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Moral Considerations and the Experience of Ego Dissolution: Insights from Psilocybin

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Abstract

Although psychedelics were banned from medical research for about fifty years, recent early-phase studies indicate they may offer unique therapeutic benefits for various mental health and substance use disorders. When effective, psychedelic experiences often involve phenomena not typically observed in other medical or psychiatric interventions, such as a diminished sense of self-importance, insights that are difficult to articulate, feelings of connection and unity with others, and encounters with "deep" reality or a divine presence. Beyond symptom relief, these experiences can lead to substantial shifts in an individual's personality and worldview. Using psilocybin as a primary example, we argue that the distinct effects of psychedelics introduce specific risks that necessitate an expanded informed consent process, extending beyond standard procedures in psychiatry. We outline key considerations for consent discussions and propose prompts for enhancing informed consent in the context of psychedelic therapy. We also address possible objections and conclude by examining ethical issues likely to emerge as psychedelics transition from tightly controlled research settings to broader clinical practice.

Keywords: Moral considerations, Ego, Psilocybin, psychedelics

Introduction

Early studies on psilocybin-assisted psychotherapy suggest it can produce lasting symptom reduction for treatment-resistant depression (TRD), as well as for depression and anxiety related to cancer [1–5]. Initial trials have also demonstrated promising outcomes for psilocybin in supporting smoking cessation and reducing alcohol dependence [6–8], while safety profiles appear favorable with minimal adverse effects [9]. Similarly, studies investigating MDMA for social anxiety in autistic individuals [10] and PTSD [11, 12], LSD for anxiety [13], and ayahuasca for TRD [14] have shown encouraging results. Ongoing clinical trials aim to replicate these findings [15, 16], with further studies anticipated, highlighting the resurgence of psychedelics in psychiatric research and the potential for eventual mainstream clinical use.

The therapeutic effects of psychedelics seem closely linked to the unique, "mind-manifesting" experiences they induce. In psilocybin studies, participants frequently report gaining ineffable knowledge, feeling deep interconnectedness, encountering profound reality or God, and experiencing a reduced sense of self, often described as "ego dissolution." These mystical-type experiences correlate with both therapeutic benefits [3] and broader personality changes [17].

Despite their growing clinical relevance and transformative potential, psychedelics have received limited attention in medical ethics. Some scholars have explored psilocybin and MDMA for moral enhancement [18] or couples therapy [19], and others have considered ethical issues in early research on psilocybin for disorders

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of consciousness [20]. Nevertheless, the most pressing ethical concerns likely lie in the increasing psychiatric use of psychedelics and their potential for widespread benefit.

This paper addresses that gap by focusing on psilocybin, one of the most extensively studied psychedelics. We argue that psilocybin carries novel risks—such as undesired personality shifts or traumatic memory reactivation—as well as potential benefits. We propose guidance for informed consent in both research and clinical contexts, emphasizing the need for an enhanced consent process beyond typical medical practice. After discussing potential objections, we conclude with ethical considerations relevant to the transition of psilocybin from clinical trials to routine psychiatric practice.

Two clarifications regarding terminology are necessary. First, while some define "psychedelic" narrowly as classic serotonergic compounds like psilocybin, LSD, ayahuasca, and ibogaine [21, 22], others apply the term more broadly to any substance that produces "mind-manifesting" effects [23]. Although we focus on psilocybin, our discussion generally applies to serotonergic psychedelics and may, in part, extend to non-serotonergic substances like MDMA, though full treatment of these is beyond our scope.

Second, personality change is central to this discussion, though the concept is inherently vague. Here, we define personality broadly as the narrative traits and values that make an individual distinct. This broad definition captures the range of changes influenced by psilocybin, aligning with everyday understandings of personality—even if less precise than some psychological definitions. For example, one might describe a friend's personality based on their care for family, lifestyle preferences, and values, contrasting with another who is more individualistic and focused on different priorities. While this broad framing sacrifices some technical specificity, it is appropriate given that psilocybin-assisted psychotherapy can lead to ethically significant personality shifts.

Personality change and neurobiology of psilocybin-assisted psychotherapy

The therapeutic potential of psilocybin has been most rigorously examined in individuals facing anxiety and depression in the context of terminal illness, as well as those with treatment-resistant depression (TRD); thus, these groups will be the primary focus, while recognizing that outcomes may not directly extend to other psychiatric conditions or alternative dosing regimens, such as microdosing. Evidence indicates that clinical improvements are strongly linked to the mystical dimensions of the psychedelic experience, which are evaluated through experiences of inner and outer unity, sacredness, elevated mood, transcendence, and ineffability [3]. Parallel findings associate therapeutic gains with "oceanic boundlessness," characterized by a sense of unity, spiritual insight, blissful affect, heightened self-reflection, and disembodiment [24]. Importantly, not every participant achieves these states, yet those who do tend to experience greater therapeutic benefit [3, 24].

In addition, participants frequently describe psilocybin sessions as among the most profound or meaningful events of their lives [1, 3, 17], often reporting encounters with "a great plane of consciousness," enhanced interpersonal connectedness, and the recognition that life and death are interwoven in a continuous cycle [25].

Personality changes induced by psilocybin have been examined using validated tools such as the NEO Personality Inventory-Revised (NEO PI-R), which assesses traits along the Five-Factor Model: openness, conscientiousness, extraversion, agreeableness, and neuroticism [26–28] **(Table 1).** Findings consistently show reductions in neuroticism and increases in openness, conscientiousness, and extraversion, reflecting the deep sense of connection often reported during the psychedelic experience [25, 26].

Higher scores on each trait correspond to the features listed, whereas lower scores indicate the opposite tendencies

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Table 1. Key characteristics of the five-factor model traits (Adapted from [28])

Extraversion	Agreeableness	Conscientiousness	Neuroticism	Openness
Sociable	Considerate	Organized	Anxious	Creative
Outgoing	Non-judgmental	Dependable	Sensitive	Reflective
Energetic	Generous	Goal-oriented	Worrisome	Curious

Talkative	Helpful	Productive	Tense	Insightful
Enthusiastic	Trusting	Disciplined	Vulnerable	Original
Warm	Honest	Responsible	Self-critical	Evaluates unconventionally
Rapid personal tempo	Altruistic	Motivated	Self-pitying	Introspective

However, therapeutic psilocybin appears to promote personality changes that extend beyond those captured by standard measures such as the NEO PI-R. For example, it can enhance participants' sense of spirituality [3], with some describing experiences of feeling "reborn in a way" [25]. Interestingly, even individuals without prior spiritual inclinations sometimes report newfound spiritual awareness during treatment [29]. Likewise, in patients facing life-threatening cancer, psilocybin may foster feelings of transcendence over mortality [1, 3].

Psilocybin also appears to strengthen individuals' sense of interconnectedness [29, 30]. Participants frequently report a profound awareness of global connectedness, perceiving links among humans, animals, and the natural environment, and describing deeper emotional bonds with family members, including feeling "more emotionally open" toward loved ones [25]. Individuals with TRD often contrast this heightened connection with the previous sense of disconnection and emotional avoidance they experienced under earlier treatments [29].

The neurobiological mechanisms underlying these changes remain under investigation. Neuroimaging studies suggest that psilocybin may acutely reduce functional connectivity within meta-cognitive networks such as the default-mode network, leading to "disintegration" or loss of a rigid sense of self, alongside increased global connectivity that may underlie enhanced sensory perception [22, 31, 32]. Notably, these networks typically reintegrate shortly after the psychedelic state, suggesting that psilocybin may exert therapeutic effects in part by restructuring neural pathways associated with depression [22, 33].

This type of cognitive "reset" may also relate to increased openness and feelings of connection, potentially explained through a psychodynamic lens whereby psilocybin facilitates access to previously latent thoughts, a mechanism proposed for LSD [34]. Given the pharmacological similarities between LSD and psilocybin, this interpretation may apply to psilocybin as well. Relatedly, interviews with patients using LSD [34] and psilocybin [29] indicate that the intervention may modify cognitive frameworks for approaching challenges, resembling the cognitive restructuring techniques used in psychotherapies such as cognitive behavioral therapy (CBT). Emerging evidence from ayahuasca studies suggests that psychedelics may similarly enhance cognitive flexibility and mindfulness-related skills, including decentering [35, 36]. Another proposed mechanism is that psilocybin increases suggestibility, rendering participants more receptive to therapeutic interventions [9]. Overall, psilocybin's mechanisms are likely multifaceted, encompassing several of these pathways alongside others yet to be fully identified.

Why enhanced consent?

Certain effects of psilocybin may be difficult for patients to anticipate prior to treatment, necessitating enhanced consent procedures that go beyond typical informed consent processes used for many psychotropics. Importantly, this enhanced process still relies on the established principles of informed consent but is more extensive than those applied when prescribing standard psychiatric medications.

Ethicists and legal scholars generally agree that clinicians must provide information that a reasonable patient would want to know regarding the treatment [37, 38] iv. Core elements of disclosure include the nature of the intervention, potential risks and benefits, and available alternatives [38]. While debate persists regarding the level of detail required, the consensus is that disclosure standards should vary with the invasiveness and complexity of the intervention—for example, disclosure for surgery is more detailed than for a blood draw [39].

For many psychiatric interventions, explaining these essential elements can be accomplished quickly. For instance, when prescribing SSRIs such as escitalopram, clinicians typically cover common side effects like gastrointestinal upset and sexual dysfunction, along with rare but severe effects such as serotonin syndrome. Likewise, for second-generation antipsychotics, disclosure may include frequent side effects like weight gain, dizziness, or orthostatic hypotension, as well as rare but serious reactions including dystonia or neuroleptic malignant syndrome. After providing this information, clinicians can answer questions and offer informational

materials if desired. In research contexts, the main additional concern is ensuring participants understand that they may be randomized and might not receive the experimental agent. In line with ongoing efforts to simplify consent documents and discussions [39, 40], many consent procedures in psychotropic research remain relatively straightforward.

This simplicity is partly justified because a reasonable person is expected to focus on the most common and severe outcomes. For SSRIs and antipsychotics, patients are unlikely to prioritize mechanisms or subtle personality effects, which are minimal compared to the profound changes sometimes seen with psychedelics. By contrast, with psilocybin, simply explaining potential relief from depression or the possibility of hallucinations may not adequately convey the profound psychological and personality changes described above, which could be critical to a patient's decision-making.

Disclosure topics in enhanced consent

In particular, three aspects of psilocybin treatment warrant special attention during consent due to their novelty and potential unexpectedness for patients: changes in personality and values, rare psychiatric side effects, and the possible inclusion of therapeutic touch during sessions. These elements require an enhanced disclosure process to ensure that participants can make fully informed decisions.

Shifts in values and personality

Two considerations regarding changes in values and personality warrant attention. First, some of the personality shifts described above may be unwelcome if the new values conflict with the individual's prior beliefs. For example, nonspiritual, agnostic, or atheist participants might perceive the emergence of spiritual or religious feelings, including belief in God, as a loss if it contradicts their former values or creates tension in personal relationships. Conversely, religious individuals who consider mystical experiences to require deep spiritual work or divine intervention could find it troubling if the experience appears reducible to a biochemical process.

Second, because psychedelic experiences are often described as ineffable, the intensity of these experiences and their potential to alter personality may be difficult to fully convey during consent discussions. For instance, atheist participants may not anticipate experiencing profound spiritual states themselves, even if they understand that others might have such encounters. Enhanced consent processes can help patients better appreciate the possibility and nature of these personality changes.

Mental health risks

The second category involves rare but significant mental health risks, including severe anxiety during the experience, psychosis, and re-exposure to trauma. Transient anxiety, often labeled "mild" or "moderate," is frequently cited as a primary risk in the literature [4], yet surveys of mostly recreational psilocybin users indicate that 39% ranked their most challenging "trip" among the five most difficult experiences of their lives [41]. While controlled clinical settings may differ substantially from recreational use [41], these data underscore the need to take severe anxiety seriously, particularly as clinical applications expand beyond tightly monitored research environments.

Psychosis represents another potential risk. Notably, no psychotic episodes have been reported in clinical trials, likely due to careful patient screening that excludes individuals at elevated risk [9]. However, as psilocybin becomes more widely used in clinical practice, screening may be less rigorous, and the consistency of safety monitoring and adherence to protocols may decline compared with research settings. Some authors argue that fears of long-term psychological effects, including psychosis, are largely unsubstantiated [20], citing cross-sectional studies showing no association between lifetime psychedelic use and recent psychotic symptoms [42]. Nevertheless, surveys of psilocybin users have identified a few self-reports of persistent psychosis [43]. While these reports alone cannot establish causation or statistical significance, they suggest caution.

Additional considerations temper the view that concerns about psychosis are negligible. For example, substance-induced psychosis is generally expected to resolve shortly after substance cessation, and the DSM defines persistent symptoms lasting more than a month as evidence for a primary psychotic disorder despite substance exposure [44]. Thus, lifetime psychedelic use complicated by substance-induced psychosis may not correlate with current symptoms, limiting the reassurance provided by cross-sectional findings. Furthermore, hallucinogen use has been associated with increased schizophrenia risk, and use by individuals with schizophrenia is linked to higher rates of violent behavior [45, 46]. Therefore, although the absolute risk of

psychosis is likely low for most individuals, it remains clinically significant and must be addressed in enhanced consent discussions, alongside reassurance that risk is extremely low under controlled conditions.

Finally, trauma re-exposure constitutes a third mental health concern. Participants may relive prior traumatic events or experience apparently new, putative "memories" during the psychedelic session [4, 29], and clinicians may not be able to verify the accuracy of such experiences [4]. As a result, it is essential to inform patients of this possibility and to ensure clinicians are prepared to manage these occurrences. Careful discussion of potential trauma re-exposure is therefore a critical component of the informed consent process.

Therapeutic touch

The use of physical touch—such as a supportive pat on the shoulder for a patient experiencing grief or acute distress during a psychedelic session—raises significant ethical considerations in psychedelic psychotherapy. Touch in psychotherapy has historically been controversial, particularly within psychodynamic frameworks [47, 48], and surveys indicate wide variability in how therapists employ it [49, 50]. Because some psychedelic therapists incorporate touch into their practice [51], it is important to address the unique consent challenges associated with its use in this context.

At first glance, one might assume that touch presents no special issues: therapists should only use it if it is likely to benefit the patient and is acceptable to them [51]. Concerns about exploiting vulnerable patients are at least partly mitigated in many current protocols, which typically require two therapists to be present, providing a built-in safeguard.

However, ethical complexities arise when patients' preferences regarding touch may shift during the psychedelic experience. A patient may anticipate being receptive to touch beforehand, yet experience new feelings—especially during intense anxiety or trauma—while in the psychedelic state. This creates a challenge for consent, as both the patient and therapist may be uncertain which preference should be honored.

Although one might argue that patients should have the right to revise their preferences as long as they retain decision-making capacity, assessing capacity during a psychedelic session can be difficult. Standard capacity assessment evaluates whether patients can maintain a stable preference, understand relevant information, appreciate the consequences of their choices, and reason about this information [52]. In the context of a distressing psychedelic state, applying this standard can be problematic.

Two specific issues complicate capacity assessment during therapy. First, stable preference over time is required to establish capacity; if the patient's preferences fluctuate, this criterion may not be met, particularly under severe anxiety. Second, the patient's ability to comprehend, appreciate, and rationally manipulate information may be limited during intense psychedelic experiences, further challenging capacity determination.

Given these complexities, we propose two guiding principles for consent regarding therapeutic touch. First, unless immediate safety concerns arise—such as the risk of a patient falling [51] or becoming dangerously agitated—any refusal of touch must be respected at all times, even if the patient initially requested it. Second, the psychedelic psychotherapy community should establish standardized guidelines for handling situations in which patients change their minds about touch. The Multidisciplinary Association for Psychedelic Studies (MAPS) emphasizes that consent should be obtained both before and during therapy, ensuring that no patient is touched against their will. MAPS recommends identifying "simple and specific words and gestures" in advance that patients can use to communicate their preferences during sessions [51]. As research in psychedelic therapy expands, further guidance will be necessary, including legal and ethical input on how to respond to evolving patient preferences and how these standards align with existing medical practice and law.

Having outlined key considerations for enhanced consent, we present discussion prompts for this process in **Table 2.**

Table 2. Suggested disclosure information and questions for consent to psilocybin

Category	Disclosure / Information
Information about the Experience	"You may experience a sense of communicating with higher powers or perceiving deeper realities. Such experiences can occur in people with or without prior spiritual or religious beliefs. Because these experiences are often ineffable, it may be difficult to fully understand or convey them before having them yourself."

	"You may notice profound feelings of connection that might have seemed unusual to you before. These could involve connections with other people—potentially all of humanity—as well as with animals and the natural world."
	"You may experience a sense of losing your individual self, feeling that everything is interconnected, or sensing unity with all that exists."
Information about Potential Long-Term Changes	"You may become more open to new experiences and different perspectives."
	"You may develop or deepen a sense of spirituality, even if you previously did not identify as spiritual."
	"You may feel a stronger connection to the natural environment."
	"You may notice increased sociability, openness to new ideas, and a greater willingness to engage with novel experiences."
	"These changes may be noticeable to you and those around you, potentially affecting how others perceive you."
Information about Mechanism	"The benefits of psilocybin may be linked to these experiential effects and related changes in personality. Embracing the experience rather than resisting it has been found to enhance therapeutic outcomes, whereas resistance can increase anxiety and reduce benefits."
	"Some benefits may also arise from the suggestive effects enabled by the drug. For example, patients with cancer have experienced reductions in depressive symptoms, possibly because the experience helps them perceive that their illness does not control their mood or sense of meaning."
Therapeutic Touch	"During challenging moments in the psychedelic session, therapists may offer physical support, such as holding your hand, if desired. This would only occur with your consent. We can discuss in advance how to communicate your preferences about touch during the session."
Questions for Subjects' Reflection	"Would any of the potential changes described be difficult or uncomfortable for you?"
	"Do you have any additional questions about the experience, its potential risks, or its possible benefits?"

Enhanced consent and current practice

Do current research procedures sufficiently meet the demands of enhanced consent? In many cases, they may—particularly during preparatory sessions designed to orient participants to psychedelic psychotherapy. The early guidelines developed during the modern resurgence of psychedelic research by Johnson, Richards, and Griffiths (2008) highlight that psychedelic-naïve participants may struggle to fully grasp the nature of the experience, necessitating additional time for discussion beyond standard consent procedures. These guidelines emphasize that participants should be informed about a wide range of potential effects of psilocybin, including those reviewed above, with particular attention to psychedelic-induced psychiatric symptoms during the consent process.

Notably, these preparatory sessions are often described separately from formal informed consent. They serve multiple purposes: introducing participants to session logistics, fostering a therapeutic alliance, providing a comprehensive discussion of possible psychedelic experiences, and offering strategies for managing challenging episodes. However, we argue that such sessions should be regarded as integral to informed consent, not merely preparatory steps. They represent an extended, iterative process that enhances participant understanding and supports truly informed decision-making.

Despite their importance, there is a lack of systematic reviews detailing the protocols of preparatory sessions or the specifics of consent processes across different psychedelic studies. Consequently, it is difficult to determine definitively how well current research practices meet the standards we propose. By outlining these standards, we aim to support their consistent application in both ongoing research and future clinical practice.

Is psilocybin relevantly different?

One potential objection to our argument is that psilocybin may not differ substantially from conventional psychotropics such as SSRIs. Concerns about personality changes are not unique to psychedelics; SSRIs have been noted for their effects on personality for over two decades

[53], with evidence that they decrease neuroticism and increase conscientiousness [26, 54–56]. Likewise, various forms of psychotherapy—including CBT, supportive, psychodynamic, inpatient, and mixed modalities—can also produce personality changes, sometimes exceeding those observed with antidepressants [57]. This raises the question: "Does psilocybin truly differ in a meaningful way regarding personality change?" The answer appears to be yes.

Several key distinctions set psilocybin apart from standard psychiatric interventions. First, while preliminary, the personality changes associated with psilocybin differ in both type and magnitude. Beyond shared reductions in neuroticism and increases in conscientiousness, psilocybin produces substantial increases in extraversion and openness, effects not typically observed with conventional antidepressants [26]. The enhancement in openness may be particularly central to psilocybin's therapeutic mechanism, making this difference ethically and clinically significant.

Second, patients can often use their prior experience with conventional therapies to inform ongoing treatment decisions. Experiencing part of a psychopharmacologic or psychotherapeutic process allows patients to reassess their willingness to continue, supporting a longitudinal, iterative approach to consent. In contrast, psilocybin's effects frequently manifest rapidly and after a single dose, leaving little opportunity for incremental reassessment. This amplifies the ethical importance of ensuring participants understand potential personality changes before engaging in psilocybin treatment.

Finally, many of psilocybin's effects—such as inducing ineffable insights into universal interconnectedness, existential truths, or perceptions of God—do not clearly map onto the Five-Factor Model of personality. Such experiences are atypical of conventional antidepressants and are rarely central features of standard psychotherapy. Even when existential insights arise in traditional therapy, the process is usually gradual, comprehensible, and within the patient's control, allowing them to decide how to integrate these changes. In contrast, psilocybin often elicits rapid, intense, and ineffable experiences, making the potential for personality and value shifts more immediate and less predictable.

Suggestibility and capacity to consent

Two additional objections merit consideration. First, some may argue that enhanced consent could reduce psilocybin's capacity to induce suggestibility, potentially diminishing its therapeutic effect if suggestibility contributes to its mechanism [5, 9]. Learning about possible personality changes or the role of suggestibility might make participants less receptive to suggestion, thereby lowering therapeutic impact and complicating research by introducing disclosure-related effects [17].

However, withholding such information would deny participants material facts relevant to their decision-making, contrary to standard principles of informed consent [37], unless explicitly waived. Moreover, this objection supports the need for enhanced consent: participants may not wish to undergo treatment that increases suggestibility to beliefs they would not normally endorse. Additionally, if future trials incorporating enhanced consent demonstrate smaller effect sizes, this could provide valuable insight into the role of suggestibility in psilocybin's therapeutic action, potentially informing the development of other novel interventions.

A second objection asserts that patients cannot truly consent if psilocybin induces experiences that are ineffable. When evaluating the value of an event, we often rely on imagining what it would be like to experience it [58]. If the experience or its outcomes cannot be anticipated, some ethicists argue that one may lack the necessary information to make an autonomous, rational choice [59]. In the case of psilocybin, one could question whether individuals can give fully informed consent to experiences that are difficult or impossible to conceptualize in advance.

We contend, however, that the inability to fully imagine an experience does not invalidate consent. Consent is routinely accepted for life decisions that cannot be fully anticipated—such as starting a job, entering a marriage, or moving to a new place. Likewise, consent to traditional psychotherapy is considered valid, even though it may alter personality or worldview in ways that participants cannot fully foresee.

The ethics of transitioning to mainstream use

Historical concerns about personality-altering interventions, though often ultimately unfounded, caution us to interpret preliminary psilocybin data carefully. Similar apprehensions have arisen around SSRIs, organ transplants, deep brain stimulation, and face transplants. For instance, early worries that heart or face transplants could alter personality largely proved speculative [60–63], and systematic review of deep brain stimulation showed personality changes in only 8 of 150

uncontrolled studies [61]. These examples highlight the need for careful interpretation of initial findings.

Current evidence regarding psilocybin's effects on personality remains preliminary, reinforcing the need for cautious ethical conclusions. Nonetheless, the arguments above support implementing enhanced consent practices for psilocybin, at least until further data clarify its effects.

As psilocybin moves from research to mainstream psychiatric practice, four ethical issues warrant attention. First, if psilocybin induces personality changes that are not fully captured by the Five-Factor Model, additional research is needed, potentially including development of new instruments to assess these effects, given the importance of personality in mental health.

Second, psilocybin, like other novel therapies, presents ethical challenges due to limited knowledge of its mechanisms, safety, and long-term benefits. Standardized policies are needed to mitigate risks such as anxiety, psychosis, and trauma exposure. Lessons from ketamine therapy suggest that enthusiasm for novel treatments can sometimes lead to deviations from safety protocols [64, 65]. Implementing formal safeguards, such as FDA Risk Evaluation and Mitigation Strategies (REMS), may help maintain safety during clinical use [66].

Third, intense psychotherapy is generally employed alongside psychedelic administration, though the necessity and extent of therapy remain untested. Despite this uncertainty, the precautionary principle suggests continuing supportive and integration therapy during clinical psilocybin use to help monitor and manage risks, including psychosis and trauma re-exposure.

Finally, participants consistently report profoundly positive experiences. For individuals screened to minimize psychosis risk, the potential benefits appear substantial. If replicated in Phase III trials, these benefits may create a strong ethical imperative to transition psilocybin into mainstream psychiatric practice, while maintaining appropriate safeguards.

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References

1. Ross S, et al. Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. J Psychopharmacol. 2016;30(12):1165–80. doi:10.1177/0269881116675513
2. Johnson MW, Griffiths RR. Potential therapeutic effects of psilocybin. Neurotherapeutics. 2017;14(3):734–40. doi:10.1007/s13311-017-0542-y
3. Griffiths RR, et al. Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: a randomized double-blind trial. J Psychopharmacol. 2016;30(12):1181–97. doi:10.1177/0269881116675513
4. Carhart-Harris RL, et al. Psilocybin with psychological support for treatment-resistant depression: six-month follow-up. Psychopharmacology (Berl). 2018;235(2):399–408. doi:10.1007/s00213-017-4771-x
5. Carhart-Harris RL, et al. Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. Lancet Psychiatry. 2016;3(7):619–27. doi:10.1016/S2215-0366(16)30065-7
6. Johnson MW, et al. An online survey of tobacco smoking cessation associated with naturalistic psychedelic use. J Psychopharmacol. 2017;31(7):841–50. doi:10.1177/0269881116684335
7. Johnson MW, Garcia-Romeu A, Griffiths RR. Long-term follow-up of psilocybin-facilitated smoking cessation. Am J Drug Alcohol Abuse. 2017;43(1):55–60. doi:10.3109/00952990.2016.1170135
8. Garcia-Romeu A, et al. Cessation and reduction in alcohol consumption and misuse after psychedelic use. J Psychopharmacol. 2019;33(9):1088–101. doi:10.1177/0269881119845793
9. Johnson MW, Richards WA, Griffiths RR. Human hallucinogen research: guidelines for safety. J Psychopharmacol. 2008;22(6):603–20. doi:10.1177/0269881108093587
10. Danforth AL, et al. Reduction in social anxiety after MDMA-assisted psychotherapy with autistic adults: a randomized, double-blind, placebo-controlled pilot study. Psychopharmacology (Berl).

2018;235(11):3137–48. doi:10.1007/s00213-018-5045-3
11. Mithoefer MC, et al. 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for post-traumatic stress disorder in military veterans, firefighters, and police officers: a randomised, double-blind, dose-response, phase 2 clinical trial. Lancet Psychiatry. 2018;5(6):486–97. doi:10.1016/S2215-0366(18)30135-4
12. Ot'alora GM, et al. 3,4-Methylenedioxymethamphetamine-assisted psychotherapy for treatment of chronic posttraumatic stress disorder: a randomized phase 2 controlled trial. J Psychopharmacol. 2018;32(12):1295–307. doi:10.1177/0269881118806297
13. Gasser P, et al. Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. J Nerv Ment Dis. 2014;202(7):513–20. doi:10.1097/NMD.0000000000000113
14. Sanches RF, et al. Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a SPECT study. J Clin Psychopharmacol. 2016;36(1):77–81. doi:10.1097/JCP.0000000000000436
15. ClinicalTrials.gov. The safety and efficacy of psilocybin in participants with treatment resistant depression (P-TRD). 2018. Available from: https://clinicaltrials.gov/ct2/show/NCT03775200
16. ClinicalTrials.gov. A multi-site phase 3 study of MDMA-assisted psychotherapy for PTSD. 2018. Available from: https://clinicaltrials.gov/ct2/show/NCT03537014
17. Griffiths RR, et al. Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. J Psychopharmacol. 2008;22(6):621–32. doi:10.1177/0269881108094300
18. Earp BD. Psychedelic moral enhancement. R Inst Philos Suppl. 2018;83:415–39.
19. Earp BD, Savulescu J. Love drugs: the chemical future of relationships. Redwood City: Redwood Press; 2020.
20. Peterson A, Tagliazucchi E, Weijer C. The ethics of psychedelic research in disorders of consciousness. Neurosci Conscious. 2019;2019(1):niz012.
21. Nichols DE, Johnson MW, Nichols CD. Psychedelics as medicines: an emerging new paradigm. Clin Pharmacol Ther. 2017;101(2):209–19. doi:10.1002/cpt.557
22. Carhart-Harris RL. The entropic brain - revisited. Neuropharmacology. 2018;142:167–78. doi:10.1016/j.neuropharm.2018.03.010
23. Multidisciplinary Association for Psychedelic Studies. MDMA: the movie - is MDMA a psychedelic? MAPS Bulletin.
24. Roseman L, Nutt DJ, Carhart-Harris RL. Quality of acute psychedelic experience predicts therapeutic efficacy of psilocybin for treatment-resistant depression. Front Pharmacol. 2018;8:974. doi:10.3389/fphar.2017.00974
25. Belser AB, et al. Patient experiences of psilocybin-assisted psychotherapy: an interpretative phenomenological analysis. J Humanist Psychol. 2017;57(4):354–88.
26. Erritzoe D, et al. Effects of psilocybin therapy on personality structure. Acta Psychiatr Scand. 2018;138(5):368–78. doi:10.1111/acps.12904
27. MacLean KA, Johnson MW, Griffiths RR. Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness. J Psychopharmacol. 2011;25(11):1453–61. doi:10.1177/0269881111420188
28. McCrae RR, John OP. An introduction to the five-factor model and its applications. J Pers. 1992;60(2):175–215.
29. Watts R, et al. Patients' accounts of increased "connectedness" and "acceptance" after psilocybin for treatment-resistant depression. J Humanist Psychol. 2017;57(5):520–64.
30. Carhart-Harris RL, et al. Psychedelics and connectedness. Psychopharmacology (Berl). 2018;235(2):547–50. doi:10.1007/s00213-017-4701-y
31. Carhart-Harris RL, et al. Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. Proc Natl Acad Sci U S A. 2012;109(6):2138–43. doi:10.1073/pnas.1119598109
32. Carhart-Harris RL, et al. The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs. Front Hum Neurosci. 2014;8:20. doi:10.3389/fnhum.2014.00020

33. Carhart-Harris RL, et al. Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms. Sci Rep. 2017;7(1):13187. doi:10.1038/s41598-017-13282-7
34. Gasser P, Kirchner K, Passie T. LSD-assisted psychotherapy for anxiety associated with a life-threatening disease: a qualitative study of acute and sustained subjective effects. J Psychopharmacol. 2015;29(1):57–68. doi:10.1177/0269881114555249
35. Murphy-Beiner A, Soar K. Ayahuasca's 'afterglow': improved mindfulness and cognitive flexibility in ayahuasca drinkers. Psychopharmacology (Berl). 2020;237(4):1161–75. doi:10.1007/s00213-019-05455-3
36. Soler J, et al. Exploring the therapeutic potential of ayahuasca: acute intake increases mindfulness-related capacities. Psychopharmacology (Berl). 2016;233(5):823–9. doi:10.1007/s00213-015-4162-0
37. Faden RR, Beauchamp TL. A history and theory of informed consent. New York: Oxford University Press; 1986.
38. Berg JW, et al. Informed consent: legal theory and clinical practice. 2nd ed. New York: Oxford University Press; 2001.
39. Grady C. Enduring and emerging challenges of informed consent. N Engl J Med. 2015;372(9):855–62. doi:10.1056/NEJMra1411250
40. Schenker Y, Meisel A. Informed consent in clinical care: practical considerations in the effort to achieve ethical goals. JAMA. 2011;305(11):1130–1. doi:10.1001/jama.2011.333
41. Carbonaro TM, et al. Survey study of challenging experiences after ingesting psilocybin mushrooms: acute and enduring positive and negative consequences. J Psychopharmacol. 2016;30(12):1268–78. doi:10.1177/0269881116662634
42. Krebs TS, Johansen P-Ø. Psychedelics and mental health: a population study. PLoS One. 2013;8(8):e63972. doi:10.1371/journal.pone.0063972
43. Carbonaro TM, et al. Survey study of challenging experiences after ingesting psilocybin mushrooms: acute and enduring positive and negative consequences. J Psychopharmacol. 2016;30(12):1268–78. doi:10.1177/0269881116662634
44. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). Arlington: American Psychiatric Association; 2013.
45. Lamsma J, Cahn W, Fazel S. Use of illicit substances and violent behaviour in psychotic disorders: two nationwide case-control studies and meta-analyses. Psychol Med. 2020;50(11):1826–35. doi:10.1017/S0033291719002920
46. Nielsen SM, et al. Association between alcohol, cannabis, and other illicit substance abuse and risk of developing schizophrenia: a nationwide population based register study. Psychol Med. 2017;47(9):1668–77. doi:10.1017/S0033291717000162
47. Gutheil TG, Gabbard GO. The concept of boundaries in clinical practice: theoretical and risk-management dimensions. Am J Psychiatry. 1993;150(2):188–96. doi:10.1176/ajp.150.2.188
48. Gabbard GO. Boundary violations. In: Bloch S, Green SA, editors. Psychiatric ethics. 4th ed. Oxford: Oxford University Press; 2009. p. 251–70.
49. Phelan J. Exploring the use of touch in the psychotherapeutic setting: a phenomenological review. Psychotherapy (Chic). 2009;46(1):97–111.
50. Stenzel CL, Rupert PA. Psychologists' use of touch in individual psychotherapy. Psychotherapy (Chic). 2004;41(3):332–45.
51. Multidisciplinary Association for Psychedelic Studies. MAPS MDMA-assisted psychotherapy code of ethics. MAPS Bulletin. 2019;29(1):24–7.
52. Appelbaum PS. Assessment of patients' competence to consent to treatment. N Engl J Med. 2007;357(18):1834–40. doi:10.1056/NEJMcp074045
53. Kramer PD. Listening to Prozac. New York: Penguin Books; 1997.
54. Bagby RM, et al. Selective alteration of personality in response to noradrenergic and serotonergic antidepressant medication in depressed sample: evidence of non-specificity. Psychiatry Res. 1999;86(3):211–6. doi:10.1016/s0165-1781(99)00041-5
55. Quilty LC, Meusel L-AC, Bagby RM. Neuroticism as a mediator of treatment response to SSRIs in major depressive disorder. J Affect Disord. 2008;111(1):67–73. doi:10.1016/j.jad.2008.02.006
56. Noordhof A, et al. Change in self-reported personality during major depressive disorder

treatment: a reanalysis of treatment studies from a demoralization perspective. Personal Disord. 2018;9(1):93–100. doi:10.1037/per0000264
57. Roberts BW, et al. A systematic review of personality trait change through intervention. Psychol Bull. 2017;143(2):117–41. doi:10.1037/bul0000088
58. Paul LA. Transformative experience. Oxford: Oxford University Press; 2014.
59. Savulescu J. Rational desires and the limitation of life-sustaining treatment. Bioethics. 1994;8(3):191–222. doi:10.1111/j.1467-8519.1994.tb00395.x
60. Sanner MA. Living with a stranger's organ--views of the public and transplant recipients. Ann Transplant. 2005;10(1):9–12.
61. Gilbert F, Viaña JNM, Ineichen C. Deflating the "DBS causes personality changes" bubble. Neuroethics. 2018;11(3):297–310. doi:10.1007/s12152-018-9369-0
62. Kiwanuka H, et al. Evolution of ethical debate on face transplantation. Plast Reconstr Surg. 2013;132(6):1558–68. doi:10.1097/PRS.0b013e3182a80883
63. Powell T. Face transplant: real and imagined ethical challenges. J Law Med Ethics. 2006;34(1):111–5. doi:10.1111/j.1748-720X.2006.00012.x
64. Segal A, Sisti D. Research moratoria and off-label use of ketamine. Am J Bioeth. 2016;16(4):60–1. doi:10.1080/15265161.2016.1148526
65. Schatzberg AF. A word to the wise about ketamine. Am J Psychiatry. 2014;171(3):262–4. doi:10.1176/appi.ajp.2013.13101493
66. Johnson MW, et al. The abuse potential of medical psilocybin according to the 8 factors of the Controlled Substances Act. Neuropharmacology. 2018;142:143–66.