic criteria changes and epistemic risk. This figure illustrates a hypothetical progression over time (t) demonstrating how psychedelic experiences may induce changes in epistemic criteria. Initially, individuals share a consensus notion of reality based on common epistemic frameworks (t_1). Following psychedelic therapy and an associated alien-abduction-like experience (t_2), there is an increased prioritization of revelation-based epistemic criteria, leading to the adoption of novel metaphysical or paranormal beliefs (t_3). These epistemic criteria and associated beliefs persist, leading to epistemic conflicts, social isolation, psychological distress and alienation from the individual's original social group and cultural context (t_4). Finally, the patient physically assaults a loved one because of a dispute over his or her new belief (t_4).

entities perceived as beyond the self," who interacted with users playing various roles, such as guides, caretakers, or controllers, and often conveyed personal or universal knowledge to them, taking various forms, such as human, animal, or otherworldly creatures. Additionally, most or all participants reported the appearance of "distinctly different worlds or realms'' during their experiences, which were described as highly intense and profound. Notably, many participants reported intuitive or telepathic communication with the entities. In addition to these types of experiences, similar studies with other psychedelic substances (Davis et al., 2020) reported that 69 % of participants claimed to have received messages or predictions about the future as a result of these encounters. Most participants stated that the experience had been one of the most meaningful of their lives, with lasting positive changes in satisfaction, purpose, and meaning in life. Experiences of "God" or "ultimate reality" have also been described in other studies (Griffiths et al., 2019). Other notable phenomenological features include loss of the notion of space and time, disembodied sensations, alterations in memory, processing, language, and sense of self, and a nuanced understanding of personal and self-referential experiences (Michael et al., 2023). Similarities between the psychedelic experience and near-death experiences have been reported, with the former showing association with reduced persistent psychopathological symptoms (Sweeney et al., 2022). The similarity of the psychedelic experience to the psychotic experience, suggests that these substance-induced states can be used to create models of psychosis for the study of this psychiatric symptom (Wieβner et al., 2023). All this indicates that the wide variety of psychedelic phenomenologies and their respective associations to symptom relief should be studied in depth (Miceli McMillan and Fernandez, 2023).

4. The psychedelic problem: changes in beliefs and personality

Psychedelic consumption positively predicts liberal political views, openness and relationship with nature, while it negatively predicts authoritarian political views, which appears to be associated with the experience of ego dissolution during the psychedelic experience (Lyons and Carhart-Harris, 2018). A recent study (Nour et al., 2017) suggests that psychedelic use can lead to lasting changes in personality traits, beliefs, and attitudes. This has been replicated in other studies (Lyons and Carhart-Harris, 2018) observing that psilocybin treatment also produced a significant increase in relatedness to nature and a decrease in authoritarian views in patients with treatment-resistant depression one week after consumption and remained evident 7–12 months post-treatment. However, the possibility that these experiences conveyed some kind of knowledge, either about the world or about one's own conscious and unconscious mental states, about our motivations, personality traits or about autobiographical memories, is an under-researched question in the clinical setting, although the term "psychedelic" (which manifests the soul) that arose as an evolution of the concept "psychotomimetic" (which imitates states of psychosis) certainly has epistemic implications. Its relevance for philosophy, specifically for epistemology, seems evident, and has recently been addressed (Hauskeller and Sjöstedt-Hughes, 2022; Letheby, 2021).

5. Explaining psychedelic-induced changes: metaphysical belief theory vs predictive self-binding theory

Responding to the question of knowledge acquired through psychedelic states, we can differentiate between two streams: metaphysical belief theory (Timmermann et al., 2021) and predictive self-binding theory (Letheby, 2021).

The first considers changes in metaphysical or fundamental beliefs about the nature of reality to be catalysts for symptom reduction and increased well-being. The concept of mystical experience, characterized by a profound sense of interconnectedness, altered perceptions of space and time, positive emotions, the belief of having accessed a fundamental reality, and the challenge of articulating the experience, stands as a significant predictor of positive outcomes in psychedelic therapy. It should be mentioned that the mystical qualities of psychedelic experience, measured with instruments such as the *Mystical Experience Questionnaire* (MEQ) (Pahnke, 1969) and its revised version MEQ-30 (MacLean et al., 2012), also show strong associations with psychological well-being and relief of various psychopathological symptoms (Griffiths et al., 2006; Ko et al., 2022). The mystical experience referred to is conceptualized in the manner of William James (James et al., 2003). In it, the individual experiences a transformative process that leads to the loss of personal identity and a profound feeling of oneness with all reality, including the divine. This phenomenon, described as *consensus mysticum*, has common features in various cultures. Rudolph Otto (1926) describes it as overwhelming and fascinating. William James identifies key features of mystical experiences, such as their ineffable, noetic, anti-naturalistic, transitory, passive, pantheistic and optimistic nature. James asserts that these experiences have authority only over those who have experienced them, break the conventional boundaries of consciousness, and offer hypotheses that others may dismiss. Such experiences, documented in a number of studies, have sparked debates about their necessity for therapeutic success (Ko et al., 2022). This perspective has culminated in the metaphysical belief theory (Jylkkä et al., 2024; Sjöstedt-Hughes, 2023; Timmermann et al., 2021), which suggests that the main benefit of psychedelic therapy derives from the adoption of comforting, albeit supernatural, beliefs following a mystical experience. It further postulates that psychedelic substance-induced experiences can lead to a profound and lasting change in worldview, providing existential solace and boosting the therapeutic benefits of psychedelics. In support of this view, research (Timmermann et al., 2021) indicates that psychedelic experiences can induce lasting changes in individuals' beliefs about reality, correlating these changes with improvements in mental health.

Another recent clinical trial shows that a large proportion of people who use psychedelics attribute consciousness to both animate and inanimate objects (Nayak and Griffiths, 2022). Participants reported higher attribution of consciousness after consumption to: a) non-human primates (63 % before; 83 % after; 85 % now), b) quadrupeds (62 % before; 80 % after; 83 % now), c) insects (34 % before; 59 % after; 61 % now), d) fungi (21 % before; 57 % after; 62 % now), e) plants (26 % before; 62 % after; 65 % now), f) natural inanimate objects (8 % before; 27 % after; 29 % now), and g) artificial inanimate objects (4 % before; 15 % after; 17 % now). This higher attribution of consciousness was significant and long-lasting, not diminishing even years after the experience. The same study (Nayak and Griffiths, 2022) also showed significant increases in beliefs in telepathy (30 % before; 62 % after; 64 % now), telekinesis (11 % before; 20 % after; 23 % now), communication with the dead (25 % before; 42 % after; 45 % now), and out of body mind travel (30 % before; 70 % after; 72 % now), among others; and also decreases in superstitious beliefs. Additionally, psychedelic use appears to be associated with a decrease in the number of people who identify as atheists (35.8 % before; 13 % after). The percentage of participants of the same study who identified themselves as "believers" (e.g., in Ultimate Reality, Higher Power, and/or God, etc.) increased from 28.8 % before use to 58.8 % afterwards, where changes remained after an average of 8,4 years (Nayak and Griffiths, 2022). Similar results have been found in other trials (Davis et al., 2020; Griffiths et al., 2019). All these changes in basic beliefs were sustained over time and associated with higher scores on the MEQ30.

A highly relevant study conducted by an interdisciplinary team of pharmacologists, psychologists and philosophers shows that psychedelic use appears to change fundamental beliefs about the nature of reality (Timmermann et al., 2021). The development of a specific questionnaire on metaphysical beliefs (*Metaphysical Beliefs Questionnaire*) for this study can be considered as one of the first psychometric philosophical tools. The results of this study seem to point to the existence of a causal relationship between the use of psychedelics, the change of

metaphysical beliefs (specifically, about the nature of reality, consciousness and destiny) and symptom relief and increased psychological well-being. The effect of psychedelics seems to specifically favor panpsychistic, dualistic and fatalistic (deterministic type) beliefs, to the detriment of naturalistic, physicalistic or materialistic positions.

Following this line of work, some recent philosophical approaches consider that states induced by psychedelic substances give access to knowledge about the nature of reality, that is, they behave as a kind of instrument for metaphysical research (Sjöstedt-Hughes, 2015). The apparent therapeutic power of intense psychedelic experiences (including mystical ones), the complex phenomenology and the associated changes in beliefs have led some philosophers to postulate the need to introduce the metaphysical debate into the therapeutic and experimental realm (Sjöstedt-Hughes, 2023). According to Sjöstedt-Hughes (2023), both researchers and patients would benefit from having a metaphysical conceptual framework to interpret and integrate psychedelic experiences. His proposal suggests presenting patients and researchers with a simplified outline of the different metaphysical theories or positions in the form of a *Metaphysics Matrix*, and implementing a questionnaire (*Metaphysics Matrix Questionnaire* or MMQ) to introduce rational argumentation in the psychotherapeutic setting in contrast to the "revelation" of the mystical experience.

Gładziejewski (2023), postulated that psychedelic experiences, by allowing epistemic subjects to elicit experiences whose core structure differs from ordinary states of consciousness, enable a radical and transient broadening of cognitions that can inform metaphysical inquiry. In this sense, psychedelic experiences may provide epistemic benefits otherwise unattainable by (a) invalidating arguments "from experience" that favor certain commonsense metaphysical claims; (b) challenging claims of (in)conceivability and their supposed modal consequences that figure in metaphysical debates; and (c) supporting metaphysical projects that presuppose states of consciousness with non-ordinary phenomenal characteristics, such as non-dual or egoless forms of consciousness. However, profound sensations of having true insights into the nature of reality could simply be the result of faulty metacognitive monitoring of reality or a modification in the weighting of priorities induced by psychedelics. Similarly, there is the problem of determining what to make of the differences in metaphysical beliefs that emerge after psychedelic experiences in different people. How to assess which experience is more credible? In turn, there appears to be evidence that preexisting expectations can significantly influence psychedelic experiences (Colloca et al., 2023; McGovern et al., 2022), shaping perceptions in ways that confirm certain beliefs, a phenomenon known as cognitive penetrability.

On the other hand, Letheby (Letheby and Gerrans, 2017; Letheby, 2021), proposes an innovative approach to understanding the effects of psychedelics on the human psyche, distinguishing itself from metaphysical belief theory by focusing on the generation of new self-perceptions during psychedelic experiences. This theory is based on the integration of two fundamental concepts, predictive processing and self-binding theory, to explain how psychedelics might facilitate psychological flexibility and insight. It suggests that psychopathologies may arise from overly rigid self-representations that are resistant to new and potentially contradictory information. Psychedelics, may relax these rigid self-concepts, increasing receptivity to new information and facilitating meaningful personal insights. This relaxation of self-representations is believed to alter certain neural networks, mainly the default mode network, leading to the dissolution of the ego, a state of increased malleability of the self, which can pave the way for new perspectives and insights. This theory emphasizes the psychological over the mystical or metaphysical, suggesting that the primary value of psychedelic experiences lies in the generation of personal insights that can lead to psychological transformation and beneficial outcomes, such as reduced depression and substance abuse. In contrast to metaphysical belief theory, which focuses on the alteration of beliefs as a catalyst for change, predictive self-binding theory posits that changes in self-representation and the perceptions derived from these changes are the central mechanisms of action in psychedelic therapy. Acevedo et al. (2024) results supported the predictive self-binding theory by showing that psychological perception was the sole predictor of both beneficial and negative outcomes, mediating the impact of ego dissolution and therapeutic intention on positive outcomes.

Consequently, these theories posit that changes in beliefs explain therapeutic benefits. Nevertheless, the metaphysical beliefs theory does not consider the possibility that certain changes in beliefs may be considered risks or even epistemic harms. In contrast, the predictive-self binding theory does consider the possibility of epistemic harms but maintains that therapeutic benefits outweigh them.

Both metaphysical belief theory and predictive self-binding theory may coexist and complement each other in explaining therapeutic improvements. Clinical observations suggest significant variability, as some individuals experience predominantly mystical states and others primarily gain personal insights. Additionally, some individuals experience a combination of both or neither. Therefore, both theories can offer valuable explanatory frameworks without necessarily competing or being mutually exclusive. However, further empirical research is required to clarify the conditions and mechanisms under which each type of experience contributes to therapeutic outcomes.

6. The psychedelic problem: epistemic risks

The interpretation or valuation of these experiences has traditionally been considered positive or negative depending on the social context. Religious or mystical experiences have traditionally been considered virtuous or desirable in various cultures (Escohotado, 1995), while hallucinations or psychotic delusions are considered pathological or undesirable in modern Western scientific societies. Nevertheless introspective or mystical-type experiences and their association to psychological benefits should be further studied (Millière et al., 2018). Stripping away the supernatural character of mystical experience, some authors speak of bodily self-experiences and mental self-experiences (Mosurinjohn et al., 2023), thus decomposing mystical experience into empirically supported constructs of psychology and neuroscience. In turn, the personality changes associated with these experiences pose an ethical challenge that must be addressed. The immense variety of psychedelic experiences and their diverse interpretations have led on the one hand to some controversy about the possible dangers of psychedelic-assisted therapies and on the other hand points directly to the philosophical challenge represented by psychedelic phenomenology. Garb and Earleywine (2022) recognize the difficulty of discussing psychedelic experiences and attribute that to the implicit recognition of the existence of the mystical by researchers, the mystical being a non-falsifiable concept from a naturalistic and scientific perspective. They therefore propose a fictionalist philosophical approach, based on research in logic and linguistics. This approach would allow researchers to engage in discussions of mystical experiences without committing themselves to their ontological status. By employing non-factual narrative prefix operators, researchers could treat reports of mystical experiences as meaningful narratives without asserting their factual truth. Non-factual prefix operators are linguistic tools used to treat statements or accounts as if they do not represent actual facts, i.e. to point out that what is being said should not be taken literally or as a true fact, but rather as part of a narrative, hypothesis, fiction or speculation. This allows for the exploration of ideas and situations without claiming that these correspond directly to reality. In the clinical setting, it refers to expressions such as "imagine that … " or "suppose that … ". This perspective would offer more flexibility, allowing researchers to explore the impact of these experiences on therapy outcomes without being constrained by a rigid belief in their mystical nature. It would also facilitate dialogue between proponents and detractors of mystical interpretations without affecting the empirical commitment involved in scientific activity. It would also provide cognitive flexibility, allowing

individuals undergoing psychedelic-assisted therapies to view their thoughts as hypotheses rather than absolute truths. This mindset aligns somewhat with cognitive-behavioral models, allowing patients to reevaluate their cognitions and behaviors to potentially reduce the suffering associated with their psychological problems.

Other more radical criticisms such as those of Sanders and Zijlmans (2021) speak of a conceptual clash between scientific values and the supernatural and mystical beliefs that seem to have infiltrated the field of clinical research. The critique implies that researchers themselves are responsible for introducing anti-scientific and anti-empirical biases and beliefs through the use of instruments such as the MEQ and the *Altered States of Consciousness Questionnaire* (Studerus et al., 2010), which seem to suggest the existence of "pure consciousness," "ultimate reality," etc. The problem therefore lies in the use of the mystical framework, which can lead to a "black box" mentality among researchers, treating certain aspects of the psychedelic state as "beyond scientific investigation". This phenomenon, termed "psychedelic exceptionalism," occurs when psychedelic experiences are considered so sacred or important that normal scientific rules do not apply. Sanders and Zijlmans argue against labelling psychedelic experiences as "ineffable," "paradoxical," or "empty," emphasizing that the mystical label does not adequately explain psychological phenomena. The aforementioned psychometric tools would bias the data and hinder a more nuanced understanding of participants' experiences. They also insist on the possible misinterpretation of psychedelic research results when mystical terminology is used. This has led to interpretations of mysticism that lack supernatural aspects. Confusing the phenomenal aspects of the mystical experience with the beliefs associated with mystical experiences can create unrealistic expectations for researchers, for trial participants, and for future patients. This is why these authors argue for the need to develop new conceptual frameworks for psychedelic research, which we will discuss below.

Alleged encounters with intelligent entities (Lutkajtis, 2021), with the divine or with deceased persons (Podrebarac et al., 2021), are relatively common among psychedelic users. Patients often state this with a high degree of certainty and refer to a "direct contact with reality". This has sparked a debate about the epistemic risks or harms associated with psychedelic use (Letheby, 2016). This has been raised by journalist and science popularizer Michael Pollan: Do psychedelics offer comforting delusion to the sick and dying? This directly alludes to the obvious epistemic-ethical conflict faced by psychedelic-assisted therapy (PAT) and is known as the "comforting delusion objection" (CDO) (Pollan, 2015). In the wake of this controversy, Letheby has recently presented one of the most systematic analyses to date of the epistemic risks of PAT. In *Philosophy of Psychedelics* (Letheby, 2021) the CDO argument is reformulated as follows:

1. Naturalism is true.
2. If the epistemic status of psychedelic therapy is poor, then we should hesitate to recommend or prescribe it.
3. If naturalism is true, then the epistemic status of psychedelic therapy is poor.
4. Therefore, we should hesitate to recommend or prescribe psychedelic therapy.

As we can see, the first premise presupposes the veracity and desirability of naturalism, the foundation of scientific thought and developed technological societies. Although there is no single way of conceptualizing naturalism (Horst, 2009), it is understood by Letheby as the metaphysical doctrine that considers the mind as a physical or material process and denies the existence of non-natural entities such as God, the soul and supernatural qualities. From there, Letheby introduces the idea that PAT introduces elements and forms beliefs that contradict this metaphysics. Therefore, PAT poses a risk to the patient.

Letheby (2021) himself presents us with three lines of argument for dealing with CDO. First, psychedelic therapy understood in a naturalistic way does not inherently promote non-naturalistic metaphysical beliefs. Contrary to initial appearances, the mechanism of therapy does not necessarily involve the promotion of these beliefs, nor is it an inevitable side effect. Second, he introduces the concept developed by Bortolotti of "epistemic innocence" which refers to the status of faulty cognitions that, despite their epistemic costs, provide significant epistemic benefits that could not be achieved by less costly means (Bortolotti, 2015). Psychedelic states are, according to Letheby (2021), "epistemically innocent," meaning that although they carry some epistemic risks, they also offer significant benefits that often cannot be obtained by other means. He suggests that transformative psychedelic experiences do not always involve non-naturalistic metaphysical hallucinations. On the contrary, they often lead to profound changes in self-perception, granting individuals new perspectives on their lives (i.e., introspection). The third line of argument states that some aspects of psychedelic therapy contain elements of a "naturalistic spirituality," understood as a heightened sense of connection, aspiration, and reflection on the vastness and beauty of the natural world accompanied by a profound humility and reduction of the ego. This spirituality would not necessarily conflict with the naturalistic conceptual framework.

We offer here some objections to Letheby's argument. First, his initial argument (i.e., that the mechanism of therapy does not necessarily involve the promotion of non-naturalistic beliefs) seems to contradict some empirical evidence previously mentioned (Nayak and Griffiths, 2022; Timmermann et al., 2021). While it is true that there are still few studies establishing such strictly causal relationships between psychedelic consumption and dramatic changes in beliefs, these experiments should be taken into account given their profound epistemic and ethical implications. Another objection refers to Letheby's second argument which implies that the therapeutic potential of psychedelic experiences is associated with the transformative power of introspection. However, it is not clear how to determine the epistemic innocence attributed to psychedelic states: how would one calculate the benefit-risk balance without having previously designed and validated a specific instrument to determine the epistemological framework before and after psychedelic use? Additionally, how can we talk about this balance without establishing associations between these epistemic frameworks and well-being and health variables? And finally, the third argument is particularly complex, given that the author does not detail what exactly this "naturalistic spirituality" consists of and how it differs from "spirituality in general". The very concept of spirituality is vague (Nelson, 2009) and has many meanings (Zinnbauer et al., 2015). How to implement this supposed "naturalistic spirituality" in the psychotherapeutic setting also seems unclear and raises new complex problems of philosophical, religious, cultural, and ideological compatibility.

Greif and Šurkala (2020) argue that the alleged epistemic harm may not outweigh the benefits of PAT, especially if the use is palliative or compassionate. From this utilitarian point of view, if PAT is beneficial and helps people cope with serious situations, even if it provokes delusions and irrational beliefs, it might be perfectly permissible. It follows that these authors subordinate epistemology to welfare. This pragmatic approach seems more reasonable in severe cases or when psychedelics are used in moderation, as in compassionate use, but might not be justifiable for cases of habitual or low use. CDO also raises another problem when it presupposes naturalism. Naturalism, understood by Greif and Šurkala as physicalism or materialism, is a metaphysical assumption that can be questioned without contradicting the critical spirit that characterizes modern philosophy and science. This stance on naturalism, physicalism or materialism is similar to what has been defined as object naturalism, as opposed to subject naturalism (Price, 2004).

From this follows a final pertinent objection to CDO, which addresses the challenges associated with diagnosing metaphysical delusions in the context of psychiatry. The International Classification of Diseases (ICD-11) (Meagher et al., 2008) defines delusion as a manifestly false, firmly held belief that is difficult to modify by contradictory evidence. Religious beliefs are excluded from this definition. However, when it comes

to metaphysical beliefs such as the existence of God, the immaterial nature of reality or the concept of an afterlife, psychedelic-induced experiences have the potential to induce and reinforce such beliefs by giving them apparent (albeit altered) empirical support. This point opens the possibility of rethinking the criteria used to define delusions from a psychopathological perspective.

At first glance Greif and Šurkala's (2020) pragmatic approach seems to simplify and to some extent invalidate the epistemological debate suggested by Letheby (2021). However, it remains to be seen whether epistemic risk may entail other harms to patients that could not be precisely established to date. In this sense, it may be that the patient's depressive symptoms have subsided, but leaving the patient in a state of suggestibility that makes him or her easy prey for cults, gurus or being a victim of abusive relationships. Although direct empirical evidence for persistent suggestibility beyond the acute dosing session remains limited (Dupuis, 2021), existing literature does show lasting changes in beliefs following psychedelic experiences, e.g., increase in paranormal beliefs like telepathy and clairvoyance (Nayak and Griffiths, 2022; Timmermann et al., 2021). These persistent changes could indicate long lasting modifications in underlying epistemic criteria, a possibility that we hypothesize might involve prolonged states of relaxed epistemic vigilance, openness to new beliefs, or a decreased threshold for accepting new ideas. However, more rigorous, longitudinal empirical research is necessary to clearly determine whether and to what extent suggestibility itself persists beyond the acute psychedelic experience, potentially contributing to epistemic risks.

These problems have given rise to proposals to neutralize the possible biases that therapists and researchers may introduce (Johnson, 2020) so as not to encourage ideological and sectarian tendencies in patients and experimental subjects. However, we consider that in light of the transformative power of psychedelic states and the potential vulnerability of the patient, the responsibility of therapists and researchers should not remain mere neutrality. On the other hand, there are positions that prioritize epistemological pluralism over specific epistemologies arguing in favor of epistemic agency and cognitive liberty, despite this potentially contravening a naturalistic epistemology (Zeller, 2024). Therefore, the potential associations between different types of epistemologies and therapeutic outcomes and well-being (but also suggestibility and gullibility) should be determined.

Recent developments in assessing adverse events in PAT have also highlighted the necessity of monitoring post-acute dosing impacts on patients' worldviews and spirituality. Palitsky et al. (2024) introduced a comprehensive framework that identifies 54 potential adverse event constructs warranting systematic assessment in PAT, including those related to changes in meaning and psychosocial health and potential negative consequences of altered epistemic beliefs. This approach also brings attention to the potential for adverse events arising from the imposition of therapists' religious or ideological beliefs during PAT. This concern reveals the ethical implications of altering epistemic beliefs, emphasizing the need for therapists to maintain epistemic humility and respect for patients' pre-existing belief systems to prevent epistemic harms and preserve therapeutic integrity. Palitsky et al. (2024) discuss epistemic beliefs primarily at the level of explicit and conscious worldviews or spiritual beliefs (i.e., what people explicitly believe about reality, spirituality, or metaphysical entities). Their emphasis lies on how explicit belief content, when altered by psychedelic-assisted therapies, can lead to clinical and psychosocial consequences. It is nonetheless worth mentioning that Palitsky's epistemic beliefs focus primarily on explicit belief content changes (conscious, articulable beliefs about reality, spirituality, and worldview), while our epistemic criteria focus on deeper, implicit criteria (often unnoticed by the individual) that determine how beliefs are evaluated, formed, and justified in the first place.

Corlett et al. (2013) also point to a direct relationship between altered prediction error signaling induced by ketamine administration and psychosis-like symptoms, suggesting that disruptions in these cognitive processes may underpin the emergence and persistence of delusional beliefs. These findings indicate the importance of investigating drug-induced cognitive disturbances, particularly altered epistemic processes and their potential harmful consequences (e.g., psychosis), across various clinical and non-clinical contexts.

7. Therapeutic benefit versus epistemic harm: a novel avenue for exploration

What do we do with patients who, after PAT, start to believe in telekinesis, telepathy, clairvoyance, that they communicate with aliens or the dead, or are certain that reality is a computer simulation? Strassman (2000) has documented a large number of cases of participants in clinical trials with N, N-dimethyltryptamine (DMT) who claim not only to have experienced contact with intelligent entities under the effects of the substance, but that these entities are real. The attribution of consciousness to inanimate objects, belief in supernatural intelligent entities or the paranormal are obviously in conflict with the rational spirit of philosophy and science, not to say that they can be considered symptoms of a psychopathology. Several studies have linked prolonged use of psychedelics, poly-substance use, and absorptive capacity (linked to the personality trait of openness to experience), among other variables, to these types of experiences, beliefs, and ways of thinking (Zhou et al., 2022). Other studies show associations between use of substances such as LSD and cannabis with anomalous and paranormal beliefs and experiences (Thalbourne, 2001). In view of the evidence, a new *Acid Panic* cannot be ruled out (Henríquez-Hernández et al., 2023). This is why these issues should be addressed systematically and empirically as soon as possible.

Do psychedelics simply change beliefs, or do they affect the epistemic criteria on which beliefs are grounded? Changes in the latter imply that the underlying norms that govern the formation and justification of our beliefs, both conscious/explicit and unconscious/implicit, could be affected by psychedelic consumption, reorganizing the priority we give to empirical evidence, reason, emotion or authority. This apparent reconfiguration of the cognitive and affective infrastructure that determines our perceptions of the world, the dynamics of our social interactions and our personal well-being through the use of a substance needs to be further explored if regulation is to occur in the clinical setting. This proposal should motivate the design of both observational and clinical studies to examine how such changes in epistemic criteria occur, and what other variables are involved in order to address unexplored risks. In addition psychological variables (e.g. personality, suggestibility), the influence of both set and setting variables on epistemic changes should be carefully investigated.

To date, several fundamental questions have not been addressed and need to be explored:

- Does the use of psychedelics result in alterations to the epistemic criteria that guide the evaluation, acquisition, and validation of knowledge and beliefs?
- In the context of psychedelic therapy, is the change in beliefs (metaphysical, paranormal, political, etc.) mediated by change in epistemic criteria?
- In the context of psychedelic therapy, are the occurrence of insights and personality change mediated by change in epistemic criteria?
- Is there a correlation between specific epistemic criteria and specific beliefs?
- In the context of psychedelic therapy, could changes in beliefs and epistemic criteria be predicted by pre-existing psychological variables (e.g., openness)?
- Do variables of set and setting predict changes in epistemic criteria and fundamental beliefs?
- In the context of psychedelic therapy, should a naturalistic epistemology be included in the preparation for and integration of psychedelic experiences to minimize epistemic risks?

- Can certain epistemic changes constitute harm in themselves, independent of emotional, physical or interpersonal harm?
- Can epistemic harm cause subsequent emotional or physical harm?
- Can epistemic harm, in turn, cause harm to interpersonal relations?
- Are therapeutic benefits positively correlated with epistemic risks? If so, is psychedelic therapy ethical?

8. Further research

To empirically test the hypothesis that psychedelics induce alterations in epistemic criteria, future research should prioritize the development and validation of an Epistemic Criteria Questionnaire (ECQ), a tool that would systematically measure the prioritization of epistemic criteria (evidence, reason, authority, intuition, emotion, revelation, and faith, and maybe others). With such a tool, correlational, longitudinal, and clinical studies could determine if shifts in epistemic criteria correlate with sustained changes in beliefs, psychological well-being, social relationships, or susceptibility to epistemic harm. Establishing these relationships empirically is essential for understanding the broader ethical and clinical implications of psychedelic therapy. The ECQ could also serve to explore epistemic changes beyond psychedelics, providing insight into how epistemic criteria may shift across various contexts, interventions, and life experiences.

CRediT authorship contribution statement

Lucas F. Borkel: Writing – original draft, Investigation, Conceptualization. **Jaime Rojas-Hernández:** Writing – original draft, Investigation, Conceptualization. **Domingo J. Quintana-Hernández:** Writing – review & editing, Investigation. **Luis Alberto Henríquez-Hernández:** Writing – review & editing, Validation, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Acevedo, E.C., Uhler, S., White, K.P., Al-Shawaf, L., 2024. What predicts beneficial outcomes in psychedelic use? A quantitative content analysis of psychedelic health outcomes. J. Psychoact. Drugs 1–10.

Bogenschutz, M.P., Johnson, M.W., 2016. Classic hallucinogens in the treatment of addictions. Prog. Neuro Psychopharmacol. Biol. Psychiatr. 64, 250–258.

Borkel, L.F., Rojas-Hernández, J., Henríquez-Hernández, L.A., Santana Del Pino, Á., Quintana-Hernández, D.J., 2024. Set and setting predict psychopathology, wellbeing and meaningfulness of psychedelic experiences: a correlational study. Expet Rev. Clin. Pharmacol. 17 (2), 165–176.

Bortolotti, L., 2015. The epistemic innocence of motivated delusions. Conscious. Cognit. 33, 490–499.

Carhart-Harris, R.L., Leech, R., Hellyer, P.J., Shanahan, M., Feilding, A., Tagliazucchi, E., et al., 2014. The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs. Front. Hum. Neurosci. 8, 20.

Castellanos, J.P., Woolley, C., Bruno, K.A., Zeidan, F., Halberstadt, A., Furnish, T., 2020. Chronic pain and psychedelics: a review and proposed mechanism of action. Reg. Anesth. Pain Med. 45 (7), 486–494.

Colloca, L., Nikayin, S., Sanacora, G., 2023. The intricate interaction between expectations and therapeutic outcomes of psychedelic agents. JAMA Psychiatry 80 (9), 867–868.

Corlett, P.R., Cambridge, V., Gardner, J.M., Piggot, J.S., Turner, D.C., Everitt, J.C., et al., 2013. Ketamine effects on memory reconsolidation favor a learning model of delusions. PLoS One 8 (6), e65088.

Davis, A.K., Clifton, J.M., Weaver, E.G., Hurwitz, E.S., Johnson, M.W., Griffiths, R.R., 2020. Survey of entity encounter experiences occasioned by inhaled N,N-dimethyltryptamine: phenomenology, interpretation, and enduring effects. J. Psychopharmacol. 34 (9), 1008–1020.

Dupuis, D., 2021. Psychedelics as tools for belief transmission. set, setting, suggestibility, and persuasion in the ritual use of hallucinogens. Front. Psychol. 12, 730031.

Escohotado, A., 1995. Historia General de las Drogas, (three volumes). Alianza, Spain.

Evans, J.S.B., 2002. Logic and human reasoning: an assessment of the deduction paradigm. Psychol. Bull. 128 (6), 978.

Flanagan, T.W., Nichols, C.D., 2018. Psychedelics as anti-inflammatory agents. Int. Rev. Psychiatr. 30 (4), 363–375.

Garb, B.A., Earleywine, M., 2022. Mystical experiences without mysticism: An argument for mystical fictionalism in psychedelics. Journal of Psychedelic Studies 6 (1), 48–53. https://doi.org/10.1556/2054.2022.00207.

Gładziejewski, P., 2023. From altered states to metaphysics: the epistemic status of psychedelic-induced metaphysical beliefs. Rev. Philosophy Psychol. 1–23.

Greif, A., Šurkala, M., 2020. Compassionate use of psychedelics. Med. Healthc. Philos. 23 (3), 485–496.

Griffiths, R.R., Hurwitz, E.S., Davis, A.K., Johnson, M.W., Jesse, R., 2019. Survey of subjective" God encounter experiences": comparisons among naturally occurring experiences and those occasioned by the classic psychedelics psilocybin, LSD, ayahuasca, or DMT. PLoS One 14 (4), e0214377.

Griffiths, R.R., Richards, W.A., McCann, U., Jesse, R., 2006. Psilocybin can can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. Psychopharmacology 187, 268–283.

Hauskeller, C., Sjöstedt-Hughes, P. (Eds.), 2022. Philosophy and Psychedelics: Frameworks for Exceptional Experience. Bloomsbury Publishing.

Henríquez-Hernández, L.A., Rojas-Hernández, J., Quintana-Hernández, D.J., Borkel, L.F., 2023. Hofmann vs. Paracelsus: do psychedelics defy the basics of toxicology?-A systematic review of the main ergolamines, simple tryptamines, and phenylethylamines. Toxics 11 (2), 148.

Hood Jr., R.W., Hill, P.C., Spilka, B., 2009. The Psychology of Religion: an Empirical Approach. Guilford Press.

Horst, S., 2009. Naturalisms in philosophy of mind. Philos. Compass 4 (1), 219–254.

Ichikawa, J.J., 2020. Faith and epistemology. Episteme 17 (1), 121–140.

James, M., Carrette, J., James, W., Taylor, E., 2003. The Varieties of Religious Experience: A Study in Human Nature. Routledge.

Johnson, M.W., Garcia-Romeu, A., Cosimano, M.P., Griffiths, R.R., 2014. Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction. J. Psychopharmacol. 28 (11), 983–992.

Johnson, M.W., 2020. Consciousness, religion, and gurus: pitfalls of psychedelic medicine. ACS Pharmacol. Transl. Sci. 4 (2), 578–581.

Johnson, M.W., 2022. Classic psychedelics in addiction treatment: the case for psilocybin in tobacco smoking cessation. Disruptive Psychopharmacol. 213–227.

Jylkkä, J., Krabbe, A., Jern, P., 2024. Endorsement of Metaphysical Idealism Mediates a Link between Past Use of Psychedelics and Wellbeing.

Kamal, S., Jha, M.K., Radhakrishnan, R., 2023. Role of psychedelics in treatment-resistant depression. Psychiatric Clinics 46 (2), 291–305.

Ko, K., Knight, G., Rucker, J.J., Cleare, A.J., 2022. Psychedelics, mystical experience, and therapeutic efficacy: a systematic review. Front. Psychiatr. 13, 917199.

Kuhn, D., Weinstock, M., 2012. What is epistemological thinking and why does it matter?. In: Personal Epistemology. Routledge, pp. 121–144.

Lawrence, D.W., Carhart-Harris, R., Griffiths, R., Timmermann, C., 2022. Phenomenology and content of the inhaled N, N-dimethyltryptamine (N, N-DMT) experience. Sci. Rep. 12 (1), 8562.

Letheby, C., 2016. The epistemic innocence of psychedelic states. Conscious. Cognit. 39, 28–37.

Letheby, C., 2021. Philosophy of Psychedelics. Oxford University Press.

Letheby, C., Gerrans, P., 2017. Self unbound: ego dissolution in psychedelic experience. Neuroscience of Consciousness 2017 (1), nix016.

Litjens, R.P., Brunt, T.M., Alderliefste, G.J., Westerink, R.H., 2014. Hallucinogen persisting perception disorder and the serotonergic system: a comprehensive review including new MDMA-related clinical cases. Eur. Neuropsychopharmacol. 24 (8), 1309–1323.

Luoma, J.B., Chwyl, C., Bathje, G.J., Davis, A.K., Lancelotta, R., 2020. A meta-analysis of placebo-controlled trials of psychedelic-assisted therapy. J. Psychoact. Drugs 52 (4), 289–299.

Lutkajtis, A., 2021. Entity encounters and the therapeutic effect of the psychedelic mystical experience. J. Psychedelic Stud. 4 (3), 171–178.

Lyons, T., Carhart-Harris, R.L., 2018. Increased nature relatedness and decreased authoritarian political views after psilocybin for treatment-resistant depression. J. Psychopharmacol. 32 (7), 811–819.

MacLean, K.A., Leoutsakos, J.M.S., Johnson, M.W., Griffiths, R.R., 2012. Factor analysis of the mystical experience questionnaire: a study of experiences occasioned by the hallucinogen psilocybin. J. Sci. Stud. Relig. 51 (4), 721–737.

Madsen, M.K., Petersen, A.S., Stenbæk, D.S., Sørensen, I.M., Schiønning, H., Fjeld, T., et al., 2022. Psilocybin-induced reduction in chronic cluster headache attack frequency correlates headache attack frequency correlates with changes in hypothalamic functional connectivity. medRxiv.

McGovern, HT, Leptourgos, P, Hutchinson, BT, Corlett, PR, 2022 Jun. Do psychedelics change beliefs? Psychopharmacology (Berl) 239 (6), 1809–1821. https://doi.org/10.1007/s00213-022-06153-1. Epub 2022 May 4. PMID: 35507071.

Meagher, D.J., MacLullich, A.M., Laurila, J.V., 2008. Defining delirium for the international classification of diseases, 11th revision. J. Psychosom. Res. 65 (3), 207–214.

Miceli McMillan, R., Fernandez, A.V., 2023. Understanding subjective experience in psychedelic-assisted psychotherapy: the need for phenomenology. Aust. N. Z. J. Psychiatr. 57 (6), 783–788.

Michael, P., Luke, D., Robinson, O., 2021. An encounter with the other: a thematic and content analysis of DMT experiences from a naturalistic field study. Front. Psychol. 12, 5731.

Michael, P., Luke, D., Robinson, O., 2023. An encounter with the self: a thematic and content analysis of the DMT experience from a naturalistic field study. Front. Psychol. 14, 1083356.

Morgan, C., McAndrew, A., Stevens, T., Nutt, D., Lawn, W., 2017. Tripping up addiction: the use of psychedelic drugs in the treatment of problematic drug and alcohol use. Curr. Opinion in Behav. Sci. 13, 71–76.

Mosurinjohn, S., Roseman, L., Girn, M., 2023. Psychedelic-induced mystical experiences: an interdisciplinary discussion and critique. Front. Psychiatr. 14, 1077311.
Millière, R., Carhart-Harris, R.L., Roseman, L., Trautwein, F.M., Berkovich-Ohana, A., 2018. Psychedelics, meditation, and self-consciousness. Front. Psychol. 9, 1475.
Nayak, S.M., Griffiths, R.R., 2022. A single belief-changing psychedelic experience is associated with increased attribution of consciousness to living and non-living entities. Front. Psychol. 13, 1035.
Nelson, J.M., 2009. Psychology, Religion, and Spirituality.
Nichols, D.E., 2016. Psychedelics. Pharmacol. Rev. 68 (2), 264–355.
Nour, M.M., Evans, L., Carhart-Harris, R.L., 2017. Psychedelics, personality and political perspectives. J. Psychoact. Drugs 49 (3), 182–191.
Otto, R., 1926. The Idea of the Holy: an Inquiry into the Non-rational Factor in the Idea of the Divine and its Relation to the Rational. H. Milford, Oxford university press.
Pahnke, W.N., 1969. Psychedelic drugs and mystical experience. International Psychiatry Clinics 5 (4), 149–162.
Palitsky, R., Kaplan, D.M., Perna, J., Bosshardt, Z., Maples-Keller, J.L., Levin-Aspenson, H.F., et al., 2024. A framework for assessment of adverse events occurring in psychedelic-assisted therapies. J. Psychopharmacol. 38 (8), 690–700.
Podrebarac, S.K., O'Donnell, K.C., Mennenga, S.E., Owens, L.T., Malone, T.C., Duane, J. H., Bogenschutz, M.P., 2021. Spiritual experiences in psychedelic-assisted psychotherapy: case reports of communion with the divine, the departed, and saints in research using psilocybin for the treatment of alcohol dependence. Spirituality in Clinical Practice 8 (3), 177.
Pollan, M., 2015. The trip treatment. In: The New Yorker, vol. 9.
Pollan, M., 2019. How to Change Your Mind: what the New Science of Psychedelics Teaches Us about Consciousness, Dying, Addiction, Depression, and Transcendence. Penguin.
Price, H., 2004. Naturalism without representationalism. Naturalism in Question, pp. 71–88.
Ragnhildstveit, A., Slayton, M., Jackson, L.K., Brendle, M., Ahuja, S., Holle, W., et al., 2022. Ketamine as a novel psychopharmacotherapy for eating disorders: evidence and future directions. Brain Sci. 12 (3), 382.
Rojas-Hernández, J., Borkel, L.F., Quintana-Hernández, D.J., del Pino, Á.S., Henríquez-Hernández, L.A., 2024. Pattern of psychedelic substance use: a comparison between populations in Spain and South America using the Psychedelic Use Scale (PUS). Curr. Psychol. 43 (45), 35083–35098.
Sanders, J.W., Zijlmans, J., 2021. Moving past mysticism in psychedelic science. ACS Pharmacol. Transl. Sci. 4 (3), 1253–1255.
Scheidegger, M., 2021. Psychedelic medicines: a paradigm shift from pharmacological substitution towards transformation-based psychiatry. Ayahuasca healing and science 43–61.
Schindler, E.A.D., Sewell, R.A., Gottschalk, C.H., et al., 2021. Exploratory controlled study of the migraine-suppressing effects of psilocybin. Neurotherapeutics 18, 534–543. https://doi.org/10.1007/s13311-020-00962-y.
Sjöstedt-Hughes, P., 2015. Noumenautics: Metaphysics-Meta-Ethics-Psychedelics.
Sjöstedt-Hughes, P., 2023. On the need for metaphysics in psychedelic therapy and research. research. Front. Psychol. 14, 1128589.
Strassman, R., 2000. DMT: the Spirit Molecule: A Doctor's Revolutionary Research into the Biology of Near-Death and Mystical Experiences. Simon and Schuster.
Studerus, E., Gamma, A., Vollenweider, F.X., 2010. Psychometric evaluation of the altered states of consciousness rating scale (OAV). PLoS One 5 (8), e12412.
Sweeney, M.M., Nayak, S., Hurwitz, E.S., Mitchell, L.N., Swift, T.C., Griffiths, R.R., 2022. Comparison of psychedelic and near-death or other non-ordinary experiences in changing attitudes about death and dying. PLoS One 17 (8), e0271926.
Thalbourne, M.A., 2001. The paranormal and its place in human relationships: Some hypotheses. Australian Journal of Parapsychology 1 (1), 72–85.
Timmermann, C., Kettner, H., Letheby, C., Roseman, L., Rosas, F.E., Carhart-Harris, R.L., 2021. Psychedelics alter metaphysical beliefs. Sci. Rep. 11 (1), 22166. https://www.nature.com/articles/s41598-021-01209-2.
Van Amsterdam, J., Opperhuizen, A., van den Brink, W., 2011. Harm potential of magic mushroom use: a review. Regul. Toxicol. Pharmacol. 59 (3), 423–429.
Wießner, I., Falchi, M., Palhano-Fontes, F., Feilding, A., Ribeiro, S., Tófoli, L.F., 2023. LSD, madness and healing: mystical experiences as possible link between psychosis model and therapy model. Psychol. Med. 53 (4), 1151–1165.
Wolfson, P.E., 2014. The transformative power of ketamine: psychedelic states and a personal history of transformation. Int. J. Transpersonal Stud. 33 (2), 14.
Zagzebski, L.T., 2012. Epistemic Authority: A Theory of Trust, Authority, and Autonomy in Belief. Oxford University Press.
Zeller, M., 2024. Psychedelic therapies and belief change: are there risks of epistemic harm or epistemic injustice? Philos. Psychol. 1–32.
Zhou, K., De Wied, D., Carhart-Harris, R., Kettner, H., 2022. Predictors of hallucinogen persisting perception disorder symptoms. Delusional Ideation and Magical Thinking Following Naturalistic Psychedelic Use.
Zinnbauer, B.J., Pargament, K.I., Cole, B., Rye, M.S., Butfer, E.M., Belavich, T.G., et al., 2015. Religion and spirituality: unfuzzying the fuzzy. Sociol. Relig. 29–34.