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ORIGINAL RESEARCH

These aren't the beliefs you're looking for: on the limits of affect-neutral accounts of psychedelic therapy

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Abstract

A recurring finding in psychedelic-assisted therapy is that the subjective intensity and quality of the psychedelic experience contribute more to therapeutic outcomes than the administered dose. To explain why such experiences are therapeutic, many have appealed to what these may reveal or enable, such as the types of mental representations that can be acquired, the expansion of what can enter awareness, or the revision of high-level beliefs about the self and the world. Across these proposals, some form of belief disruption is often assigned a causal role. In this paper, I argue that even if psychedelics do work by loosening beliefs or expanding awareness, this alone is not sufficient to explain why the resulting changes should be beneficial rather than neutral or harmful. By implicitly taking for granted the typically positive character of many psychedelic experiences, existing theories risk describing processes that could just as easily worsen distress as alleviate it, and so fail to reflect the literature's predominantly positive outcomes. Ultimately, I argue that without a positive shift in affective valence, there is no clear reason why psychedelic experiences should lead to therapeutic outcomes.

Keywords Psychedelics · Psychotherapy · Beliefs · Phenomenology · Cognitive science · Affect

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1 Introduction

In the last decade, research into psychedelics has surged, driven by their extensive clinical benefits. Various theories have been proposed to explain how these substances induce such changes. However, in this paper I argue that none of these theories are entirely satisfactory. Instead, I propose that the key to achieving therapeutic effects lies in the positive affective valence of psychedelic experiences, a component that has been overlooked. While positive affect *alone* is undoubtedly insufficient, I contend that it is *required* for clinical outcomes. If individuals do not find their experiences enjoyable, they are unlikely to derive therapeutic benefits from them.

Section 2 reviews the literature on the clinical benefits of psychedelics and outlines Letheby's criticisms of preliminary explanations for these benefits. Section 3 describes Letheby's (2021) alternative perspective on what he believes is responsible for psychedelics' therapeutic effects. Section 4 introduces another theory, proposed by Lyon (2023), regarding how psychedelics facilitate healing. Finally, in Sect. 5, I argue that neither theory is complete, as both lack a mechanism ensuring positive outcomes. I show that neither can explain why outcomes are predominantly positive rather than neutral or even harmful, and demonstrate how incorporating the positive affect reliably found in psychedelic experiences naturally fills this explanatory gap. I conclude that, without integrating affect, no belief-based theory can adequately explain why psychedelics so often improve mental health.

2 Psychedelics' therapeutic outcomes

2.1 What are psychedelics?

Psychedelics represent a class of psychoactive substances that induce significant alterations in consciousness. These altered states are characterized by vivid visual hallucinations, distortions in the perception of time, changes in the sense of self, and profound emotional experiences (Preller & Vollenweider, 2016). Among the most recognised hallucinogens are psilocybin (the active component in magic mushrooms), lysergic acid diethylamide (LSD), N,N-Dimethyltryptamine (DMT), and 3,4-Methylenedioxymethamphetamine (MDMA).[1] Despite their unique effects, these substances share similar psychotropic properties (Preller & Vollenweider, 2016).

The primary mechanism by which psychedelics exert their effects is believed to be through their interaction with the serotonin 5-HT2A receptor (Barrett et al., 2017; Kometer et al., 2013). This receptor can be thought of as a docking station where serotonin typically binds. Psychedelics mimic serotonin by binding to these receptors but induce different receptor behaviors. This interaction is thought to be responsible not only for their hallucinogenic properties but also their potential therapeutic effects.

[1] Displaying characteristics similar to both amphetamines and hallucinogens, MDMA is positioned somewhere between a stimulant and a hallucinogen, rather than a "classic" hallucinogen (Holze et al., 2019). MDMA is also recognized as an empathogen or entactogen.

However, not all psychedelics exert their effects through the serotonin system. Some psychedelics act on different receptors and involve distinct mechanisms. For example, ketamine primarily interacts with the NMDA receptor, while salvinorin A (found in salvia) activates the kappa opioid receptor. For clarity, when referring to psychedelics in this paper, I will be exclusively referring to serotonergic psychedelics, those affecting the serotonin 5-HT2A receptor, such as LSD, psilocybin, and DMT.

Historically, psychedelics garnered significant research interest in the 1950s and 1960s, particularly concerning substance abuse and psychiatric treatment. Early studies demonstrated benefits in various psychiatric contexts, including the treatment of alcoholism, obsessive-compulsive disorder (OCD), and neurosis (Abramson et al., 1955; Smart & Storm, 1964; Mechaneck et al., 1968; Vojtěchovský et al., 1972; Savage, 1973). However, the rise of the 1960s counterculture movement, coupled with political and social upheaval, led to substantial stigmatization of these substances (Strassman, 2000). Consequently, nearly all research into their potential benefits was halted (Liester, 2015).

This stagnation persisted until the 1990s and 2000s when pioneering studies began to revisit the effects of psychedelics (Hermle et al., 1992; Strassman et al., 1994; Griffiths et al., 2006). The promising results from these studies rekindled scientific interest, leading to an increasing number of investigations that have yielded further positive findings regarding their use. Recent investigations have focused on the therapeutic potential of psychedelics for treating mental health disorders such as depression, post-traumatic stress disorder (PTSD), and end-of-life anxiety. This resurgence in research, often referred to as the "psychedelic renaissance", has begun to reshape both the scientific and public perception of these substances (Sessa, 2012; Hadar et al., 2022).

2.2 Psychedelics' range of therapeutic benefits

The therapeutic potential of psychedelics has gained significant attention due to their promising results across a wide range of disorders and conditions. They not only show promise in treating multiple disorders, but in some instances, outperform treatments specifically designed for those conditions. Given the widespread prevalence of mental health and substance abuse issues, discovering effective treatments is of utmost importance. Here, I will review different therapeutic avenues in which psychedelics may offer a viable solution.

2.2.1 Major depressive disorder (MDD)

Major depressive disorder (MDD), for instance, affects 300 million people globally, with a lifetime prevalence rate between 10 - 20% and significant increases observed in the last decade (World Health Organization, 2017). Despite this, current treatment methods often fall short. Approximately half of patients discontinue antidepressants within six months of starting treatment (Solmi et al., 2021), and these treatments have small effect sizes and high relapse rates (Anagha et al., 2021; Locher et al., 2017). Therefore, new approaches to treating depression are essential. Psychedelic-

assisted therapy (PAT), where psychedelics are integrated into therapeutic sessions, has produced exceptionally positive results in treating depression. Numerous studies, reviews, and meta-analyses (Perez et al., 2023; Sanches et al., 2016; Davis et al., 2021; Rucker et al., 2016; Goodwin et al., 2023; Raison et al., 2023; dos; Santos et al., 2016) have demonstrated that psychedelics significantly reduce depressive symptoms in cases of both primary and secondary depression. These substances often show effectiveness even after a single dose, providing rapid benefits without the need for prolonged treatment plans. Moreover, the positive effects of psychedelics extend well beyond the acute drug effects, which is uncommon in pharmacotherapies.

For example, Griffiths et al. (2016) found that a single dose of psilocybin significantly reduced depressive symptoms and anxiety in patients with life-threatening cancer. These improvements, as reported by patients, clinicians, and community observers, lasted for at least six months, with clinical response rates, indicating the percentage of patients experiencing a reduction in symptoms, of 78% for depression and 83% for anxiety. Another study demonstrated that a single dose of psilocybin led to significant antidepressant effects, with response rates reaching around 80% at a 6.5-month follow-up (Ross et al., 2016). Similar antidepressant responses have been observed with single doses of ayahuasca, an Amazonian brew containing DMT (Osório et al., 2015), and DMT itself (Davis et al., 2019).

Not only are psychedelics showing great efficacy in treating depression, but they are also capable of treating patients with treatment-resistant depression. Approximately 20–60% of patients with psychiatric disorders do not respond to available standard therapies (Howes et al., 2022). Patients with treatment-resistant depression are those whose condition has not improved when using available methods, leaving them with limited options. Psychedelics, however, have demonstrated significant improvements in treating such patients (Kalfas et al., 2023; Carhart-Harris et al., 2016; Palhano-Fontes et al., 2019). Notably, Goodwin et al. (2023) found significant results as soon as the second day after treatment, and Carhart-Harris et al. (2018) reported sustained positive effects at three and six months.

In conclusion, psychedelics have demonstrated value in reducing depressive and anxiety symptoms for prolonged periods after only one dose, even in treatment-resistant cases. Their side effects, such as headache and occasional nausea, are generally limited to the session itself, a significant improvement over other medications, such as SSRIs, which can have long-term side effects (Irizarry et al., 2022). Other mental health disorders have also been studied using psychedelics and, similarly, found positive results. High treatment response rates have been observed following psychedelic-assisted therapy in PTSD and OCD (Bahji et al., 2020; Moreno et al., 2006), and ongoing research shows promise in using psychedelics for chronic pain management (Kooijman et al., 2023; Robinson et al., 2024). The positive therapeutic outcomes following psychedelic use seems to, therefore, reach different pathologies and clinical populations.

2.2.2 Substance use disorders[2]

The urgency for effective treatments is equally pronounced in substance use disorders. Tobacco addiction, for instance, results in up to half of its users dying if they do not quit, with smoking-related mortalities estimated at 8 million annually worldwide (World Health Organization, 2023). Current behavioral interventions and pharmacotherapies for smoking cessation demonstrate minimal success rates, typically below 35% at six months (Cahill et al., 2014; Mottillo et al., 2009).

So far, only one study has investigated whether psychedelics could be used for smoking cessation, and its results are very promising. In an open-label pilot study, smokers received either 2 or 3 doses of psilocybin in conjunction with cognitive behavioral therapy (CBT) aimed at quitting smoking. Remarkably, 80% of participants displayed biologically confirmed smoking abstinence, verified through breath and urine analysis, six months post-treatment (Garcia-Romeu et al., 2015). This is significantly higher than the success rates of current smoking cessation treatments.

Prior to their criminalization, the therapeutic potential of psychedelics for substance use disorders was already recognized, with early research primarily investigating LSD as a treatment (Smart & Storm, 1964; Ludwig et al., 1969; Johnson, 1969; Hollister et al., 1969). A meta-analysis of six randomized controlled studies from within that time concluded that a single dose of LSD significantly decreased alcohol misuse compared to non-psychedelic control treatments (Krebs & Johansen, 2012). LSD was also found to significantly increase opioid abstinence at six months (Savage, 1973).

More recently, psilocybin has also demonstrated promising results in the treatment of alcoholism. Bogenschutz et al. (2015) administered psilocybin along with Motivational Enhancement Therapy to participants with alcohol dependence. This combination led to a significant increase in abstinence, which was not observed with therapy alone. The positive effects were largely sustained at the 36-week follow-up. Additionally, another study found that over a 32-week double-blind trial, the psilocybin group significantly reduced their average daily alcohol intake and proportion of heavy drinking days compared to the placebo group (Bogenschutz et al., 2022).

Similarly, MDMA has also shown promise in treating alcohol use disorder. A study by Sessa et al. (2021) found that nine months post-detox, participants who received MDMA treatment reduced their alcohol consumption from an average of 130.6 units per week before detox to 18.7 units per week.

Beyond clinical populations, psychedelics may also decrease harmful substance use in the general population. A survey of 5268 adults found that nearly three-quarters reported quitting or reducing the use of non-psychedelic substances after using psychedelics. Specifically, 60.6% reduced their alcohol consumption, 55.7% cut back on antidepressant use, and 54.2% decreased their use of cocaine or crack (Glynos et al., 2024).

[2] I use "substance use disorder" over "addiction" to reflect its broader clinical scope beyond compulsive use.

2.2.3 Meaningful life experience

In addition to their clinical and mental health benefits, psychedelics frequently induce some of the most meaningful experiences of individuals' lives, an outcome that, though not directly tied to therapeutic benefits, is consistently observed and worth mentioning. Through randomized double-blind studies (2006, 2008, 2011), Griffiths and colleagues found that most naïve participants who were administered psilocybin rated their experience as among their life's top *ten* most meaningful events, with this sentiment persisting at a 14-month follow-up. In one study, 94% of participants considered the experience to be one of the top *five* most meaningful in their lives. Similar outcomes were observed in another randomized, double-blind study with LSD (Schmid & Liechti, 2018), and echoed in large-scale surveys, in which 27% and 12% of respondents reported their psychedelic experience as the *single most* meaningful event in their lives (Griffiths et al., 2019; Kajonius & Sjöström, 2024).

Taken together, these findings highlight the influential and enduring impact that psychedelics have on their users, setting them apart from conventional treatments. In clinical contexts, psychedelic-assisted therapy has consistently demonstrated superior efficacy in reducing depressive symptoms compared to other available treatments, even in treatment-resistant cases. It has shown promise in alleviating symptoms of anxiety, PTSD, and OCD and proven remarkable success in treating substance use disorders. In non-clinical populations, psychedelics are linked to lower substance use. Additionally, psychedelics often induce profoundly meaningful experiences, frequently ranked amongst people's top five meaningful life events. Collectively, these observations point to a therapeutic profile unique to psychedelics. Absent, however, is an explanation revealing the mechanisms that underwrite this efficacy, leaving us with a pressing open question: How can a substance produce such drastic, positive, and global effects across such different populations? In the remainder of this Section, I review preliminary explanations that attempt to address this question.

2.3 Neuroplasticity as an explanation

To explain the profound and wide-ranging effects of psychedelics, several theories have been put forward. One prominent line of reasoning emphasizes the physiological changes psychedelics produce in the brain as the key driver of their therapeutic outcomes. Letheby (2021) refers to these as neuroplasticity theories, which attribute the long-term improvements provided by psychedelics to their ability to stimulate neuroplasticity (Olson, 2018; Goodwin, 2016).

Neuroplasticity refers to the brain's capacity to reorganize itself by developing new neural connections, while also pruning, weakening, or strengthening existing ones throughout life. Plasticity enables the brain to adapt to novel experiences, learn new information, and recuperate from damage (Cramer et al., 2011). Enhanced plasticity is considered clinically advantageous by making the brain more malleable and capable of changing entrenched patterns of thought and behavior. Various mood and clinical disorders have been shown to have disrupted plasticity (Pittenger & Duman, 2007). By rewiring maladaptive neural circuits into more functional ones, neuroplasticity would lead to therapeutic benefits.

The theory that psychedelics promote positive outcomes by opening a window of neuroplasticity offers a compelling explanation for the enduring effects of these substances, which persist long after they have left the body. Additionally, it would help explain why they successfully treat such a wide range of disorders. Instead of targeting a specific mechanism thought to be responsible for a particular disorder, psychedelics may restructure dysfunctional neural configurations into more adaptive ones, regardless of the specific pathology. If true, psychedelics' therapeutic effects would stem from reorganizing neural networks, independent of any other effects they induce.

Research supports the notion that psychedelics enhance neuroplasticity (Calder & Hasler, 2023). They catalyze periods of rapid neuronal growth, thereby boosting the brain's capacity for neuroplastic changes. For example, animal studies have shown that psychedelics promote the expression of genes related to synaptic plasticity, such as immediate early genes and Brain-Derived Neurotrophic Factor (BDNF) (Moliner et al., 2023). Additionally, psychedelics increase the growth of dendritic spines, small protrusions on neurons where synapses form, and enhance the density of dendritic arborization (Ly et al., 2018). This growth improves synaptic connectivity, facilitating better communication between neurons and enhancing the flexibility and connectivity of neural networks. Collectively, these findings indicate clear neuroplasticity-enhancing effects of psychedelics.

While the neuroplasticity theory is compelling and may help explain the lasting benefits of psychedelics after a single dose, it is not sufficient on its own. As Letheby points out, if neuroplasticity were the sole or primary factor, the subjective experience during the psychedelic session would not influence clinical outcomes. However, evidence shows that the most significant predictor of therapeutic outcome is whether the patient has a mystical-type experience during the session. These experiences, characterized by a sense of oneness, transcendence of time and space, intensely positive emotions, and indescribable nature, often lead to profound personal insights and shifts in perspective (Stace, 1961). Studies consistently report that, across various conditions, the depth of the mystical-type experience is the strongest predictor of positive clinical outcomes (Barrett & Griffiths, 2018).

For example, in the study examining the use of psilocybin for smoking cessation, it was observed that participants who successfully quit smoking had significantly higher scores on measures of mystical experiences. Interestingly, there were no notable differences in the overall intensity of the drug effects between those who quit and those who did not, indicating that the mystical-type experiences, rather than how intensely the drug was experienced, played a crucial role in smoking cessation (Garcia-Romeu et al., 2015). Similarly, mystical-type experiences were linked to a decline in problematic alcohol use after psychedelic experiences (Garcia-Romeu et al., 2019). These findings suggest that mystical experiences are a key factor in the effectiveness of psychedelic-assisted addiction treatment.

The lack of correlation between the overall intensity of drug effects and clinical outcomes renders a theory based solely on molecular changes less convincing. If neuroplasticity were the key mechanism, the more intense experience of the drug's effects, indicating greater molecular activity, should trigger more substantial changes in the brain's neural connections and, consequently, greater therapeutic benefits.

Instead, evidence indicates that factors beyond mere neuroplasticity, particularly the depth of mystical experiences, are crucial for clinical outcomes.

Letheby notes that this is not surprising. Neuroplasticity, simply the brain's capability to reshape its structure and function, can have positive, neutral, or even adverse outcomes. It's unreasonable to assume that merely enhancing neuroplasticity will always lead to positive effects; the specific neural networks where plasticity occurs and how these networks are rewired are crucial. The therapeutic benefits likely depend on how this increased plasticity is directed, which would relate to the quality of the psychedelic experience itself.

While neuroplasticity is undoubtedly essential for brain health and likely plays a significant role in the therapeutic benefits of psychedelics, it alone *cannot* account for the positive clinical outcomes observed. To understand these outcomes, it is vital to consider the nature and content of the psychedelic experience itself. Mystical-type experiences seem to be critical in mediating these benefits.

2.4 Metaphysical theories

To understand how mystical-type experiences lead to positive clinical outcomes, Letheby highlights theories pertaining to metaphysics.[3] These theories suggest that the benefits of psychedelics stem from their capacity to induce transcendent experiences that reveal alternate realities, such as that of a spirit realm or what has been termed a "Joyous Cosmology."

2.4.1 Metaphysical Belief Theory (MBT)

The Metaphysical Belief Theory (MBT) suggests that psychedelics do not directly heal or transform individuals; rather, the mystical experiences they facilitate are responsible for these effects (Sjöstedt-Hughes, 2023; Gładziejewski, 2023). While psychedelics are one means of inducing such experiences, similar states can be triggered by near-death experiences, deep meditation, or hypnosis (Richards, 2008). These mystical experiences, which are characterized by an intense, often ineffable sense that one has encountered the fundamental metaphysical nature of reality, are so compelling that they frequently lead to lasting changes in metaphysical beliefs and personal attitudes. According to MBT, these changes in beliefs play a crucial role in the therapeutic process. This would explain why mystical-type experiences, rather than the mere intensity of drug effects, are better predictors of positive clinical outcomes.

Psychedelics have been shown to induce significant changes in metaphysical beliefs. For instance, a study by Griffiths et al. (2019) revealed that over two-thirds of individuals who identified as atheists prior to a psychedelic experience no longer identified as atheists afterwards. Additionally, Timmermann et al. (2021) found that psychedelic use led to shifts away from hard physicalism towards beliefs in panpsy-

[3] In this literature, 'metaphysics' deviates from its conventional academic definition, referring instead to a broader, more spiritual context. To maintain consistency with the terminology employed in relevant studies, I will continue using the term as inherited from previous scholars.

chism and dualism, among others, with many of these changes persisting six months later.

These shifts in metaphysical beliefs may not be merely incidental but also appear to confer therapeutic benefits. In the same study by Timmermann et al. (2021), changes in metaphysical beliefs were associated with positive mental health outcomes, including improved well-being and reduced depression in both observational and controlled research data. Similarly, Savage et al. (1964) found that increased awareness of an "ultimate reality" was associated with positive outcomes following a single LSD session. Letheby also highlights numerous cases where patients with terminal illnesses experienced reduced anxiety about dying after becoming convinced of a spiritual realm (p. 68–70). Even in healthy volunteers, changes in metaphysical beliefs were critical in producing enduring psychological benefits (Griffiths et al., 2008).

These findings suggest that the therapeutic effects of psychedelics are closely linked to the profound shifts in metaphysical beliefs they can induce. The realignment of beliefs towards a more spiritually oriented understanding of reality appears to be the cause of the lasting psychological improvements seen in both clinical and healthy populations.

The Metaphysical Belief Theory posits that the therapeutic benefits arise from the *beliefs* formed about the mystical experience rather than the experience per se. On this view, encountering an alternate, joyous reality during a mystical-type experience is not sufficient for clinical outcomes; the belief in this alternate reality must also be sustained.

This theory, however, faces significant challenges. Letheby provides many examples of patients who reported substantial therapeutic benefits without adopting new metaphysical beliefs (p. 70). If positive clinical outcomes can occur without changes in metaphysical beliefs, then these beliefs cannot be the sole mechanism driving the efficacy of psychedelics.

Furthermore, the extent to which psychedelic experiences reliably cause changes in metaphysical beliefs may be overstated. The findings from Griffiths et al. (2019) were based on a sample of individuals who reported having a God encounter while tripping, which is not representative of the general population. Thus, the claim that two-thirds of atheists changed their beliefs after a psychedelic experience is specific to this particular group. Additionally, Nayak et al. (2024) observed minimal to no shifts in metaphysical beliefs such as dualism or Atheist-Believer status in their study, contrasting with earlier research they conducted, which suggested that psychedelic experiences lead to such changes.

In conclusion, while changes in metaphysical beliefs *can* contribute to positive outcomes, they *cannot* be the primary mechanism behind the efficacy of psychedelic therapy.

2.4.2 Metaphysical Alief Theory (MAT)

Metaphysical Alief Theory (MAT) offers a different perspective. 'Alief' refers to a mental state that influences thought, emotion, and behavior, even if it is not consciously endorsed as a belief (Gendler, 2008a, 2008b). For example, one might feel and act as if something were hiding under their bed, all the while believing the space

to be completely safe. According to MAT, the therapeutic benefits of psychedelics are derived not from beliefs but from aliefs acquired or strengthened during the experience.

Letheby suggests that patients who undergo mystical-type experiences may develop an intense "mental representation of a transcendent universal consciousness" (p. 76). This mental representation, whether or not it is consciously endorsed, can profoundly impact the patient's emotional and psychological state. This theory likens the process to an "inverse PTSD," where instead of a traumatic experience embedding a negative alief, a mystical experience embeds a positive one (Garcia-Romeu et al., 2015).

Accordingly, if an individual were to take psychedelics and be relieved of his depression, MAT would argue that this is because the psychedelic experience induced a mystical-type experience, providing him with an *experience* of an alternate, joyous reality. The emotions and mental state experienced during this alternate reality would create an alief, leading to positive clinical outcomes, regardless of whether he metacognitively endorses these experiences afterwards.

However, MAT encounters similar issues as MBT, as many patients who benefited from psychedelics did not describe any non-naturalistic metaphysical content in their experiences. Letheby argues that if vivid metaphysical visions were essential for psychological change, they would be prominent in patients' recollections. Instead, many patients focus on themes like emotional catharsis and psychological insights without referencing metaphysical concepts (Gasser et al., 2015; Watts et al., 2017).

In conclusion, psychedelics offer many therapeutic benefits that often surpass traditional methods, effectively treating a wide range of disorders. These substances not only provide clinical advantages but also generate deeply meaningful experiences for many individuals. While increased neuroplasticity likely contributes to these benefits, the most significant predictor of positive outcomes is the occurrence of mystical experiences.

Attempts to explain why mystical experiences promote lasting therapeutic benefits have led to the Metaphysical Belief Theory and Metaphysical Alief Theory, both emphasizing the significance of the experiential aspect of psychedelics, albeit from different angles. The MBT emphasizes changes in metaphysical beliefs, while the MAT highlights the role of aliefs. However, many patients report clinical outcomes without changes in metaphysical beliefs or encountering non-naturalistic metaphysical content during their psychedelic experiences.

Therefore, an explanation for why mystical experiences correlate with positive outcomes, independent of metaphysical experiences, is needed. Letheby proposes that the fundamental psychological mechanisms of psychedelic therapy stem from an aspect of mystical-type experiences that is not connected to non-naturalistic ideations. In the next Section, I will explore what he proposes that aspect is.

3 Letheby's self-unbinding model

The central premise of Letheby's account is that psychedelic therapy operates through disrupting and subsequently revising mental representations of the self. Although not the only factor, Letheby stresses that these changes in self-representation are the main mechanism through which psychedelics yield their benefits. In this Section, I will lay out the foundational concepts needed to make sense of his model. First, I will explain *what* Letheby means by a self-model, distinguishing between the narrative and minimal self, and their corresponding neural correlates. Following this, through the lens of the predictive processing framework that Letheby uses for his model, I will explain *how* psychedelics disrupt the brain's model of the self, and how these disruptions lead to changes in self-representation. Finally, I will elaborate on *why* changes in one's self-model would lead to such extensive therapeutic benefits.

3.1 The self as a model

Self-representation involves the brain's construction of a self-model, which frames how we view ourselves and our place in the world. This self-model allows us to experience different dimensions of the self as belonging to one unified entity: the self (Letheby & Gerrans, 2017). These include the minimal self and the narrative self. The minimal self represents the self that exists in the "here and now", experiencing life directly and immediately (Blanke & Metzinger, 2009). This involves present-moment sensations, emotions, and thoughts as they arise, and is fundamental to our sense of agency and self-coherence (Gallagher, 2000). Over time, this "I" goes beyond the immediate perceptual range and is extended through our memories, shaping the narrative self. The narrative self represents the story we narrate about ourselves, encompassing our personal history, beliefs, and aspirations (Gallagher, 2000; Zahavi, 2010; Lebedev et al., 2015). Though integrating present experiences with our past and future projections, we experience ourselves as a cohesive and continuous entity.

One line of evidence for these different dimensions comes from research concerning the Default Mode Network (DMN) and the Salience Network (SN). In this context, a 'network' refers to a group of interconnected brain regions communicating to perform specific cognitive functions. The DMN has been implicated in self-referential tasks, such as recalling the past, projecting oneself in the future, and making conceptual judgements about one's character, and plays a critical role in maintaining the narrative self (Buckner et al., 2008; Spreng et al., 2009; Spreng & Grady, 2010; Raichle et al., 2001; van Veluw & Chance, 2014; Qin & Northoff, 2011; Johnson et al., 2002). The Salience Network, on the other hand, is implicated in detecting and filtering salient stimuli from the environment and coordinating the brain's response to these stimuli (Seth, 2013), and correspondingly, has been linked to maintaining the minimal self (Lebedev et al., 2015; Tagliazucchi et al., 2016; Craig, 2009).

Letheby highlights the importance of the DMN and the SN in understanding the effects of psychedelics, which are thought to both disintegrate and desegregate these networks. *Disintegration* refers to the reduced functional connectivity within these networks, weakening the cohesion of self-referential thoughts and the immediate

sense of self (Carhart-Harris et al., 2013, 2014; Palhano-Fontes et al., 2015). This reduction disrupts the brain's typical self-processing, as evident in the diminished capacity for mental time travel—projecting oneself into the past or future—seen in LSD (Speth et al., 2016). *Desegregation*, meanwhile, enhances global connectivity, enabling more interaction between regions that do not usually communicate (Daws et al., 2022). This heightened interaction can blur the boundaries between internal and external experiences, culminating in ego-dissolution (Petri et al., 2014; Tagliazucchi et al., 2016; Muthukumaraswamy et al., 2013).

Ego-dissolution is a common experience reported by individuals while tripping, characterized by a (reversible) loss of the sense of self, perceptual abnormalities, and a feeling that one is dying (Millière, 2017). Letheby points out that this dramatic transformation can be attributed to the disruption psychedelics cause on the networks. These networks are critical in maintaining a coherent self-concept by modeling the self as a distinct and indivisible entity. Therefore, when psychedelics disrupt their functional integrity, the boundaries that normally delineate the self from the external world blur, leading individuals to experience the feeling of merging with the universe or their self disintegrating.

3.2 Seeing the self as a construct

Letheby's account of how psychedelics induce changes in one's self-model draws on predictive processing (PP)[4], a theoretical framework that describes how the brain interprets and interacts with the world. According to PP, the brain continuously makes predictions about sensory inputs and updates these predictions based on incoming data (Friston, 2009; Hohwy, 2013; Huang & Rao, 2011; Seth, 2013). It generates a model of the world from past experiences and current inputs, which helps it anticipate and interpret sensory information. This process relies on hierarchical prediction, where high-level priors (expectations) influence lower-level sensory processing (Clark, 2013). For instance, imagine hearing footsteps coming up the stairs. Based on the familiar pace, you predict that it's your sibling. This assumption (high-level prior) shapes your interpretation of any subsequent sounds or activities on the stairs. You might attribute a dropped item or a door closing to your sibling, without ever seeing them or having definitive proof. Only a significant discrepancy, such as hearing a deeper voice than anticipated, would prompt you to revise your initial prediction to this person not being your sibling after all.[5]

Under normal circumstances, these predictions and the resulting perception of reality are *phenomenally transparent* (Metzinger, 2003, 2014), meaning that we experience our mental models of the world as reality itself, not as representations. For example, when looking at a chair, it doesn't strike us as a construct of our minds, where visual data is assembled into a chair. One would simply see the chair directly.

[4] While Letheby heavily relies on PP to articulate his theory (see Colombo, 2022), a rejection of PP does not necessarily entail a rejection of Letheby's model.

[5] This example, while not specific to PP and also compatible with non-PP models of the mind, illustrates how high-level priors can shape lower-level sensory inputs, and is sufficient for understanding the core principles of Letheby's model.

This transparency, Letheby argues, extends to our self-model, where our sense of self and related beliefs are experienced as direct truths rather than constructs.

However, when influenced by psychedelics, this normal processing undergoes significant changes. According to the REBUS model (RElaxed Beliefs Under pSychedelics)[6], psychedelics reduce the precision of high-level priors, effectively loosening their influence over sensory and perceptual processing (Carhart-Harris & Friston, 2019). This weakening allows lower-level data to have more impact on cognitive processing, potentially leading to a phenomenological state where the usual seamless experience of reality becomes disrupted. As a result, Letheby argues what was once a transparent and direct experience of the self and the world can become *opaque* and evidently constructed.

This means that individuals become aware that what they perceive and believe are not direct realities but constructs of the mind. In some cases, psychedelics can even induce a state of global opacity, where the entire experienced world is perceived as a mental construction (Metzinger, 2003; Letheby, 2021, p. 141–144). Rather than experiencing thoughts and the external world as direct facets of reality, individuals under the influence of psychedelics may view them as subjective interpretations or constructs, prompting a reevaluation of foundational beliefs about themselves and the world. In Letheby's view, this shift is crucial for therapeutic outcomes.

To illustrate, consider Joe, whose depression stems from a deep-seated belief that he is unworthy, resulting in his loneliness. Under psychedelics, he may revisit this thought; however, with his usual sense of self disintegrated, experience it as a "mere thought" stripped of its usual emotional weight. As Letheby quotes, "To see thoughts and feelings as mere thoughts and feelings is ipso facto to disidentify with them" (p. 141). This disintegration of the 'I', or the phenomenal unit of identification, means that its associated thoughts and feelings no longer carry the same personal significance, reducing their impact and the defensive behaviors they typically provoke. This shift in perception would allow Joe to reframe and alter his deeply entrenched negative self-perceptions, facilitating a path away from his loneliness.

Putting it all together, Letheby's predictive self-model theory posits that the self is usually constructed through a hierarchically organized set of predictions. This construction becomes evident when psychedelics disrupt the predictive processing mechanisms that underlie self-representation, allowing for the relaxation of negative beliefs about the self. As a result, the rigid and often maladaptive thought patterns and self-models characteristic of many psychological disorders become malleable. Letheby contends that the therapeutic potential of psychedelics stems from their ability to render the brain's self-representation open to change, enabling therapeutic outcomes that are challenging to achieve with conventional treatments.

3.3 The cascading effects of self-model revision

While it may seem straightforward that transforming one's self-model from "unworthy" to "worthy" would yield positive outcomes, it seems excessive to attribute the broad spectrum of changes observed both clinically and anecdotally to mere changes

[6] Which is guided by the free-energy principle (FEP) (Feldman & Friston, 2010).

in self-representation. For example, how someone who otherwise has healthy self-esteem but is addicted to smoking cigarettes would experience clinical improvements out of changes in self-representation is far less intuitive.

Borrowing from Dennett's concept of the "self as a center of narrative gravity" (1992), Letheby proposes that this is due to the self-model acting as a center of representational gravity, where changes to the self-model would propagate through all levels of perception, emotion, and behavior.

Letheby & Gerrans (2017) previously described the self-model as a central organizing principle in cognitive processing. This self-model regulates how attention is allocated, salience is attributed, and the formation of all mental representations. Thus, by revising the self-model, the entire landscape of one's phenomenological experience, from perceptual attention and emotional engagement to memory recall and future projection, is fundamentally transformed. This transformation impacts processes ranging from the concrete sensorimotor level to more abstract cognitive operations.

At the sensorimotor level, our perception of the world is inherently egocentric, structured around where the self is in space (Blanke & Metzinger, 2009; Revonsuo, 2006). Changes at this level would therefore alter how we perceive our environment. At higher cognitive levels, the self-model determines how information is interpreted and prioritized, assigning specific emotional weights and personal significance to different experiences.

This dynamic can result in the rigid entrenchment of dysfunctional self-models, which Letheby notes is common in psychological disorders. The more deeply ingrained our beliefs about our identity are, the less likely we are to act, think or feel in ways that contradict these beliefs. However, by altering dysfunctional self-models, dysfunctional behaviors and thoughts can also be changed.

Consider the example of Claire, a smoker with high self-esteem. Through the use of psychedelics, her self-model shifts from identifying as a smoker to a non-smoker. This change cascades through her cognitive processes, altering her perception of smoking, thoughts about and emotional reactions to cigarettes. As a result, so too do her behaviors, allowing her to fight the urge for a cigarette, previously deemed inconsistent with her identity as a smoker.

To support his theory, Letheby draws on empirical research linking psychedelics' sustained therapeutic benefits to (1) self-related insights and (2) decentering.

First, Letheby highlights that episodes of acute insightfulness, where individuals gain clarity about personal issues, recognize previously unacknowledged emotional responses, and reassess their life priorities, are strongly linked to the enduring benefits of psychedelics, including symptom reduction (Carhart-Harris et al., 2016; Ross et al., 2016). These insights contribute to a restructuring of the narrative self, which Letheby identifies as a critical factor in psychedelics' therapeutic outcomes.

Second, Letheby discusses how psychedelic therapy enhances mindfulness-related capacities, which involve maintaining an open, non-judgmental attitude toward one's internal experiences (Soler et al., 2016, 2018). This enhancement facilitates a process known as "decentering", where individuals shift from a rigid, narrative-based self-identity to a detached perspective, allowing them to view their thoughts and emotions as temporary, subjective experiences rather than as core elements of their identity.

This increased capacity for decentering, which parallels Letheby's concept of shifting from transparent to opaque mental models, has been associated with reduced symptoms in conditions like depression and anxiety, providing further empirical support for his model (Mian et al., 2020).

In conclusion, in this Section, I outlined Letheby's explanation for how psychedelic-assisted therapy yields long-term therapeutic benefits through his self-unbinding model. By disrupting the neural networks underlying self-representation, psychedelics may prompt a shift from a unified self-model to a more flexible and revisable one. This transformation is marked by a move from phenomenal transparency, where self-perceptions are experienced as direct realities, to opacity, where they are understood as mental constructs. These mechanisms are seemingly critical in alleviating symptoms in various mental disorders.

4 Lyon's revealing the hidden mind account

In this Section, I will consider an alternative perspective, offered by Lyon, as to how psychedelics may facilitate healing. Lyon's central thesis is that the benefits of psychedelics are primarily derived from their capacity to reveal hidden mental content, which in itself promotes well-being. While he acknowledges other potential therapeutic mechanisms[7], Lyon emphasizes the revelation of hidden mental elements as the main pathway through which psychedelics exert positive effects. Through mind-revealing[8] experiences, individuals can gain insights into obscured parts of their psyche, enabling them to correct dysfunctional behaviors and thought patterns. In unpacking his thesis, I will first define *what* it means for something to be hidden in the mind. Then, I will describe *how* Lyon proposes psychedelics reveal the hidden mind, by allocating attentional resources to parts of the mind that normally do not receive attention. Lastly, I will discuss *why* revealing previously hidden aspects of the mind is supposedly conducive to well-being.

4.1 Revealing the hidden mind

Revealing the hidden mind involves bringing unconscious elements of our psyche into conscious awareness. To understand this process, it's essential to recognize the role of attention in shaping our conscious experience. Lyon emphasizes that attention and awareness, while distinct, are interrelated (Lopez, 2022). Attention may function

[7] For example, he mentions that some forms of depression are due to inflammation and correspondingly, psychedelics have been found to have anti-inflammatory properties (Flanagan & Nichols, 2018). Thus, if a person suffering from this form of depression were to find relief after taking psychedelics, it's plausible that the benefits would primarily be due to the reduction of inflammation rather than any transformative psychological experiences (p. 254).

[8] Lyon refers to experiences that reveal hidden parts of the mind as "psychedelic experiences". This is regardless of whether they occur spontaneously or are induced by psychedelics or meditative practices. For clarity, in this paper, when referring to psychedelic experiences, I will solely be referring to experiences induced by psychedelics, and will refer to experiences that reveal the hidden mind as "mind-revealing".

as a prioritizing filter, determining what enters our awareness and how we perceive it (Serences & Yantis, 2006). Given our limited cognitive resources, attention must be allocated to relevant tasks, inevitably leaving aspects of our mind outside of our immediate awareness.

To illustrate, consider having an exam soon, which is constantly occupying your thoughts. However, while out grocery shopping, your attention momentarily shifts to what items you need to buy, leaving thoughts of the exam temporarily outside of your awareness. Once attention can be allocated back to the exam, it reenters your awareness.

In contrast, some unattended content lies not merely outside our immediate awareness but is genuinely inaccessible. Buried memories, repressed desires, and subconscious beliefs all exist within our mental repository yet are hidden from conscious access. Lyon stresses that these hidden elements can significantly influence our behaviors and decision-making. Research highlights that we hold many social biases, implicitly learn, and make decisions influenced by factors we are completely unaware of (Greenwald & Banaji, 1995; Reber, 1989; Nisbett & Wilson, 1977). Thus, hidden aspects of our minds can shape our actions and interactions without us ever realizing it.

Nevertheless, just because these aspects are hidden or inaccessible does not mean they are permanently sealed from our consciousness. For example, epiphanies and sudden recollections of long-lost memories exemplify how unconscious content can surface into conscious awareness. Such "mind-revealing" experiences demonstrate how the hidden mind can momentarily manifest in our consciousness.

4.2 Psychedelics expand awareness

According to what Lyon refers to as the Osmond-Grof hypothesis (p. 112), psychedelics bring unconscious elements into conscious experience by *amplifying* the mind. Lyon expands on this idea, suggesting that psychedelics create an attentional surplus by temporarily increasing the amount of attentional resources available, thus "amplifying" mental processes. As our allocation of attentional resources is limited, when psychedelics create an attentional surplus, it facilitates elements that typically don't receive attention to come into awareness. This expands awareness, enabling the revelation of previously hidden elements.

Lyon identifies two ways in which psychedelics may achieve this: (1) by lifting metabolic constraints on the brain, thereby generating new attentional resources, or (2) by freeing up attentional resources from their existing patterns of allocation. The first mechanism is supported by studies showing that psychedelics can increase metabolic activity in certain brain regions (Vollenweider et al., 1997, 1998; Gouzoulis-Mayfrank et al., 1999). The second mechanism aligns with the entropic brain hypothesis (Carhart-Harris et al., 2014) and the REBUS model (Carhart-Harris & Friston, 2019), which suggest that psychedelics disrupt the normal functioning of networks such as the DMN, the SN, and the Dorsal Attention Network (DAN). This disruption releases attentional resources from their typical patterns, allowing them to be redistributed towards novel mental processes.

Lyon suggests that the randomness and unpredictability in how the attentional surplus is redistributed can account for the phenomenological variability of psychedelic experiences. For example, the commonly experienced visual hallucinations may arise when attentional resources are redistributed into the underlying processes of the visual system, an aspect normally hidden from our consciousness. These visual hallucinations may reveal the foundational elements of visual perception, such as edge detection, depth perception, and pattern recognition, that are integrated seamlessly below our awareness. When psychedelics bring these processes into awareness, it allows individuals to witness the construction of visual scenes in real-time, resulting in characteristic distorted and fragmented visuals.

The unpredictable redistribution of attentional resources can also explain the contrasting experiences of phenomenological transparency and opacity that occur under psychedelics. Lyon and Farennikova (2022) previously conceptualized the attentional system as a coin balanced on its edge: tipping it may cause it to land on heads (increasing opacity), or it may equally[9] land on tails (increasing transparency). As a result, individuals taking psychedelics may experience either state depending on how their attentional resources are reallocated. Some may even experience *both* states, alternating between plunging *deeper* into their experience and *detaching* from it, as their attentional resources flow "forward" and "back" throughout their mind's hierarchical structures.

Lyon similarly represents the phenomenon of mystical-type experiences through changes in the traditional allocation of attention. A critical aspect of attention is that it is selective: something is being attended to more than something else, creating a distinction between the subject (the observer) and the object (the observed). However, in cases where the attentional surplus is extreme, Lyon suggests selective attention may be dissolved. Instead, attention is uniformly distributed across all mental content, thereby losing its inherently selective nature.[10] The dissolution of this selective focus removes the illusory boundaries between subject and object, or self and other, aligning with the concept of non-duality often described in mystical experiences, manifesting as ego-dissolution, unity, emptiness, or pure awareness. In such states, because attention is undiscriminating and all-encompassing, every aspect of the mind is equally exposed; thus, these experiences are *maximally* mind-revealing. As Lyon's thesis is that psychedelics exert their positive effects through revealing the hidden mind, and mystical-type experiences result in complete mind revelation, this would explain why having these experiences predicts therapeutic outcomes.

In conclusion, psychedelics reveal hidden elements of the mind by enabling a redistribution of attentional resources into parts that are normally concealed. How the resources are redistributed can explain their phenomenological variability.

[9] But if there is any bias at all, Lyon argues that it leans towards increased transparency, as it is more consistent with patient reports (p. 281) and many psychological conditions treated with psychedelics involve feelings of disconnection (Carhart-Harris et al., 2018).

[10] Some theoretical frameworks might consider the idea of uniformly distributed attention across all mental content as incoherent. For example, biased competition models of attention argue that attention serves as a mechanism for 'biasing' the competition among signals, allowing some to be more prominent in conscious awareness while others are suppressed (Desimone & Duncan, 1995). In such models, if no single "option" or cognitive signal is favoured, then, strictly speaking, attention does not occur.

4.3 Why confronting the concealed is therapeutic

According to Lyon, many psychological conditions are psychocryptic, meaning they are mind-concealing. For instance, in conditions like depression, individuals may struggle to access non-depressive thoughts or memories, perpetuating a cycle of negative thinking. A mind-revealing experience, therefore, can offset this by unlocking these concealed parts of the mind.

Lyon identifies hidden mental elements, such as suppressed traumatic memories, as core drivers of psychological suffering, exerting control from the shadows and influencing behavior and decision-making in ways that can lead to distress (p. 228). The therapeutic power of psychedelics lies in their ability to bring these hidden drivers into conscious awareness, providing an opportunity for individuals to confront and resolve the underlying causes of their suffering.

Psychedelics' capacity to induce mind-revealing experiences can be therapeutic in and by themselves or through their resulting increase in mindfulness, extending the benefits beyond the trip. Lyon argues that important life lessons, such as "comparison is the thief of joy," "it's better to be kind than right," "sleep is vital," etc., often make a significant impact when first learned but tend to diminish in our consciousness as time passes. This fading effect leads to a cyclic pattern where we must continually relearn these lessons. Mindfulness helps us break this cycle by anchoring these insights into our everyday consciousness. This process is crucial because, despite the wealth of life lessons available, such information is useless if not actively remembered and implemented. Thus, by cultivating mindfulness, individuals can maximize the benefits of the insights unearthed from their hidden minds.

Returning to the example of Claire, who knows smoking is harmful yet in moments of craving, has this knowledge eclipsed by the urge to smoke. Lyon asserts that by developing the ability to bring into awareness the hidden mental elements that drive undesirable behaviors, we can break free from their grip. If Claire were to take psychedelics and have insights into her smoking behavior revealed to her from a different lens, mindfulness can help her keep these harmful impacts of smoking in her awareness even during cravings, thus empowering her to resist the urge. Alternatively, psychedelics might reveal an optimal state of consciousness where Claire no longer feels the need to smoke, disrupting the habitual dynamics that lead to her smoking behavior. While mindfulness in this context might not be essential, Lyon believes it would maximize the overall benefits of psychedelics. He supports these assertions with research, citing studies that show mindfulness training can enhance the positive effects of psychedelic experiences and mitigate their negative aspects (Griffiths et al., 2018; Smigielski et al., 2019).

To recapitulate, Lyon's thesis posits that psychedelics create an attentional surplus, broadening the scope of what can be brought into conscious awareness. This expanded awareness can reveal dysfunctional thought patterns, forgotten memories, and healthier modes of being. Exposing the underlying causes of one's psychological issues would provide a means to their resolution, leading to substantial therapeutic benefits. Mindfulness may maximize the therapeutic benefits of these revelations by ensuring their integration into daily life.

5 Mechanisms underlying positive outcomes

So far, I have outlined the numerous benefits provided by psychedelic-assisted therapy and discussed why initial theories explaining these benefits fall short. I introduced two new theories, those of Letheby and Lyon, and detailed their mechanisms for how psychedelics confer their therapeutic benefits. Here, I turn to a line of psychedelic research not mentioned as of yet, which may challenge their explanations: microdosing.

5.1 What is microdosing?

Microdosing refers to the practice of taking repeated sub-perceptual doses of a psychedelic substance, typically about 1/10th to 1/20th of a full dose, or a *macrodose* (Fadiman, 2011). Sub-perceptual means that the doses are so small that the user does not experience the alterations in perception and cognition often associated with macrodoses, such as visual hallucinations or ego-dissolution. Despite the absence of these pronounced effects, microdosing has received considerable attention, predominantly through anecdotal reports suggesting a range of beneficial effects on cognitive and emotional well-being (Johnstad, 2018).

However, compared to the extensive body of research on macrodoses, scientific investigation into microdosing has been relatively scant. This gap may stem from challenges such as defining a standardized microdose, accounting for individual variability in drug response, the potential influence of placebo effects, and the absence of a scientific consensus on what constitutes effective microdosing (Horsley et al., 2018; Kuypers et al., 2019; Cavanna et al., 2022; Polito & Liknaitzky, 2022). Nonetheless, enough research has been conducted to draw some conclusions about its effects.

In terms of acute effects, microdosing appears to positively influence both subjective experiences and behavioral outcomes. Murphy et al. (2024) reported that single administrations of 10 µg and 20 µg of LSD increased ratings of vigor, elation, and enjoyment. Similarly, Bershad et al. (2019) found that LSD microdoses significantly enhanced the vigor subscale of mood measures, which includes feelings of being lively, active, energetic, and cheerful. In studies examining repeated dosing, participants reported increased feelings of awe, higher engagement in activities, and greater satisfaction with those activities on microdosing days (van Elk et al., 2022; Pop & Dinkelacker, 2024).

Regarding mental health outcomes, microdosers exhibit less depression, anxiety, and stress compared to non-microdosing controls, and score lower on measures of dysfunctional attitudes and negative emotionality (Rootman et al., 2021; Anderson et al., 2019a, 2019b). Over a one-month period, a study observed that microdosers experienced significantly improved mood and better mental health relative to controls (Rootman et al., 2022). Moreover, repeated, spaced microdoses were followed by improvements in depression in another study (Fadiman & Korb, 2019). Overall, across many studies and reviews, increased positive mood and decreased negative mood were a common outcome of microdosing (Lea et al., 2020; Ona & Bouso, 2020; Lo et al., 2024; Polito & Liknaitzky, 2022; Johnstad, 2018).

Despite both microdosing and full-dose psychedelic therapy delivering clinical benefits, they appear to employ different neural mechanisms. For example, while macrodoses often lead to significant increases in dendritic spine density and changes in gene expression related to neural plasticity, these effects are not observed with microdosing. Cameron et al. (2019) showed that chronic, intermittent low doses of DMT did not produce the same biochemical and structural changes seen with a single high dose, though they did produce antidepressant-like effects. Interestingly, this chronic dosing also altered metabolism in male rats, leading to significant weight gain despite eating *less* food, a phenomenon not observed following a single high dose. Similarly, microdosing enhances pain tolerance and has shown promise in pain management in a way that macrodosing does not (Lyes et al., 2023; Murphy et al., 2024; Fadiman & Korb, 2019).

Kiilerich et al. (2023) noted that many serotonergic receptors typically affected by high doses of psilocybin, such as the 5-HT2A, were not impacted by microdosing. However, increases were seen in receptor levels linked to approach-avoidance decisions and motivation-related behaviors. This suggests that microdosing might achieve its therapeutic effects by influencing particular pathways of the serotonin system rather than the extensive serotonin system modifications observed with macrodosing.

Distinct mechanisms being targeted by microdosing and macrodosing psychedelics would not be entirely surprising. Many medications exhibit dose-dependent effects, targeting different pathways and treating different conditions at varying dosages. For instance, the antipsychotic Quetiapine is used to treat schizophrenia at high doses (800 mg) by acting on serotonergic, muscarinic, alpha-adrenergic, and histaminergic receptors. However, at a low dose (50 mg), it is used to treat insomnia due to its sedative effects mediated through histamine receptor blockade (Curry & Richards, 2022). Similar dose-dependent effects are seen with other medications, such as aspirin and dexamethasone (Cadavid, 2017; Dogra & Vijayashankar, 2024).

These distinct targeted mechanisms highlight why, despite both producing clinical benefits, microdoses and macrodoses have different phenomenological experiences. The visual hallucinations, significant alterations in cognition and memory, and mystical-type experiences accompanied by macrodoses are not present in microdosing. These mystical experiences are a significant predictor of positive clinical outcomes in full-dose therapy. The absence of such experiences in microdosing further suggests that different mechanisms may underlie the therapeutic effects of microdosing versus full-dose psychedelics.

5.2 Below the threshold for explanatory accounts

This discussion naturally leads to the question: Is a theory of psychedelic-assisted therapy successful in explaining its positive outcomes by considering the mechanisms targeted by microdoses, macrodosing, or both? In this first instance, I will consider the case of microdosing.

5.2.1 Letheby's account

Letheby's theory on the therapeutic effects of psychedelics hinges on the disruption and subsequent revision of one's self-representation, a process driven by the disintegration of the Default Mode Network (DMN) and the Salience Network (SN). According to the REBUS framework integral to his theory, the loosening of high-level priors under psychedelics promotes a state of increased phenomenal opacity, allowing individuals to view their mental constructs as mere constructs rather than direct reflections of reality.

However, neither the phenomenological, cognitive, nor neural effects observed in microdoses align with the mechanisms of Letheby's theory. At the neural level, microdosing's subtle effects are insufficient to trigger the significant network disintegration necessary for the REBUS to take effect. Additionally, the absence of perceptual distortions and ego-dissolution indicates that high-level priors remain largely intact, preventing any increase in phenomenal opacity. Current research does not show any increase in phenomenal opacity from microdosing either, and the lack of anecdotal reports further indicates that these effects are absent.

This isn't surprising, as Letheby himself acknowledges that his framework is tailored for moderate to high doses that *significantly alter* consciousness, stating that microdoses lack the potency to induce an altered state of consciousness required for therapeutic benefits (p. 16). Thus, by his own lights, Letheby's framework does not provide a basis for understanding how non-consciousness-altering doses could offer significant therapeutic benefits.

5.2.2 Lyon's account

Lyon's theory, which attributes therapeutic outcomes to the revelation of hidden mental content, also fails to explain the effects of microdosing. For his theory to be applicable, microdoses would need to result in an attentional surplus, thereby expanding awareness and revealing previously hidden aspects of the mind.

However, current research does not support the idea of an attentional surplus resulting from microdosing. Lyon's model suggests this surplus could come from reallocating existing attentional resources or creating new ones. Yet, the reallocation requires the REBUS to take effect, which, as established, does not occur with microdosing. Moreover, creating new attentional resources seems unlikely, given the minimal neural impact of sub-perceptual doses and lack of user reports indicating increased attention. Even if microdoses *did* somehow increase the brain's metabolic capacity, creating new attentional resources, the absence of profound insights, visual hallucinations, or unearthed memories suggests that any attentional surplus would be insufficient to validate Lyon's theory at this dosage. Therefore, if microdosing yields positive outcomes without revealing hidden mental content, Lyon's theory is unable to explain these therapeutic effects.

In conclusion, both Letheby and Lyon's theories fail to account for the therapeutic effects of psychedelics when taken in microdoses. According to Letheby and Lyon, for psychedelics to have therapeutic effects, they must first cause significant network disintegration or an attentional surplus leading to expanded awareness. Microdosing

has demonstrated clinical benefits, yet it does not induce network disintegration nor create an attentional surplus. Therefore, the therapeutic effects of microdosing cannot be due to the mechanisms proposed by Letheby and Lyon.

5.3 Disruption, revelation, and the absence of clinical telos

This leaves open the second case: Can Letheby and Lyon's theories successfully explain the therapeutic effects of psychedelics when taken in high doses? In this subsection, I argue that their views, as they currently stand, *cannot* fully explain the observed therapeutic benefits. Although both Letheby and Lyon provide comprehensive accounts of *how* psychedelics can mediate profound changes in cognition, perception, and attention, neither account adequately addresses *why* these changes should result in positive outcomes. I argue that their explanations show no natural trajectory towards a positive result.

5.3.1 Letheby's account

Consider the example of Claire again, the smoker who uses psychedelics in an attempt to quit. According to Letheby's theory, the psychedelics alter her high-level priors about reality and herself, resulting in a phenomenally opaque state where she perceives her thoughts as mere constructs. In one scenario, this altered state enables Claire to change her self-model from smoker to non-smoker, which then propagates through her perception and cognition, ultimately helping her quit smoking.

However, it is just as conceivable that upon reaching the opaque stage, Claire discards the wrong beliefs from her self-model. Letheby doesn't explain why, at the *choice point*, someone would redefine their self-model to be aligned with their pre-existing goals when they are themselves detached from their usual sense of self and its associated goals. Additionally, from a perspective where reality is apprehended as a mere construct, she could come to see the notion of fighting an addiction as futile and discard the hope of being clean from her self-model rather than the addiction itself. Consequently, she could adopt a new identity as a 'true addict,' abandoning her efforts to quit and possibly even smoking more.

In both scenarios, all of Letheby's criteria are met: altered high-level priors, increased phenomenal opacity, and revised self-model. Yet, only in the first one does Claire experience a positive outcome. In the second case, Claire is now *worse* off having taken psychedelics. The difference in outcomes between the two scenarios has nothing to do with the mechanisms underlying Letheby's theory, but rather depends on the nature of the mental constructs that are reinforced during the experience.

As discussed in Sect. 2.3, neuroplasticity theories fail to account for the benefits of psychedelic therapy because increased plasticity alone does not ensure positive outcomes; the direction in which plasticity is guided is crucial. Letheby himself raised this limitation, yet his theory similarly fails to account for how changes in the self-model lead to beneficial results.

Perhaps, Letheby might counter this critique by arguing that psychedelics liberate individuals like Claire from their habitual ways of being, providing an opportunity to revisit and modify their self-models. Since Letheby restricts his theory to psyche-

delic-assisted therapy (PAT) rather than recreational psychedelic use, the underlying assumption is that Claire, with the support of a therapist, intends to change her self-model from smoker to non-smoker. The therapist's role would be to guide and redirect any negative self-reconceptions that arise during the session into more positive and constructive thoughts. Therefore, the trajectory of the experience would lie in the hands of the therapist and the intrinsic motivation of the patient. If something were to go amiss, it would be due to the therapist failing to adequately redirect the session rather than the mechanisms underlying his theory being flawed.

However, if the fate of the session lies in the hands of the clinician's competence, this seems like a pretty significant aspect to forgo mentioning in a comprehensive theory of PAT. If Letheby truly intended for the therapist to play a critical role in ensuring a positive trajectory, it would be unreasonable for him to not explicitly state this. The absence of this crucial element in Letheby's framework suggests that it is not an intended component of his theory. Furthermore, assuming that the patient's motivation for improvement would steer the outcome is overly optimistic. The changes in self-modeling are only possible after experiencing a shift from a usually transparent reality to an opaque one, according to Letheby's model. However, experiencing an opaque state for the first time can be quite distressing, and realizing that one's self, loved ones, and reality are all mental constructs rather than shared objective truths might just as easily lead to cynicism or nihilism rather than improvement, despite initial motivations. Such a revelation could provoke a sense of existential despair, where life feels meaningless when perceived as a mere fabrication, making it difficult to see the value in pursuing personal growth or change. It's unclear why someone would embrace this altered state constructively instead of becoming fixated on the unsettling idea that everything they experience as real is, in fact, illusory.

This indicates that Letheby's account lacks a component that ensures the experience will follow a positive trajectory. Without such a mechanism, Letheby's account is incomplete. Even if Letheby were to revise his model to emphasize the therapist's role in steering the experience toward a beneficial outcome, as mentioned in Sect. 2, the widespread reports of positive therapeutic effects from psychedelics in non-clinical or unguided contexts indicate that this addition would be neither sufficient nor necessary. Rather, it suggests that there is an inherent aspect of the psychedelic experience itself, beyond the influence of a therapist, that contributes to these benefits. Ultimately, Letheby's model assumes that changes in self-models will lead to positive outcomes but does not explain why this should be the case.

5.3.2 Lyon's account

A similar conclusion can be drawn from Lyon's account. Consider Joe, the lonely man seeking to alleviate his depression through psychedelics. According to Lyon, psychedelics expand his awareness, revealing hidden content from his mind. He discovers that his loneliness is due to his own antagonistic behaviors with others, a realization previously hidden from his consciousness. Ideally, this revelation prompts Joe to change his behavior, becoming kinder and more mindful of others, thereby improving his relationships and reducing his loneliness.

However, this positive outcome is not guaranteed. Joe could just as easily become overwhelmed by the realization that he is the source of his problems, leading to increased self-loathing and further isolation. He could believe that his negative traits are unchangeable and withdraw further from social interactions, exacerbating his depression. In this case, the expanded awareness and revelation of hidden content result in a negative rather than a positive outcome.

Lyon's account presupposes that unveiling hidden content will lead to positive changes, but this assumption is wrong. Traumatic memories or distressing revelations might be better left hidden, as their exposure could be too overwhelming to address constructively, perhaps explaining why they were hidden to begin with. Additionally, the assumption that uncovering buried memories invariably leads to resolution overlooks the complexity of processing trauma; some distressing content may have no clear solution when exposed. For instance, Loftus and colleagues (1996) found that after recovering memories of childhood sexual abuse, 67% of patients exhibited suicidal ideation or attempts, compared to 10% before.

Lyon might argue that these distressing hidden memories are responsible for the individual's psychological suffering in the first place, and that bringing them to light is necessary for treatment. Once exposed, they can be addressed, freeing the individual from their grip, a path to recovery that would not be possible had they remained subconscious. This reasoning, however, overlooks conditions like PTSD, where the traumatic episodes are already present in the person's mind. It's the very *presence* and accessibility of these memories that is problematic. Therefore, Lyon's theory requires a mechanism to ensure that once these memories are revealed, they can be resolved. Unfortunately, this is not guaranteed, as some traumatic experiences may require a lifetime to address effectively, and others might remain unresolved indefinitely. Consequently, exposing someone to their hidden traumatic content via psychedelics could leave them *worse off* than if they had never used the drug.

This reveals a significant gap in Lyon's theory; it lacks a reliable mechanism to ensure that exposure to hidden content leads to beneficial outcomes. Thus, Lyon's model fails to explain why high-dose psychedelic therapy generally leads to positive therapeutic effects.

In conclusion, both Letheby and Lyon's frameworks of how psychedelics lead to therapeutic benefits assume a positive arc to the experience, which is not guaranteed by their proposed mechanisms. If their theories *were* complete, we would expect the results of psychedelic-assisted therapy to be more varied, with a more balanced share of negative and positive experiences. However, as discussed in Sect. 2, this is not the case. The results of psychedelic-assisted therapy, both in clinical and non-clinical populations, have been overwhelmingly positive, with very few negative outcomes observed in recreational use. This indicates a critical component missing from their accounts, a factor that biases the outcomes toward overwhelmingly positive results.

5.4 Positive affect as necessary for therapeutic outcomes

I argue that this factor is positive affect, and incorporating it as a necessary component in their models would help explain why psychedelic interventions generally result in favorable outcomes.

5.4.1 Mystical qualities as inherently positive

A potential reason why positive affect has been overlooked in theories of PAT may stem from the way mystical-type experiences are conceptualized and assessed. These experiences are crucial predictors of therapeutic outcomes and are central to theories about the mechanisms targeted by psychedelics. However, the tools used to measure these experiences, such as the Mystical Experiences Questionnaire (MEQ), tend to emphasize positive emotions.

Hoffman (2022) notes that positive valence is a fundamental dimension in the psychometrics of mystical-type experiences. For example, the MEQ assesses the mystical quality of an experience based on feelings of sacredness, freedom from limitations, experiences of pure being, spiritual height, and reverence, qualities that are inherently positive (Barrett et al., 2015). Given that the MEQ includes a separate factor for positive mood, this reinforces the idea that high scores typically indicate a positive experience. Therefore, the strong association between high scores on the MEQ and positive outcomes suggests that positive affect plays a critical role in the therapeutic effects of psychedelics.

The significance of positive emotional states in mystical experiences becomes particularly relevant when considering that both mystical and psychotic experiences might originate from the same mechanisms. Brouwer and Carhart-Harris (2021) pointed out the numerous cognitive and neural similarities between these two experiences, and proposed that they are both a form of a pivotal mental state (PiMS), a hyper-plastic state that mediates rapid learning when psychological change is sensed as needed. However, their relationship has been overlooked due to a bias in focusing on their differing outcomes, rather than the underlying processes leading up to them.

To illustrate, the authors identify shared characteristics between mystical and early and acute psychotic experiences such as altered self-experience, magical thinking, and perceptual abnormalities (Crespi et al., 2019; Grof & Grof, 1989; Hunt, 2000, 2007; Jackson, 1997; Lukoff, 1985, 2007, 2019; Parnas & Henriksen, 2016; Powers & Corlett, 2018; Ross & McKay, 2018; Willard & Norenzayan, 2017), all of which serotonergic psychedelics consistently elicit (Carhart-Harris, 2007; Carhart-Harris & Friston, 2010; Kraehenmann et al., 2017; Nour et al., 2016). However, psychosis typically involves negative affect, whereas spiritual and psychedelic experiences are marked by positive affect (Liechti et al., 2017; Carrigan & Barkus, 2017). Accordingly, though both states involve anomalous self-experiences, in severe psychosis the experience of one being fragmented typically feels invasive and torturing, whereas in psychedelic-induced spiritual experiences, individuals often report positive sensations and a sense of unity or interconnectedness during moments of ego-dissolution (Millière, 2017; Nour et al., 2016; Roseman et al., 2018).

Despite their shared mechanisms, mystical experiences typically result in profound personal growth and emotional healing, while psychotic experiences do not. One explanation for this divergence could be their contrasting emotional valence; mystical experiences are generally pleasurable, suggesting that positive affect is crucial for their positive outcomes. Likewise, positive affect may not merely be a by-product of tripping but a fundamental driver of its therapeutic effects.

5.4.2 Psychedelic experiences as predominantly positive

Beyond mystical elements, psychedelic experiences are themselves marked by an abundance of distinct positive emotions, including feelings of euphoria, gratitude, awe, and uncontrollable laughter (Goldy et al., 2024). While the initial "come up", the onset of the drug's effects, can sometimes involve anxiety, the subsequent peak and "come down" are predominantly positive, often described as awe-inspiring, blissful, and peaceful (Brouwer et al., 2025).

Despite this, much of the existing literature on psychedelics tends to emphasize their more unusual or 'cosmic' features over the straightforward pleasure they provide (Bøhling, 2017). Understandably, increased positive affect can result from consuming countless substances and frequently occurs in psychedelic experiences that lack any therapeutic outcomes. Given the unique therapeutic potential demonstrated by psychedelics, it may seem less pertinent—when identifying the mechanisms responsible—to focus on a feature so ubiquitous in ordinary life. However, as discussed earlier, the mystical qualities that strongly correlate with therapeutic success are themselves intrinsically positive. In what follows, I argue that this is not incidental, and that psychedelic experiences lead to clinical benefits *in virtue* of the positive emotions they induce. Contra an affect-neutral view, I show that psychedelic experiences that fail to increase positive affect will be clinically ineffective.

5.4.3 Why neutrality will not do

To see why, consider how psychedelics are thought to exert their effects. While the exact mechanisms involved remain debated (see van Elk & Yaden, 2022), many accounts converge on the idea that psychedelics disrupt the dynamics that ordinarily constrain our experience of reality, thereby temporarily loosening rigid patterns and destabilizing beliefs underlying pathology (McGovern et al., 2022, 2024). However, regardless of how this disruption has been accounted for in therapeutic outcomes, whether by revising *self-related* beliefs[11] (Letheby) or enabling *hidden mental content* to surface (Lyon), belief revision on its own is neutral; it is not inherently therapeutic. Nothing in these accounts explains what orients the resulting patterns or beliefs to reconfigure in more adaptive ways. Positive affect, however, can readily account for this orientation.

Affect influences not only *what* people think about, but *how* they think, biasing attention, accessible memories, interpretation, and judgment in affect-congruent directions (Bless & Fiedler, 2012; Fielder, 2012; Forgas, 1995; Bower & Forgas, 2000; Isen, 1987; Sedikides, 1995; Clore & Palmer, 2009). For instance, individuals induced into a positive mood tend to generate more positive spontaneous thoughts and optimistic beliefs, recall more positive memories, and form more lenient social judgments (Rice & Fredrickson, 2017; Niedenthal, 1990; Forgas, 2008). Conversely, negative affect constrains cognitive flexibility, priming critical self-evaluations and

[11] Letheby (2024) has since distanced himself from his "self-unbinding" theory, acknowledging pathologies sustained by non self-related beliefs (Van Eyghen, 2023), and now favors REBUS as the most plausible account.

pessimistic interpretations of ambiguous situations (Fredrickson, 2001; Johnson & Tversky, 1983; Lerner & Keltner, 2001).

Moreover, affect is deeply implicated in the formation and revision of beliefs (Müller-Pinzler et al., 2022; Bromberg-Martin & Sharot, 2020; Frijda & Mesquita, 2000; Boden & Berenbaum, 2010). Beliefs are often generated in order to make sense of one's affective state, while affect itself can serve as *epistemic evidence*, increasing the credibility and perceived truthfulness of one's beliefs (Forgas, 1995; McMartin & Pickavance, 2024). For example, jealousy can make one's suspicions feel more valid, while the absence of fear in a dangerous situation can falsely signal that a situation is safe. Hence, both the formation and endorsement of beliefs are strongly embedded within the emotional landscape in which they emerge.

This has direct implications for psychedelic-assisted therapy. If psychedelics do facilitate therapeutic change by loosening rigid, pathological beliefs, then, without a concurrent improvement in affective state, these beliefs may just as easily be revised in ways that perpetuate the pathology.

To illustrate, consider Joe again, who is depressed and convinced of his own incompetence. If his psychedelic experience fails to induce positive affect and remains imbued with the same negative tone, then, even if his pathological beliefs become more labile, his cognitive processes still remain largely constrained by mood-congruent content. In seeking coherence between his experiential state and his self-understanding, Joe is likely to generate new, yet equally self-defeating, beliefs that rationalize his persisting affect.

Even with a therapist present to guide the belief-revision process toward more constructive content, two problems still remain. First, because they are incongruent with Joe's emotional state, these positive propositions may feel untrue, prompting rejection and making them unlikely to be internalized. Second, even if these new beliefs were internalized, if they inherit the same emotional tone as the ones underlying the pathology, this will do little to improve his well-being. For even a belief positive in content ("I am capable") will be clinically inert if endorsing it feels no different from endorsing its pathological antecedent. Joe may come to believe that he is competent, but now being competent does not matter anymore; there is still *something* wrong with him.

Contrast this with an experience filled with hope, compassion, or humor; his thought process is now naturally steered toward exploring positive content, thinking in more optimistic ways about himself, with his positive mood making these thoughts seem more true. Here, Joe could even keep the same propositional content of the pathological belief ("I'm incompetent"), but if he instead finds humor or acceptance in it, the belief's pathological grip would dissolve. In this way, what matters most therapeutically is not that beliefs are revised into healthier forms, but that endorsing these beliefs *feels* better. Absent a positive shift in valence, it remains unclear how clinical populations will experience any meaningfully beneficial belief change.

Here, one might respond that loosening the pathological beliefs also dissolves the negative affective associations attached to them, thereby creating a neutral psychological landscape amenable to healthier belief replacement absent explicitly positive emotions. Suppose we grant this. A view that discards positive affect still encounters a further problem: explaining the long-term integration of these new beliefs into daily

life. A distinctive aspect of psychedelic-assisted therapy (PAT) is the persistence of therapeutic outcomes long after the acute experience ends. Such persistence requires that healthier beliefs are not only formed but also actively reinforced and repeatedly chosen in everyday life. Yet the mere possession of a belief does not guarantee its influence on future action. Beliefs are not uniformly accessible; which beliefs are accessible, and their salience, depends on context and the rewards associated with them (Sheeran, 2002; Grodniewicz, 2024; Bendaña & Mandelbaum, 2021; Sommer et al., 2023). Thus, some additional factor must sustain the accessibility and motivational pull of these newly formed beliefs, and here positive affect offers an explanation.

In addition to shaping cognition, positive affect significantly influences behavior through nonconscious motivational processes. Specifically, when mental representations of behavioral states are linked with positive affect, they trigger a cascade of nonconscious mechanisms that orient individuals toward cues associated with those states, enhancing their incentive salience (Van Cappellen et al., 2018). This generates a motivational "wanting" to re-experience those states, prompting individuals to exert greater effort in pursuing them and to gravitate toward actions aligned with them (Custers & Aarts, 2005; Kiviniemi et al., 2007). Crucially, for this self-reinforcing loop to form, positive affect must be present during the behavior itself, not merely follow from it, as these processes are driven to repeat what felt good *in the moment.* For instance, studies show it is not those who felt good after exercising or meditating who were most likely to sustain these behaviors, but those who experienced positive affect during the activity (Cohn & Fredrickson, 2010; Rhodes & Kates, 2015).

Applied to PAT, the "behavior" in question can be understood as the act of *endorsing the belief* itself. If Joe were to form the belief that he is competent while immersed in positive emotions, the very act of endorsing the belief would evoke positive affect. Nonconsciously, this association increases the likelihood that supportive thoughts will spontaneously arise, that cues reinforcing competence will capture attention, and that actions confirming the belief will be pursued. Consciously, each recollection of the belief rekindles optimism, forging a virtuous cycle in which belief, affect, and behavior continuously reinforce one another. Over time, the belief becomes more accessible, more likely to guide future action, and more resistant to displacement when confronted with situations that may challenge it.

By contrast, if Joe were to form this belief in a neutral affective context, it would lack this self-reinforcing mechanism. Studies show that mental representations formed in neutral affect do not increase participants' desire to achieve associated states, enhance their effort in pursuing them, or reliably predict future action—even when the individual holds positive attitudes toward those states (Lawton et al., 2009; Lowe et al., 2002; Custers & Aarts, 2005). Nonconsciously, Joe would be less likely to generate supportive thoughts, attend to cues, or gravitate toward behaviors affirming his competence. As a result, the belief would remain less validating and less accessible; when confronted with situations that challenge it, the belief could be overridden or re-rationalized (e.g., "I'm competent, but the world is against me"), thereby reinstating pathological thinking by another route.

In short, belief revision devoid of positive affect lacks the motivational strength required to sustain long-term behavioral changes. This limitation is especially critical

in clinical populations suffering from conditions like substance use disorders. During moments of intense craving, revised beliefs must compete directly against the intense immediate gratification offered by addictive substances. Without the reinforcing influence of positive affect, healthier beliefs risk becoming inaccessible, unconvincing, or behaviorally ineffective when they are most needed.

In sum, the positive emotions induced by psychedelic experiences are essential to support enduring therapeutic outcomes. Positive affect ensures that loosened beliefs not only reshape into more adaptive forms, but also resonate affectively, remain accessible, are motivating to retrieve, and rewarding enough to enact.

5.4.4 Affect and downstream clinical effects

Up to this point, I have argued that the mechanisms described by Letheby and Lyon, when instantiated along a negative trajectory, can plausibly account for adverse outcomes following psychedelic use. I further contended that even when psychedelic experiences are not overtly distressing, if they fail to elicit positive affect, they remain insufficient for producing therapeutically meaningful outcomes.

It follows, then, that if affect plays the role I have described, there should be empirical evidence linking the valence of psychedelic experiences to clinical outcomes. Empirical data indeed corroborates this, in that the items from the Altered States of Consciousness (ASC) scale that most highly correlated with PAT clinical outcomes involved positive feelings (Roseman et al., 2018). Specifically, statements like "I felt particularly profound" and "I experienced a profound inner peace" were among the highest predictors of positive results. Conversely, in psychedelic experiences where negative affect was present, the duration of these negative experiences predicted negative long-term outcomes (Carbonaro et al., 2016). Symptoms such as depression, anxiety, and dissociation persisted for weeks or even months among those who reported a negative experience while tripping (Ona, 2018). Additionally, higher levels of anxiety and confusion during sessions correlated with less favorable outcomes in treating depression (Roseman et al., 2018). Collectively, these findings demonstrate a clear connection between the affective quality of psychedelic experiences and their downstream clinical effects, with negative affect leading to poorer outcomes.

There are some exceptions to this, where negative, challenging experiences resulting from psychedelics have been shown to co-occur with positive clinical outcomes (Haijen et al., 2018; Carbonaro et al., 2016; Roseman et al., 2018; Wolff et al., 2022). However, as Hoffman (2022) observes, closer scrutiny reveals that even in such cases, positive affect remains indispensable, as these experiences are therapeutically valuable *only* if they culminate in positive affect, whether in the form of cathartic release, insight, emotional resolution, or a sense of relief (Carhart-Harris et al., 2018; Roseman et al., 2019). This aligns with research suggesting that positive emotions experienced after negative ones can neutralize their aftereffects (Fredrickson, 2001; Fredrickson et al., 2000; Josephson, 1996; Werner-Seidler et al., 2016).

In these instances, it may be that the pleasure or relief derived from catharsis significantly outweighs any earlier distress, rendering the breakthrough enjoyable in itself. Alternatively, the resolution or insights gained, though not pleasurable per

se, may instead evoke positive affect in virtue of what they represent: a potential for redemption, and the new hope they inspire. In either case, it is *only* once the challenging experience has transformed into a positively valenced one that it bears any clinical potential, which helps explain why prolonged periods of negative affect predict poorer long-term outcomes. The less time spent enjoying the experience, the narrower the interval for the therapeutic processes to successfully unfold.

In conclusion, positive affect is indispensable for achieving therapeutic outcomes from psychedelic experiences. Any theory of their therapeutic effects must, therefore, include positive affect to achieve full explanatory power.

6 Concluding remarks

In this paper, I argued that affect-agnostic accounts fail to capture how psychedelics lead to positive therapeutic outcomes. I showed how two prominent frameworks, those of Letheby and Lyon, can just as easily describe mechanisms by which psychedelics leave individuals worse off than before if they do not respond positively to the processes the authors outline. I then demonstrated that belief revision, in general, is unlikely to be clinically effective if it occurs within a psychedelic experience marked by a neutral or emotionally flat tone. This is a serious limitation, as it does not reflect the overwhelmingly positive outcomes observed in both clinical and non-clinical contexts. Something more is needed to explain why these mechanisms reliably result in therapeutic rather than harmful or neutral effects.

I argued that this gap can be addressed by recognizing positive affect as a necessary component of therapeutic efficacy. Psychedelic experiences are often very pleasurable and emotionally uplifting, a feature that should not be overlooked. While insufficient on its own, I contend that positive affect must be included in any full explanatory account of psychedelic therapy.

Perhaps, while different dosing strategies may engage different mechanisms, it could be said that the common denominator of psychedelic-assisted therapy is that of positive affect. Even in microdosing, where the effects are too subtle to induce mind-altering states, positive affect reliably manifests as positive mood, feelings of awe, and elation. Thus, for all their strange and distinct effects, the therapeutic efficacy of psychedelics may ultimately be mediated by something much simpler: the happiness they bring.

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