



Psychedelic-assisted psychotherapy: where is the psychotherapy research?

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Abstract

Rationale Psychedelic-assisted psychotherapy (PAP) has emerged as a potential treatment for a variety of mental health conditions, including substance use disorders and depression. Current models of PAP emphasize the importance of psychotherapeutic support before, during, and after ingestion of a psychedelic to maximize safety and clinical benefit. Despite this ubiquitous assumption, there has been surprisingly little empirical investigation of the “psychotherapy” in PAP, leaving critical questions about the necessary and sufficient components of PAP unanswered.

Objectives As clinical trials for psychedelic compounds continue the transition from safety- and feasibility-testing to evaluating efficacy, the role of the accompanying psychotherapy must be better understood to enhance scientific understanding of the mechanisms underlying therapeutic change, optimize clinical outcomes, and inform cost-effectiveness.

Results The present paper first reviews the current status of psychotherapy in the PAP literature, starting with recent debates regarding “psychotherapy” versus “psychological support” and then overviewing published clinical trial psychotherapy models and putative models informed by theory. We then delineate lessons that PAP researchers can leverage from traditional psychotherapy research regarding standardizing treatments (e.g., publish treatment manuals, establish eligibility criteria for providers), identifying mechanisms of change (e.g., measure established mechanisms in psychotherapy), and optimizing clinical trial designs (e.g., consider dismantling studies, comparative efficacy trials, and cross-lagged panel designs). Throughout this review, the need for increased research into the psychotherapeutic components of treatment in PAP is underscored.

Conclusions PAP is a distinct, integrative, and transdisciplinary intervention. Future research designs should consider transdisciplinary research methodologies to identify best practices and inform federal guidelines for PAP administration.

Keywords Psychedelic · Psychedelic-assisted psychotherapy · Psychotherapy · Psilocybin · Psychotherapy models · Review

“There is considerable variation in dosage and method of managing patients while they are under the influ-

ence of [lysergic acid diethylamide; LSD]. Further, there is no uniformity in views expressed as to how the drug facilitates psychotherapy. This is inevitable, since there is no universally accepted theoretical basis for psychotherapy, and each psychotherapist develops techniques of management of patients under the drug in accordance with the principles of his general psychotherapy.” - Whitaker (1964).

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High-dose administration of a classic psychedelic (e.g., psilocybin or LSD) paired with psychotherapy or “psychological support” before, during, and after dosing sessions is increasingly being studied as a potential therapeutic intervention for multiple disorders (Bogenschutz et al. 2022; Carhart-Harris et al. 2021). This tight combination of pharmacological and psychological treatments is arguably unlike anything else in psychiatry and represents a potential paradigm shift for the field (Schenberg 2018). There are two

major rationales for this unusual, combined approach: (1) *Safety*: High doses of psychedelics can confer acute psychological risks that are thought to be mitigated with therapeutic support (Schlag et al. 2022); and (2) *Efficacy*: psychedelics appear to transiently relax prior beliefs (Carhart-Harris and Friston 2019), increase suggestibility (Carhart-Harris et al. 2015), and promote neuroplasticity (Nardou et al. 2023). Such increased sensitivity to context (i.e., extra-pharmacological variables) necessitates a nuanced understanding of the optimal dose and modality of psychotherapy to pair with clinical administration of a psychedelic compound to maximize participant safety and clinical effectiveness (Devenot et al. 2022; Hartogsohn 2016).

In order to determine the role of psychotherapy in PAP outcomes, a critical preliminary step would be to clearly define and distinguish “psychotherapy” from “psychological support,” a term Carhart-Harris and colleagues (2016) introduced to the psychedelic literature because they believed the psychotherapeutic component “wasn’t clearly enough formalised” (Carhart-Harris 2024). The American Psychological Association (APA) defines psychotherapy as “any psychological service provided by a trained professional that primarily uses forms of communication and interaction to assess, diagnose, and treat dysfunctional emotional reactions, ways of thinking, and behavior patterns,” (APA 2023). By this definition, the so-called “psychological support” provided in many PAP trials constitutes “psychotherapy.” Hence, moving forward, the present paper will primarily use the term “psychotherapy” as a description of this interpersonally supportive component of PAP.

Current approaches to psychotherapy in psychedelic-assisted psychotherapy (PAP) are largely the product of trial-and-error from early psychedelic researchers and contemporary community or “underground” psychedelic practitioners. Although these sources of knowledge have been incredibly valuable for the field, systematic study of the psychotherapy in PAP has been lacking (Feduccia et al. 2023). Indeed, although the drug component in trials has frequently been manipulated (e.g., by comparing different dosages of the same psychedelic or by using active or inert placebos), studies have rarely systematically manipulated the non-pharmacological aspects of treatment, including psychotherapy (see: Griffiths and colleagues’ 2018 study for a notable exception). Similarly, the wide variety of terms used to describe individuals supporting patients through psychedelic experiences, such as “guide” (Leary 1966), “sitter” (Thal et al. 2022a) “monitor” (Ching et al. 2023), “facilitator” (Golden et al. 2022), and “psychedelic therapist” (Aday et al. 2023a), among others, underscores the lack of consensus in the field concerning the psychotherapeutic component. This ambiguity regarding what is PAP, and the guidelines for training of psychedelic therapists, have contributed to uncertainty surrounding best practices for the field and raised the risk of

ethical and boundary violations (McNamee et al. 2023). That is, the overly broad definition of what can be considered “appropriate” PAP gives clinicians the flexibility to introduce practices that could compromise interpretation of study outcomes and potentially lead to real-world practices that are unethical or, at a minimum, not evidence-based.

The challenge of parsing psychotherapeutic versus pharmacologic effects in the overall combined ‘package’ of PAP remains a contentious area of debate (Aday et al. 2023c; Goodwin et al. 2023). Moreover, there is much the field has yet to leverage from decades of non-psychedelic psychotherapy research to optimize the psychotherapeutic aspect of treatment. Here, we outline psychotherapeutic models that have been utilized and proposed to be synergistic with psychedelics, summarize emerging debates regarding these models, as well as delineate how the field can address these issues by leveraging important lessons from traditional psychotherapy research. Throughout this review, we underscore the need for increased research to determine the content, frequency, and intensity with which psychotherapy should be embedded within psychedelic treatments, as well as the role it may play in clinical mechanisms and outcomes.

Current psychotherapy models in PAP

Contemporary clinical trials of PAP often include the same general sequence for the intervention, comprising three stages: preparation, dosing, and integration (Horton et al. 2021). Preparation sessions are largely intended to provide psychoeducation, set expectations, and identify goals for treatment, while establishing a therapeutic relationship between participant and therapist(s). It is commonly emphasized during these sessions to develop an approach over an avoidant mindset for dosing sessions (e.g., “trust, let go, be open”). During dosing sessions, psychedelics are typically administered in a relaxing environment with music and “psychotherapeutic support” from the therapists. The length of dosing sessions can vary by drug, but are typically at least six hours with psilocybin (Horton et al. 2021). Subsequent integration sessions assist participants in making meaning of their experiences and exploring ways of potentially generalizing insights from the dosing session to improve their daily lives (Johnson et al. 2008). Each phase of PAP (i.e., preparation, dosing, integration) contains distinct approaches to providing adjunctive psychotherapy, with more traditional forms of structured psychotherapy present during the preparation and integration stages of treatment, and a semi-structured, “non-directive” approach during dosing sessions (Thal et al. 2022b, 2023, 2024).

Almost all modern trials of PAP cite a foundational paper written by Johnson and colleagues (2008), titled

“Human Hallucinogenic Research: Guidelines for Safety.” These early guidelines provided the broad framework of preparation, dosing, and integration for PAP trials to examine the potential clinical benefits of PAP across a variety of conditions. Johnson and colleagues (2008) drew heavily from a model described as “psychedelic peak therapy,” which was specifically designed to induce peak, transformative, and altered states of consciousness with high doses of psychedelics, typically LSD (Grof 1980). Notably, mid-twentieth century PAP researchers and clinicians also experimented with psychotherapeutic approaches beyond psychedelic peak therapy, including psycholytic therapy, which involves the use of low doses of psychedelics in combination with ongoing psychotherapy (Grob and Grigsby 2021). Nonetheless, the psychedelic peak therapy model has been ubiquitously applied to modern PAP research—across various psychedelic drugs, research groups, and clinical diagnoses (Davis et al. 2021b; Johnson et al. 2014; Ross et al. 2016).

The psychedelic peak therapy model includes a semi-structured approach to adjunctive psychotherapy, historically described as a “non-directive supportive” framework, in which therapists minimize verbal interactions with participants during the dosing experience (Griffiths et al. 2016). Outside of dosing sessions, modern trials have incorporated other modalities of psychotherapy in the preparation and integration phases, including CBT (Johnson et al. 2014), Motivational Enhancement Therapy (Bogenschutz et al. 2015, 2022), and an eclectic treatment drawing from existential, psychodynamic, and CBT models (Ross et al. 2016). The list of approaches that have been proposed to be synergistic with PAP cascades into a myriad of psychotherapies, including Acceptance and Commitment Therapy (Sloshower et al. 2020), Internal Family Systems Therapy (IFST; Morgan 2020), Eye Movement Desensitization and Reprocessing Therapy (EMDR; Rose and Raine-Smith 2023), existential psychology (Moreton et al. 2020), mindfulness (Felsch and Kuypers 2022), psychoanalysis (Guss 2022), group psychotherapy (Trope et al. 2019), virtual reality therapy (Aday et al. 2020), and even novel modalities specifically designed for PAP (Brennan and Belser 2022; Wolfson 2022; Watts and Luoma 2020). Similarly, a range of putative psychological mechanisms of change have been identified in PAP, such as awe (Hendricks 2018), mystical-type experiences (Griffiths et al. 2016), acceptance (Wolff et al. 2020), decreased rumination (Barba et al. 2022), cognitive flexibility (Doss et al. 2021), and therapeutic alliance (Levin et al. 2024; Murphy et al. 2021). Thus, views regarding best psychotherapeutic practices for PAP vary widely beyond the standard psychedelic peak therapy framework that includes “non-directive support”, and there has been very limited empirical investigation to date of these diverse approaches in the context of PAP (Cavarra et al. 2022).

Emerging debates

Challenges related to the empirical investigation into, and operationalized definition of, the “psychotherapy” paired with psychedelics date back to the mid-20th century (Whitaker 1964). Recently, researchers have debated whether psychotherapy is even a necessary component of the treatment, with a publication from Goodwin and colleagues (2023), suggesting “the effects observed thus far in the best controlled studies of psychedelic treatment must be attributed to the drug itself and not to psychotherapy”. Yet, the same researchers expressing skepticism of the necessity of psychotherapy in PAP recently published a phase 2 clinical trial (Goodwin et al. 2022) that included (a) trained “therapists” present at each stage of the study intervention, (b) an unpublished “therapist manual” guiding therapist interactions with participants, and (c) explicit indication of initiating various forms of psychotherapy for participants tapering off prohibited medications as part of study participation, including “CBT,” or cognitive behavioral therapy. Goodwin et al.’s (2023) publication proved to be incredibly provocative, with six reply letters published from researchers across the globe expressing concern that minimizing the psychotherapeutic component of treatment could compromise the safety and efficacy of PAP (Alpert et al. 2024; Bogenschutz 2024; Deckel et al. 2024; Earleywine et al. 2024; O’Donnell et al. 2024; Schenberg et al. 2024).

The Federal Drug Administration (FDA) recently proposed standards for clinical trials involving PAP (FDA 2023), including the role of psychotherapy in future research. These guidelines acknowledge the paucity of research investigating psychotherapeutic mechanisms in PAP, calling for researchers to account for the role of psychotherapy on clinical outcomes. These guidelines go on to suggest that researchers provide separate psychotherapists for various stages of PAP (i.e., dosing sessions vs. preparation and integration), despite a lack of evidence suggesting this is (a) a safe or efficacious approach to the treatment, or (b) an effective means of mitigating expectancy effects (Aday et al. 2022). Indeed, in a recent trial where a similar approach was adapted, a participant noted “My team was different for every single dose and it seemed very haphazardly scheduled... Taking psychedelics is a moment of true vulnerability, and finding out shortly before a treatment session that you’d have to reintroduce your story to a brand new team who are essentially strangers, was quite jarring and unnerving,” (Evans 2024). Collectively, these recent reports underscore an immediate need to determine the necessity and sufficiency of psychotherapy in PAP in order to inform considerations for safety, cost-effectiveness, and clinical efficacy. The underlying complexity of this question was succinctly summarized by Dr. Johnson (2021): “Psychedelic

therapy is more psychotherapy than most pharma companies & neuroscientists know how to deal with, and more pharmacology than most psychotherapists know how to deal with.”

Informing PAP with traditional psychotherapy research

Given the large body of literature developed over the last century on standardizing clinical trial protocols, identifying mechanisms of change, and assessing the efficacy of competing approaches in traditional psychotherapy research, failure to leverage these methodological advancements to improve upon current PAP research and therapy models may represent an important missed opportunity (Table 1).

Standardizing protocols

First, in order for best practices to be established in PAP, it is evident that greater emphasis is needed on the specific content and intensity of the psychotherapy in psychedelic research papers. Descriptions of the psychotherapeutic components of PAP have typically been minimized (Brennan et al. 2023); speculatively, this may be because many of the researchers in this area are not psychotherapists themselves and that manualizing interpersonal interactions can be intrinsically challenging. Additionally, the FDA does not generally regulate psychotherapy and it is difficult to patent psychotherapeutic techniques, which may incentivize industry sponsors seeking commercialization to minimize the psychotherapeutic component of PAP. Notably, industry-sponsored clinical trials of PAP frequently use the term “psychological support” rather than explicit mention of psychotherapy when publishing primary outcomes.

While the issue of minimizing the psychotherapy in PAP is a separate issue altogether, challenges related to the standardization and replicability of behavioral intervention research have already been addressed in traditional psychotherapy literature. In 2018, an international group of psychotherapy researchers published recommendations to improve rigor in psychotherapy trials (Guidi et al. 2018). Regarding description of treatment components, the authors advocated that all potential treatment ingredients (e.g., how many hours were provided, the guiding principles and specific content of the treatment) should be listed in method sections. Ideally, researchers would also include a published manual or supplement outlining important details of the therapy to improve replicability. Defining the eligibility criteria for care providers (e.g., training, licensure) may also promote consistency of intervention delivery and mitigate risks for boundary violations (Baier et al. 2020). Clarifying how extra therapy sessions were determined and how many occurred may also improve rigor and replicability (Zeifman and Maia

Table 1 Informing PAP with lessons from psychotherapy research

<i>Standardizing Protocols</i>	<i>Identifying Mechanisms of Change</i>	<i>Assessing Efficacy of Specific Techniques</i>
<ul style="list-style-type: none"> List elements of psychotherapy in methods (e.g., hours provided, principles of treatment, etc.) Include the order in which specific techniques were deployed Publish a treatment manual or supplement Define eligibility criteria for care providers (e.g., training, licensure) Collect measures of reliability and adherence 	<ul style="list-style-type: none"> Examine established trans-theoretical principles of change <ol style="list-style-type: none"> Fostering hope, positive expectations, and motivation Facilitating the therapeutic alliance Increasing awareness and insight Encouraging corrective experiences Emphasizing ongoing reality testing Consider other mechanisms that have been established as well (e.g., mindfulness, experiential avoidance) 	<ul style="list-style-type: none"> Maintain awareness of “common factors” considerations and the Dodo Bird Verdict Utilize dismantling studies, comparative efficacy trials, and cross-lagged panel designs for identifying best practices in PAP

2023). Currently, these methodological details are not adequately provided in clinical trials of PAP. Lastly, collecting measures of reliability and adherence to therapy manuals, as is done in clinical trials of many forms of non-psychedelic psychotherapy, are substantive steps that can easily be implemented to improve standardization in PAP trials. To this end, Serfaty et al. (2020) published the Therapy Component Checklist (TCC) to measure adherence to manualized CBT. The authors concluded that the TCC provides a rapid and cost-effective method of evaluating the components of psychotherapy delivered, and that the instrument could be adapted for evaluating adherence to other psychological treatments, such as PAP. Thus, we recommend that future PAP trials include adapting the TCC to their specific treatment manual and use it to evaluate adherence throughout the study.

Identifying mechanisms of change

There are also specific psychotherapeutic mechanisms of change that have been established as fundamental to effective psychotherapy, yet remain minimally examined in PAP research. Identification of relevant mechanisms in any form of health treatment is important for improving treatment efficacy, as well as targeting populations most likely to benefit from the intervention (Baier et al. 2020). Twomey and colleagues (2023) recently surveyed a large number of psychotherapy clinicians and researchers ($N = 1,998$) from a variety of theoretical orientations regarding principles of change that guide routine psychotherapy practice. They found that there was consensus regarding five principles: (1) fostering hope, positive expectations, and motivation, (2) facilitating the therapeutic alliance, (3) increasing awareness and insight, (4) encouraging corrective experiences, and (5) emphasizing ongoing reality testing.

There is variability regarding the extent to which researchers have assessed these principles in the context of PAP. Certainly, fostering hope, positive outcome expectations, and motivations prior to dosing in PAP is considered to be integral to facilitating positive and therapeutic experiences with psychedelics; however, researchers have rarely measured expectations (Aday et al. 2022). Similarly, therapeutic alliance between therapists and participants in PAP appears predictive of greater emotional breakthrough, mystical-type experiences, and decreases in depression (Levin et al., 2024; Murphy et al. 2021), but has most often not been measured. Regarding insight, evidence is emerging that experiences of insight facilitated with psychedelics may predict persisting clinical benefits (Davis et al. 2021a; Peill et al. 2022), although further research is needed. Wolff and colleagues (2020) theorized that the state of belief relaxation conferred by psychedelics may facilitate corrective experiences (i.e., processing an emotional event or relationship in a

novel and unexpected way), but no PAP studies to-date have specifically examined corrective experiences. Lastly, to the authors' knowledge, emphasis of ongoing reality testing has not been incorporated as a fundamental aspect of PAP nor measured in any trials, but may align with purported psychological mechanisms of PAP (e.g., cognitive reframing, psychological flexibility, memory reconsolidation). Beyond these transtheoretical principles, there may be additional mechanisms of change derived from traditional psychotherapy (e.g., mindfulness, experiential avoidance; Payne et al. 2021; Zeifman et al. 2020) that are applicable to PAP, and it should also be highlighted that PAP may involve unique mechanisms that traditional psychotherapeutic frameworks do not typically consider (e.g., mystical-type experiences). In summary, many cognitive-emotional and interpersonal processes involved in PAP are also core constructs targeted in psychotherapy interventions (Wolff et al. 2024). Leveraging decades of research on how traditional psychotherapy “works”—while maintaining vigilance over what makes PAP distinct—may expedite crucial insights into relevant therapeutic elements of PAP.

Assessing efficacy of specific techniques

Another opportunity to utilize lessons from traditional psychotherapy research lies in assessing differences in treatment efficacy and safety, including the direct head-to-head empirical evaluation of psychotherapeutic approaches or techniques within a single trial. Such research has been critical for evaluating distinctions between modalities of psychotherapy, yielding information that can inform treatment assignment and responsiveness. A recent network meta-analysis of behavioral interventions for posttraumatic stress disorder (PTSD) exemplified the value of such research, with results indicating between-treatment differences in acute- and long-term treatment response, as well as PTSD remission (Yunitri et al. 2023). A similar analysis evaluating psychotherapies for late-life depression found Life Review Therapy to be the most preferred modality, when accounting for both effectiveness and acceptability. These analyses underscore the importance of head-to-head interventions, as treatments that share similar effectiveness may benefit from treatment tailoring to minimize patient dropout (see: Schnurr et al. 2022).

Despite these findings, non-psychedelic psychotherapy research also suggests that there is reason to doubt that traditional randomized controlled trials (RCTs) are sensitive to detecting differences between distinct therapeutic approaches (Wampold 2013). Indeed, this has been a simmering issue for the field of psychotherapy for almost a century (Rosenzweig 1936). That is, the high number of “common factors” among different psychotherapeutic techniques (e.g., therapeutic alliance, positive expectations, hope, reassurance) often makes it difficult to identify outcome

differences among approaches when directly compared in a clinical trial (Cuijpers et al. 2019), a phenomenon referred to as “The Dodo Bird Verdict” (Luborsky et al. 2002). Gukasyan and Nayak (2022) outlined how common factors of psychotherapy converge with key components of PAP, including “1) an emotionally charged, confiding relationship with a helping person, 2) a healing setting, 3) a rationale, conceptual scheme, or myth that provides a plausible explanation for the patient’s suffering and a means of alleviation, and 4) a ritual that requires participation of both patient and therapist, which is mutually believed to be the means of succor.”

The challenges related to common factors seem to have preliminary translation to PAP based on a single psilocybin study by Griffiths and colleagues (2018)—the only modern clinical trial of PAP to-date that has manipulated aspects of the “psychotherapeutic support” between conditions. In this trial, 75 healthy participants were randomized among three groups: (1) very low-dose (1 mg/70 kg on sessions 1 and 2) with moderate-level (“standard”) support for spiritual-practice (LD-SS); (2) high-dose (20 and 30 mg/70 kg on sessions 1 and 2, respectively) with the same “standard” support for spiritual practice (HD-SS); and (3) high-dose (20 and 30 mg/70kg on sessions 1 and 2, respectively) with “high” support for spiritual practice (HD-HS). At the six-month follow-up, compared with LD-SS, both high-dose groups showed large positive changes on longitudinal measures of interpersonal closeness, gratitude, life meaning/purpose, forgiveness, death transcendence, daily spiritual experiences, religious faith and coping, and community observer ratings. Although a small number of differences in the trial emerged between the high-dose groups (e.g., increased ratings of spiritual experiences in the group with high support for spiritual practice as expected), there were generally more similarities than differences—suggesting that drug dose was a more pertinent factor in trial outcomes than the contextual factors that were manipulated. To date, this is the only modern psychedelic trial we are aware of to directly study aspects of the surrounding psychotherapeutic intervention, beyond music (Strickland et al. 2021), which is ubiquitously thought to be crucial to clinical outcomes.

Psychotherapy researchers have attempted to address issues like the Dodo Bird Verdict with innovative study designs, such as dismantling studies, comparative efficacy trials, and cross-lagged panel models (CLPMs). A dismantling study design typically involves comparing a full treatment protocol to a “dismantled” control condition, where one or more components of the treatment thought to be an active mechanism(s) of action are removed. All other aspects of the study design and implementation are held constant between conditions, and attempts are made to ensure equivalence across nonspecific aspects of care that might influence outcomes. The rationale is that if the removed portion

of the treatment is an important “ingredient” in the overall treatment package, subsequent group comparisons should demonstrate reductions in clinically significant change in the dismantled group as compared to the group that received the complete treatment (Papa and Follette 2015). For example, narrative reformulation is an assumed active ingredient of cognitive analytic therapy (CAT) in treating depression. Kellett and colleagues (2021) compared typical CAT with a dismantled control condition that removed narrative reformulation. They found that narrative reformulation did not enhance the efficacy of CAT for depression, suggesting that it may be a redundant portion of the treatment that can be removed while maintaining treatment efficacy. In the context of PAP, dismantling studies could be leveraged to identify the timing and dose of psychotherapy needed to optimize clinical outcomes as well as explore the contribution of other factors assumed to be important in treatment (e.g., touch, music, etc.) However, it should also be noted that a stripped down approach may not be appropriate for all patients, and those requiring more support may be disadvantaged if insurance payers refuse to cover a more intensive treatment. Although there are possible safety concerns regarding removing aspects of the psychotherapeutic support with PAP, risks may be minimized if done iteratively.

Similarly, comparative efficacy and non-inferiority trials compare two active forms of treatment to assess treatment superiority after a treatment has demonstrated efficacy against an inactive control (Williams et al. 2016). Such designs could be systematically deployed to identify aspects of PAP that account for clinical change and inform best practices for the field. Although, it should be noted that these designs are limited by the need for larger sample sizes and higher costs.

Psychotherapy researchers have similarly acknowledged the drawbacks of dismantling designs as well as potential ethical limitations of withholding aspects of treatment. As an alternative, CLPMs have been put forth as a means for identifying mechanisms of change in psychotherapy (Falkenström et al. 2020). In a CLPM, two variables (X and Y) are repeatedly measured throughout treatment, which makes it possible to track session-by-session changes and focus on within-patient associations between predictors and outcomes. The primary advantage of CLPMs compared to traditional cross-sectional correlational analyses is accounting for temporality, a primary criterion for causal inference (Antonakis et al. 2010). Although CLPMs allow for greater confidence in causal inference, they are still limited by the potential for confounding variables and, therefore, require a large number of within-subject observations. This may be a particularly relevant hurdle for PAP, given that the treatment involves a limited number of sessions relative to traditional psychotherapy and can be characterized by periods of rapid, non-linear change in some cases (Palhano-Fontes et al.

2019). Nonetheless, CLPMs represent another untapped resource provided by traditional psychotherapy researchers that has been as of yet underutilized by PAP researchers.

Looking forward

As patchwork legalization of PAP begins to unfold across the world, standards for psychotherapy will undoubtedly vary by jurisdiction, as has already been seen in Oregon, Colorado, and Australia. The effects of these inconsistent standards on treatment outcomes remain mostly unknown. Given the heightened state of vulnerability and sensitivity to context conferred by psychedelics, it is critical for researchers to begin systematically studying the role of the surrounding psychotherapeutic component of treatment (Aday et al. 2023c). Relatedly, the importance of establishing clear guidelines and standards for appropriate licensure and training of psychedelic therapists is of the utmost importance (Feduccia et al. 2023; Siegel et al. 2023). Licensure and training are requirements for all psychotherapists, designed to ensure clinicians are appropriately trained and qualified to practice psychotherapy. Moreover, licensure is intended to mitigate risks for boundary violations and requires therapists to adhere to the Hippocratic oath to “do no harm.” Such considerations are paramount for PAP, as participants are given suggestibility-enhancing substances that may increase their vulnerability to therapist coercion and malpractice (Carhart-Harris et al. 2015; Barber and Dike 2023; Villiger and Trachsel 2023).

As previously outlined, the psychedelic peak therapy model could likely be better mechanistically understood and clinically optimized by leveraging the techniques developed in the context of traditional psychotherapy, and it may be the case that certain psychotherapeutic approaches may be more suitable for specific doses or conditions (Passie et al. 2022). A final critical issue to underscore, however, is the paucity of federal funding for psychedelic studies, which has forced researchers to primarily rely on philanthropic and industry support for trials (Barnett et al. 2022). Due to the difficulty of patenting and monetizing psychotherapy approaches, companies in the psychedelic industry are incentivized to focus on drug discovery and development (Aday et al. 2023b). Moreover, although the National Institute of Health (NIH) has recently released requests for applications for psychedelic research investigations, the NIH’s de-emphasis on psychotherapy research more generally (Karter 2015; Markowitz and Friedman 2020) could threaten scientific growth in understanding the role of psychotherapy in PAP. Increased federal support to study the psychotherapeutic component of PAP could shed light on

therapeutic mechanisms, optimize the treatment model, and inform cost-effectiveness.

Conclusion

Recent clinical trials of PAP have shown early therapeutic promise for a variety of health conditions. However, to date, there has been considerable ambiguity and a lack of empirical investigation regarding the psychotherapeutic component of treatment. Given the crucial role of context, including psychotherapy, in PAP outcomes, more research is needed to identify best practices associated with the treatment, and there are valuable advancements developed in the context of traditional psychotherapy that PAP researchers have yet to fully leverage. Recent state approvals for the clinical use of PAP, coupled with calls from the NIH to better understand the mechanisms underlying changes induced by PAP, necessitate investment and innovation into this research to reduce the risk of adverse effects, optimize clinical outcomes, inform cost-effectiveness, and enhance generalizability and comparability of study findings.

Declarations

Conflicts of interest JDW has been a paid consultant for Silo Pharma and Filament Health.

References

- Aday JS, Davoli CC, Bloesch EK (2020) Psychedelics and virtual reality: parallels and applications. *Ther Adv Psychopharmacol* 10:2045125320948356
- Aday JS, Heifets BD, Pratscher SD, Bradley E, Rosen R, Woolley JD (2022) Great expectations: recommendations for improving the methodological rigor of psychedelic clinical trials. *Psychopharmacology* 239:1989–2010 (Berl)
- Aday JS, Skiles Z, Eaton N, Fredenburg L, Pleet M, Mantia J, Bradley ER, Fernandes-Osterhold G, Woolley JD (2023a) Personal psychedelic use is common among a sample of psychedelic therapists: implications for Research and Practice. *Psychedelic Med* 1:27–37
- Aday JS, Barnett BS, Grossman D, Murnane KS, Nichols CD, Hendricks PS (2023b) Psychedelic commercialization: a wide-spanning overview of the emerging psychedelic industry. *Psychedelic Med* 3:150–165
- Aday JS, Carhart-Harris RL, Woolley JD (2023c) Emerging challenges for psychedelic therapy. *JAMA Psychiatry* 80:533–534
- Alpert MD, O’Donnell KC, Paleos CA, Sola E, Stauffer CS, Wagner AC, Nicholas CR, Mithoefer MC (2024) Psychotherapy in psychedelic treatment: safe, evidence-based, and necessary. *Am J Psychiatry* 181(1):76–77
- American Psychological Association (2023) Psychotherapy. In *APA Dictionary of Psychology*. <https://dictionary.apa.org/psychotherapy>. Accessed 22 May 2024

- Antonakis J, Bendahan S, Jacquart P, Lalive R (2010) On making causal claims: a review and recommendations. *Leadersh Q* 21:1086–1120
- Baier AL, Kline AC, Feeny NC (2020) Therapeutic alliance as a mediator of change: a systematic review and evaluation of research. *Clin Psychol Rev* 82:101921
- Barba T, Buehler S, Kettner H, Radu C, Cunha BG, Nutt DJ, Erritzoe D, Roseman L, Carhart-Harris RL (2022) Effects of psilocybin versus escitalopram on rumination and thought suppression in depression. *BJPsych Open* 8:e163
- Barber GS, Dike CC (2023) Ethical and practical considerations for the use of psychedelics in psychiatry. *Psychiatr Serv* 74:838–846
- Barnett BS, Parker SE, Weleff J (2022) United States National Institutes of Health grant funding for psychedelic-assisted therapy clinical trials from 2006–2020. *Int J Drug Policy* 99:103473
- Bogenschutz MP (2024) Pharmacological and nonpharmacological components of psychedelic treatments: the whole is not the sum of the parts. *Am J Psychiatry* 181(1):75
- Bogenschutz MP, Forcehimes AA, Pommy JA, Wilcox CE, Barbosa PC, Strassman RJ (2015) Psilocybin-assisted treatment for alcohol dependence: a proof-of-concept study. *J Psychopharmacol* 29:289–299
- Bogenschutz MP, Ross S, Bhatt S, Baron T, Forcehimes AA, Laska E et al (2022) Percentage of heavy drinking days following psilocybin-assisted psychotherapy vs placebo in the treatment of adult patients with alcohol use disorder: a randomized clinical trial. *JAMA Psychiatry*. <https://doi.org/10.1001/jamapsychiatry.2022.2096>
- Brennan W, Belser AB (2022) Models of psychedelic-assisted psychotherapy: a contemporary assessment and an introduction to EMBARK, a transdiagnostic, trans-drug model. *Front Psychol* 13:866018
- Brennan W, Kelman A, Belser AB (2023) A systematic review of reporting practices in psychedelic clinical trials: psychological support, therapy, and psychosocial interventions. Preprint at. <https://doi.org/10.31234/osf.io/2ab59>
- Carhart-Harris R (2024) It is, it's just we've been slow to formally teach and manualize it so that it can be recognised as such. In a sense, the shortcoming is on us. We called it psychological support because we knew it wasn't clearly enough formalised. Twitter/X. Last modified February 20, 2024. <https://twitter.com/RCarhartHarris/status/1759809514390606062>
- Carhart-Harris RL, Friston KJ (2019) REBUS and the anarchic brain: toward a unified model of the brain action of psychedelics. *Pharmacol Rev* 71:316–344
- Carhart-Harris RL, Kaelen M, Whalley MG, Bolstridge M, Feilding A, Nutt DJ (2015) LSD enhances suggestibility in healthy volunteers. *Psychopharmacology* 232:785–794
- Carhart-Harris RL, Bolstridge M, Rucker J, Day CM, Erritzoe D, Kaelen M, Bloomfield M, Rickard JA, Forbes B, Feilding A, Taylor D (2016) Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. *The Lancet Psychiatry* 3(7):619–627
- Carhart-Harris R, Giribaldi B, Watts R, Baker-Jones M, Murphy-Beiner A, Murphy R, Martell J, Blemings A, Erritzoe D, Nutt DJ (2021) Trial of psilocybin versus escitalopram for depression. *N Engl J Med* 384:1402–1411
- Caverra M, Falzone A, Ramaekers JG, Kuypers KP, Mento C (2022) Psychedelic-assisted psychotherapy—a systematic review of associated psychological interventions. *Front Psychol* 13:887255
- Ching T, Kichuk S, DePalmer G, Pittenger C, Kelmendi B (2023) Yale Program for Psychedelic Science (YPPS) manual for psilocybin combined with non-directive support in the treatment of OC. Preprint at. <https://doi.org/10.31234/osf.io/ba42z>
- Cuijpers P, Reijnders M, Huibers MJ (2019) The role of common factors in psychotherapy outcomes. *Ann Rev Clin Psychol* 15:207–231
- Davis AK, Barrett FS, So S, Gukasyan N, Swift TC, Griffiths RR (2021a) Development of the psychological insight questionnaire among a sample of people who have consumed psilocybin or LSD. *J Psychopharmacol* 35:437–446
- Davis AK, Barrett FS, May DG, Cosimano MP, Sepeda ND, Johnson MW, Finan PH, Griffiths RR (2021b) Effects of Psilocybin-assisted therapy on major depressive disorder: a Randomized Clinical Trial. *JAMA Psychiatry* 78:481–489
- Deckel GM, Lepow LA, Guss J (2024) Psychedelic assisted therapy must not be retired. *Am J Psychiatry* 181(1):77–78
- Devenot N, Seale-Feldman A, Smith E, Noorani T, Garcia-Romeu A, Johnson MW (2022) Psychedelic identity shift: a critical Approach to set and setting. *Kennedy Inst Ethics J* 32(4):359–399
- Doss MK, Považan M, Rosenberg MD, Sepeda ND, Davis AK, Finan PH, Smith GS, Pekar JJ, Barker PB, Griffiths RR, Barrett FS (2021) Psilocybin therapy increases cognitive and neural flexibility in patients with major depressive disorder. *Transl Psychiatry* 11:574
- Earleywine M, De Leo J, Bhayana D, Rajanna B, Scott K (2024) Psilocybin without psychotherapy: a cart without a horse? *Am J Psychiatry* 181(1):78–79
- Evans J (2024) Two cases of extended difficulties after Braxia's psilocybin TRD trial. Ecstatic Integration | Jules Evans | Substack. <https://www.ecstaticintegration.org/p/two-cases-of-extended-difficulties>. Accessed 22 May 2024
- Falkenström F, Solomonov N, Rubel J (2020) Using time-lagged panel data analysis to study mechanisms of change in psychotherapy research: methodological recommendations. *Couns Psychother Res* 20:435–441
- Feduccia A, Agin-Liebes G, Price CM, Grinsell N, Paradise S, Rabin DM (2023) The need for establishing best practices and gold standards in psychedelic medicine. *J Affect Disord* 332:47–54
- Felsch CL, Kuypers KPC (2022) Don't be afraid, try to meditate—potential effects on neural activity and connectivity of psilocybin-assisted mindfulness-based intervention for social anxiety disorder: a systematic review. *Neurosci Biobehav Rev* 139:104724
- Food & Drug Administration (2023) Psychedelic Drugs: Considerations for clinical investigations. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/psychedelic-drugs-considerations-clinical-investigations>. Accessed 22 May 2024
- Golden TL, Magsamen S, Sandu CC, Lin S, Roebuck GM, Shi KM, Barrett FS (2022) Effects of setting on psychedelic experiences, therapies, and outcomes: a rapid scoping review of the literature. *Curr Top Behav Neurosci* 56:35–70
- Goodwin GM et al (2022) Single-dose psilocybin for a treatment-resistant episode of Major Depression. *N Engl J Med* 387:1637–1648
- Goodwin GM, Malievskaia E, Fonzo GA, Nemeroff CB (2023) Must psilocybin always 'assist psychotherapy'? *Am J Psychiatry*. <https://doi.org/10.1176/appi.ajp.20221043>
- Griffiths RR, Johnson MW, Carducci MA, Umbricht A, Richards WA, Richards BD, Cosimano MP, Klinedinst MA (2016) Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: a randomized double-blind trial. *J Psychopharmacol* 30:1181–1197
- Griffiths RR, Johnson MW, Richards WA, Richards BD, Jesse R, MacLean KA, Barrett FS, Cosimano MP, Klinedinst MA (2018) Psilocybin-occasioned mystical-type experience in combination with meditation and other spiritual practices produces enduring positive changes in psychological functioning and in trait measures of prosocial attitudes and behaviors. *J Psychopharmacol* 32:49–69

- Grob CS, Grigsby J (2021) Handbook of Medical Hallucinogens. The Guilford
- Grof S (1980) LSD Psychotherapy. Hunter House
- Guidi J, Brakemeier EL, Bockting CL, Cosci F, Cuijpers P, Jarrett RB, Linden M, Marks I, Peretti CS, Rafanelli C, Rief W (2018) Methodological recommendations for trials of psychological interventions. *Psychother Psychosom* 87:276–284
- Gukasyan N, Nayak SM (2022) Psychedelics, placebo effects, and set and setting: insights from common factors theory of psychotherapy. *Transcult Psychiatry* 59:652–664
- Guss JA (2022) Psychoanalytic perspective on psychedelic experience. *Psychoanal Dialogues* 32:452–468
- Hartogsohn I (2016) Set and setting, psychedelics and the placebo response: an extra-pharmacological perspective on psychopharmacology. *J Psychopharmacol* 30(12):1259–1267 (**Oxford England**)
- Hendricks PS (2018) Awe: a putative mechanism underlying the effects of classic psychedelic-assisted psychotherapy. *Int Rev Psychiatry* 30:331–342
- Horton DM, Morrison B, Schmidt J (2021) Systematized review of psychotherapeutic components of psilocybin-assisted psychotherapy. *Am J Psychother* 74:140–149
- Johnson MW (2021) Psychedelic therapy is more psychotherapy than most pharma companies & neuroscientists know how to deal with, and more pharmacology than most psychotherapists know how to deal with. Twitter/X. Last modified February 7, 2021. https://twitter.com/Drug_Researcher/status/1358503193089556486. Accessed 22 May 2024
- Johnson M, Richards W, Griffiths R (2008) Human hallucinogen research: guidelines for safety. *J Psychopharmacol* 22:603–620
- Johnson MW, Garcia-Romeu A, Cosimano MP, Griffiths RR (2014) Pilot study of the 5-HT_{2A}R agonist psilocybin in the treatment of tobacco addiction. *J Psychopharmacol* 28:983–992
- Karter J (2015) NIMH funding changes threaten psychotherapy research. *Mad In America*. <https://www.madinamerica.com/2015/11/nimh-funding-changes-threaten-psychotherapy-research/>
- Kellett S, Gausden J, Gaskell C (2021) The effectiveness of cognitive analytic therapy for borderline personality disorder: utilizing a withdrawal experimental design to improve sensitivity to abandonment. *Psychol Psychother* 94(Suppl 1):96–119
- Leary T (1966) Psychedelic prayers after the Tao Te Ching, vol 1. Poets
- Levin AW, Lancelotta R, Sepeda ND, Gukasyan N, Nayak S, Wagener TL, Barrett FS, Griffiths RR, Davis AK (2024) The therapeutic alliance between study participants and intervention facilitators is associated with acute effects and clinical outcomes in a psilocybin-assisted therapy trial for major depressive disorder. *PLoS one* 19(3):e0300501
- Luborsky L, Rosenthal R, Diguier L, Andrusyna TP, Berman JS, Levitt JT, Seligman DA, Krause ED (2002) The dodo bird verdict is alive and well—mostly. *Clin Psychol Sci Pract* 9:2–12
- Markowitz JC, Friedman RA (2020) NIMH's straight and neural path: the road to killing clinical psychiatric research. *Psychiatr Serv* 71:1096–1097
- McNamee S, Devenot N, Buisson M (2023) Studying harms is key to improving psychedelic-assisted therapy—participants call for changes to research landscape. *JAMA Psychiatry* 80:411–412
- Moreton SG, Szalla L, Menzies RE, Arena AF (2020) Embedding existential psychology within psychedelic science: reduced death anxiety as a mediator of the therapeutic effects of psychedelics. *Psychopharmacology* 237:21–32 (**Berlin**)
- Morgan NL (2020) Integrating psychedelic experiences utilizing the internal family systems therapeutic model. *Int J Social Sci Manage Rev* 3:257–264
- Murphy R, Kettner H, Zeifman R, Giribaldi B, Kartner L, Martell J, Read T, Murphy-Beiner A, Baker-Jones M, Nutt D, Erritzoe D (2021) Therapeutic alliance and rapport modulate responses to psilocybin assisted therapy for depression. *Front Pharmacol* 12:788155
- Nardou R, Sawyer E, Song YJ, Wilkinson M, Padovan-Hernandez Y, de Deus JL, Wright N, Lama C, Faltin S, Goff LA, Stein-O'Brien GL (2023) Psychedelics reopen the social reward learning critical period. *Nature* 618:790–798
- O'Donnell KC, Anderson BT, Barrett FS, Bogenschutz MP, Grob CS, Hendricks PS, Kelmendi B, Nayak SM, Nicholas CR, Paleos CA, Stauffer CS (2024) Misinterpretations and omissions: a critical response to Goodwin and colleagues' commentary on psilocybin-assisted therapy. *Am J Psychiatry* 181(1):74–75
- Palhano-Fontes F, Barreto D, Onias H, Andrade KC, Novaes MM, Pessoa JA, Mota-Rolim SA, Osório FL, Sanches R, Dos Santos RG, Tófoli LF (2019) Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial. *Psychol Med* 49:655–663
- Papa A, Follette WC (2015) Dismantling studies of psychotherapy. *Encyclopedia Clin Psychol* 1478–1479. <https://doi-org.ezproxy.library.wisc.edu/https://doi.org/10.1002/9781118625392.wbecp523>
- Passie T, Guss J, Krähenmann R (2022) Lower-dose psycholytic therapy – a neglected approach. *Front Psychiatry* 13:1020505
- Payne JE, Chambers R, Likhaitzky P (2021) Combining psychedelic and mindfulness interventions: synergies to inform clinical practice. *ACS Pharmacol Transl Sci* 4(2):416–23
- Peill JM, Trinci KE, Kettner H, Mertens LJ, Roseman L, Timmermann C, Rosas FE, Lyons T, Carhart-Harris RL (2022) Validation of the psychological insight scale: a new scale to assess psychological insight following a psychedelic experience. *J Psychopharmacol* 36:31–45
- Rose J, Raine-Smith H (2023) EMDR as a preparation and integration tool in psychedelic-assisted therapy: a collaborative case study. *EMDR Therapy Quarterly*
- Rosenzweig S (1936) Some implicit common factors in diverse methods of psychotherapy. *Am J Orthopsychiatry* 6:412–415
- Ross S, Bossis A, Guss J, Agin-Liebes G, Malone T, Cohen B, Mennenga SE, Belser A, Kalliontzi K, Babb J, Su Z (2016) Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. *J Psychopharmacol* 30:1165–1180
- Schenberg EE (2018) Psychedelic-assisted psychotherapy: a paradigm shift in psychiatric research and development. *Front Pharmacol* 9:733
- Schenberg EE, King IVF, da Fonseca JE, Roseman L (2024) Is poorly assisted psilocybin treatment an increasing risk? *Am J Psychiatry* 181(1):75–76
- Schlag AK, Aday J, Salam I, Neill JC, Nutt DJ (2022) Adverse effects of psychedelics: from anecdotes and misinformation to systematic science. *J Psychopharmacol* 36:258–272
- Schnurr PP, Chard KM, Ruzek JI, Chow BK, Resick PA, Foa EB, Marx BP, Friedman MJ, Bovin MJ, Caudle KL, Castillo D, Curry KT, Hollifield M, Huang GD, Chee CL, Astin MC, Dickstein B, Renner K, Clancy CP, Collie C, Shih MC (2022) Comparison of Prolonged Exposure vs Cognitive Processing Therapy for Treatment of Posttraumatic Stress Disorder Among US Veterans: A Randomized Clinical Trial. *JAMA Netw Open* 5(1):e2136921
- Serfaty M, Shafraan R, Vickerstaff V, Aspden T (2020) A pragmatic approach to measuring adherence in treatment delivery in psychotherapy. *Cogn Behav Ther* 49(5):347–360
- Siegel JS, Daily JE, Perry DA, Nicol GE (2023) Psychedelic drug legislative reform and legalization in the US. *JAMA Psychiatry* 80:77–83
- Sloshower J, Guss J, Krause R, Wallace RM, Williams MT, Reed S, Skinta MD (2020) Psilocybin-assisted therapy of major depressive disorder using Acceptance and Commitment Therapy as a therapeutic frame. *J Context Behav Sci* 15:12–19

- Strickland JC, Garcia-Romeu A, Johnson MW (2021) Set and setting: a randomized study of different musical genres in supporting psychedelic therapy. *ACS Pharmacol Transl Sci* 4:472–478
- Thal SB, Engel LB, Bright SJ (2022a) Sober sitter or coconsumer? Psychedelics, online forums and preferences for interpersonal interactions. *Addict Res Theory* 30:382–390
- Thal SB, Wieberneit M, Sharbanee JM, Skeffington PM, Baker P, Bruno R, Wenge T, Bright SJ (2022b) Therapeutic (Sub) stance: current practice and therapeutic conduct in preparatory sessions in substance-assisted psychotherapy—a systematized review. *J Psychopharmacol* 36(11):1191–207
- Thal SB, Baker P, Marinis J, Wieberneit M, Sharbanee JM, Bruno R, Skeffington PM, Bright SJ (2024) Therapeutic frameworks in integration sessions in substance-assisted psychotherapy: a systematised review. *Clin Psychol Psychother* 31(1):e2945
- Thal SB, Wieberneit M, Sharbanee JM, Skeffington PM, Bruno R, Wenge T, Bright SJ (2023) Dosing and therapeutic conduct in administration sessions in substance-assisted psychotherapy: a systematized review. *J Humanistic Psychol*. <https://doi.org/10.1177/00221678231168516>
- Trope A, Anderson BT, Hooker AR, Glick G, Stauffer C, Woolley JD (2019) Psychedelic-assisted group therapy: a systematic review. *J Psychoact Drugs* 51:174–188
- Twomey C, O'Reilly G, Goldfried MR (2023) Consensus on the perceived presence of transtheoretical principles of change in routine psychotherapy practice: a survey of clinicians and researchers. *Psychother (Chic)* 60:219–224 (Chic)
- Villiger D, Trachsel M (2023) With great power comes great vulnerability: an ethical analysis of psychedelics' therapeutic mechanisms proposed by the REBUS hypothesis. *J Med Ethics*. <https://doi.org/10.1136/jme-2022-108816>
- Wampold BE (2013) *The great psychotherapy debate: models, methods, and findings*. Routledge
- Watts R, Luoma JB (2020) The use of the psychological flexibility model to support psychedelic assisted therapy. *J Context Behav Sci* 15:92–102
- Whitaker LH (1964) Lysergic acid in psychotherapy I: clinical aspects. *Med J Aust* 1:5–8
- Williams CM, Skinner EH, James AM, Cook JL, McPhail SM, Haines TP (2016) Comparative effectiveness research for the clinician researcher: a framework for making a methodological design choice. *Trials* 17:406
- Wolff M, Evens R, Mertens LJ, Koslowski M, Betzler F, Gründer G, Jungaberle H (2020) Learning to let go: a cognitive-behavioral model of how psychedelic therapy promotes acceptance. *Front Psychiatry* 11:5
- Wolff M, Evens R, Mertens LJ, Schmidt C, Beck J, Rutrecht H, Charniak AD, Gründer G, Jungaberle H (2024) Measuring psychotherapeutic processes in the context of psychedelic experiences: validation of the General Change Mechanisms Questionnaire (GCMQ). *J Psychopharmacol* 38(5):432–457. <https://doi.org/10.1177/02698811241249698>
- Wolfson E (2022) Psychedelic-supportive psychotherapy: a psychotherapeutic model for, before and beyond the medicine experience. *J Psychedelic Stud* 6(3):191–202
- Yunitri N, Chu H, Kang XL, Wiratama BS, Lee TY, Chang LF, Liu D, Kustanti CY, Chiang KJ, Chen R, Tseng P, Chou KR (2023) Comparative effectiveness of psychotherapies in adults with post-traumatic stress disorder: a network meta-analysis of randomised controlled trials. *Psychol Med* 53(13):6376–6388. <https://doi.org/10.1017/S0033291722003737>
- Zeifman RJ, Maia LO (2023) Methodological concerns in psychedelic research: the issues of nonequivalent psychological support and generalizability. *Eur Neuropsychopharm* 78:13–15
- Zeifman RJ, Wagner AC, Watts R, Kettner H, Mertens LJ, Carhart-Harris RL (2020) Post-psychedelic reductions in experiential avoidance are associated with decreases in depression severity and suicidal ideation. *Front Psychiatry* 11:782

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