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Trip sitting or just sitting? Session facilitators substantially influence psychedelic experiences in clinical trials but not in healthy ones

Sean P. Goldy [a,*], Nathan D. Sepeda [a], Samantha N. Hilbert [a], Bilal A. Bari [b,c], Albert Garcia-Romeu [a], Natalie Gukasyan [d], Frederick S. Barrett [a], David B. Yaden [a], Sandeep M. Nayak [a]

[a] Center for Psychedelic and Consciousness Research, Department of Psychiatry and Behavioral Science, Johns Hopkins University School of Medicine, Baltimore, MD, USA
[b] Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA
[c] McLean Hospital, Harvard Medical School, Belmont, MA, USA
[d] New York State Psychiatric Institute, Columbia University Medical Center, New York, NY, USA

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ABSTRACT

Psychedelics' characteristic acute subjective effects predict therapeutic benefits, such as decreases in depression and anxiety. Thus, optimizing treatment involves better understanding which factors shape subjective effects. Session facilitators, who support participants before, during, and after psychedelic administration sessions, form an important part of the setting of these experiences. Yet, the extent to which session facilitators influence participants' acute subjective effects is unknown. To address this gap, we analyzed data from 9 psilocybin administration studies involving 298 participants, 670 dosing sessions, and 60 facilitators—the largest dataset of its kind. Using multilevel models, we examined whether facilitators contributed to variance in participants' acute subjective effects. Results showed that facilitators accounted for negligible variance (0.8 %) in healthy volunteers, but greater variance in clinical samples (13.6 %), after controlling for study and participant differences. These findings reveal that facilitators may play a clinically meaningful role in shaping psychedelic treatment outcomes in patient populations, relative to non-patients, comparable to or exceeding therapist effects in traditional psychotherapy (~8 %). These results have direct implications for clinical trial design, training protocols, and the implementation of psychedelic treatments as they continue to scale.

1. Introduction

Classic psychedelics are being tested for their therapeutic potential across a range of disorders. Unlike many pharmacological treatments, however, their effects appear to depend to some extent on the quality of the subjective experiences they occasion. Interpersonal factors are an important part of the context in which psychedelic experiences occur, as most studies require that multiple session facilitators be present for safety concerns. Yet, the extent to which these facilitators impact the psychedelic experience in clinical and healthy normal populations is unknown, warranting further examination.

Classic psychedelics (i.e., serotonin 2A receptor [5-HT_{2A}R] partial agonists such as psilocybin, LSD, and DMT) are increasingly being studied in controlled medical contexts as treatments for various conditions, including major depressive disorder (Carhart-Harris et al., 2016, 2021; Davis et al., 2021; D'Souza et al., 2022; Goodwin et al., 2022; Raison et al., 2023; Reckweg et al., 2023; Rotz et al., 2023), anxiety and depression secondary to a life-threatening illness (Griffiths et al., 2016; Grob et al., 2011; Muttoni et al., 2019; Ross et al., 2016), and substance use disorders (Bogenschutz et al., 2015, 2022; Johnson et al., 2014, 2017; Rieser et al., 2025). They are argued to produce therapeutic outcomes in part via acute subjective effects (Olson, 2020; Yaden and Griffiths, 2021), which can vary across different dimensions of emotion, thought, and perception (Goldy et al., 2024; Yaden et al., 2024).

Crucially, mystical-type experience, commonly operationalized with the Mystical Experience Questionnaire (MEQ; Barrett et al., 2015; Maclean et al., 2012), one of the most widely used measures in psychedelic clinical trials, predicts a wide variety of therapeutic outcomes, including improvements in depression, anxiety, life satisfaction, and substance use (Davis et al., 2021a, 2021b; Garcia-Romeu et al., 2015;

* Corresponding author.
E-mail address: sgoldy1@jh.edu (S.P. Goldy).

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Goodwin et al., 2025; Griffiths et al., 2016; Gukasyan et al., 2022; Johnson et al., 2014; Roseman et al., 2018a, 2018b; Ross et al., 2016; Weiss et al., 2024). Insofar as the acute subjective effects of psychedelics are a causal component of their therapeutic benefits, it is vital to identify which factors meaningfully shape these subjective effects and their therapeutic outcomes.

Notably, psychedelic therapy has often been thought to function as a form of psychotherapy (Nayak and Johnson, 2021). Psychedelic experiences under some conditions appear to facilitate new perspectives, enhance psychological insight and, in clinical research settings, are typically surrounded by preparatory and follow-up visits with psychotherapists or trained facilitators (Gründer et al., 2024). If therapeutic psychedelic experiences act, at least in part, through mechanisms akin to psychotherapy, then a key variable to consider is the individual facilitating these experiences.

In traditional (i.e., non-psychedelic) psychotherapy research, therapist effects, or the degree to which individual therapists influence patients' therapeutic outcomes, are well-documented, with work suggesting that therapist effects spanning different therapeutic modalities can account for approximately 5–10 % of variance in patient outcomes after controlling for other variables (Firth et al., 2020; Saxon et al., 2017). Similarly, a systematic review of therapist effects in different contexts found that therapist effects on therapeutic outcomes in randomized controlled trials average 8.2 % (Johns et al., 2019). Additional work indicates that psychiatrist effects can also contribute marked variance in outcomes of psychopharmacological treatment (de Beer et al., 2024), sometimes to a greater degree than the prescribed medication itself (McKay et al., 2006).

Just as therapists impact traditional psychotherapy contexts, psychedelic session facilitators may also influence participants' subjective experiences. Current psilocybin trials in medical research contexts require two facilitators to be present during drug administration (at least one of whom must be an independently licensed mental health practitioner, in U.S. trials; U.S. Food and Drug Administration, 2023). Facilitators typically meet with participants several times before and after the dosing session to build and maintain trust, provide psychoeducation regarding potential effects of psychedelics, monitor safety, discuss experiences, and provide aftercare. Facilitator practices have been variously described as psychotherapy in treatment models that purposefully combine drug with psychotherapy (e.g., before, during, or after acute psychedelic experiences) or as non-psychotherapeutic psychological support where the drug is considered the primary active ingredient (Goodwin et al., 2024), in an ongoing, vigorous debate. Thus, quantifying facilitator effects on subjective and therapeutic outcomes is crucial to clarify whether psychedelic therapy should be viewed primarily as a pharmacological intervention or as an integrated psychotherapeutic process.

However, despite dozens of clinical trials, there is scant empirical work on therapist effects in the research literature on psychedelics, with two notable exceptions—both with significant methodological limitations. A single-blind, between-subjects study (N = 176) of LSD and psychotherapy for alcohol use disorder found "insignificant" differences in outcomes due to therapists (Ludwig et al., 1969). However, there was also no difference in outcomes between LSD and treatment-as-usual conditions, and the psychological practices employed (including hypnosis and psychoanalysis during drug effects) are not comparable to modern trials. A more recent double-blind, placebo-controlled trial (N = 29) of psilocybin with psychotherapy for anxiety and depression in life-threatening cancer diagnoses featured 3 lead and 12 secondary therapists found no differences in outcomes between the three lead therapists (Ross et al., 2016). However, this analysis did not account for the fact that each participant had 2 therapists. It was also limited by sample size of both participants and therapists.

Whether psychedelics' effects vary reliably with different session facilitators has important implications for interpretating existing findings, designing future psychedelic trials, and training facilitators if psychedelic drugs are approved as medicine. Similar facilitation methods have accompanied psychedelic drug administration in studies of both clinical populations and healthy volunteers. Thus, it also unknown whether facilitators might influence psychedelics' subjective effects and therapeutic outcomes in healthy volunteers differently than in clinical populations.

In this work, we present the largest and most comprehensive examination to date of the impact of session facilitators on variation in the acute subjective effects of psilocybin. Using the largest pooled dataset of modern psilocybin administration trials in humans, spanning over two decades and 9 studies, we assessed the extent to which facilitators influenced participants' reported experiences, indexed by the MEQ (Barrett et al., 2015; Maclean et al., 2012). The present research aims to assess to the extent to which an individual's psychedelic experience may be impacted by those supporting them throughout their experience.

2. Methods

Participant data were pooled from 9 drug administration studies conducted at the Johns Hopkins Center for Psychedelic and Consciousness Research (CPCR). Each of these studies administered at least one high (20 mg/70 kg or greater) oral dose of psilocybin. The dataset included completed clinical trials examining psilocybin in the treatment of anorexia (Gukasyan et al., in prep), major depressive disorder (Davis et al., 2021a), and cancer-related existential distress (Griffiths et al., 2016), as well as pharmacological studies involving healthy volunteers (Barrett et al., 2020; Carbonaro et al., 2018; Griffiths et al., 2006, 2008, 2011, 2018). As described in prior published work on trials conducted at the CPCR, two session facilitators were assigned to each participant. Over the course of a trial, participants met with both facilitators before, during, and after dosing sessions to develop rapport and trust, provide psychoeducation regarding the potential effects of psychedelic drugs, monitor safety, provide aftercare, and discuss participants' experiences following dosing. Across the studies, the number of dosing sessions varied, ranging from 1–5 separate dosing sessions per participant within a study. On dosing session days, participants completed self-report measures of the acute subjective effects of their experience after the immediate acute effects of drug dosing had subsided (i.e., about 6 h after administration). Only data from dosing sessions in which psilocybin (ranging from 0.68 mg to 47.43 mg) or a placebo (0 mg psilocybin) was administered were included in analyses.

2.1. Measures

Mystical Experience Questionnaire (MEQ30; Barrett et al., 2015; Maclean et al., 2012). After their dosing session, participants completed either the 30-item Mystical Experience Questionnaire or the 100-item States of Consciousness Questionnaire (which includes all of the 30-item MEQ). The MEQ assessed acute, largely positive, aspects of subjective effects encountered by participants. Items are rated on a 6-point Likert scale (0 = *None, Not at all*; 5 = *Extreme, more than any other time in your life and stronger than 5*) and compose four factors: mystical (e.g., feelings of unity), positive mood (e.g., awe), ineffability, and transcendence of space and time. The MEQ total and subscale scores were divided by the maximum possible Likert score to calculate the proportion of the highest possible score ($M_{\text{Total MEQ}}$ = 0.54, SD = 0.31).

Dose. Dose of drug administered—psilocybin or placebo (at 0 mg)—was measured in absolute milligrams administered in the given dosing session (M_{Dose} = 18.59, SD = 12.30; median = 21.16). Studies used weight-based (e.g., 10 mg/70 kg) or fixed doses (e.g., 25 mg).

Dosing session number. As some trials featured multiple separate dosing sessions (up to 5), the dosing session (e.g., #1, #2) was captured with a count variable indicating the number of sessions a given participant had encountered at a given point in time ($M_{\text{Session number}}$ = 1.97, SD = 1.10).

Number of sessions monitored. To account for different levels of

experience between facilitators, the number of sessions monitored at the date of a particular dosing session was calculated for each facilitator, at each dosing session, yielding two separate count variables. For example, the first time a monitor was present for a dosing session, their number of sessions monitored was 1, their second session would yield a 2, and so on, enabling us to control for differences in monitoring experience. ($M_{Sessions\ monitored} = 22.33$, SD = 50.57; median = 7.0).

Participant ID. A unique, de-identified ID number indicated each participant, as a categorical variable.

Session facilitator. This is a categorical variable denoting which of the 60 unique session facilitators were present during a participant's dosing session. Two facilitators were always present in a single session. To preserve facilitator anonymity in the dataset, random numbers were assigned to facilitator identity.

Study number. This is a unique categorical identifier for each of the 9 studies included in the analyses.

2.2. Analytic strategy

To investigate the relationship between session facilitators and participant mystical experience scores, we estimated multilevel models in R. Given that each participant was jointly monitored by two session facilitators in each dosing session, we implemented a multiple membership multilevel model to more accurately represent this structure (Browne et al., 2001), using the *lmerMultiMember* R package (van Paridon et al., 2025), which acts as a wrapper for *lme4*'s *lmer* function (Bates et al., 2015). Total MEQ scores were regressed onto fixed effects of dose, dosing session number, number of sessions monitored by facilitator, and study number. This model also included separate random intercept effects of participant ID and session facilitator, to account for the hierarchical structure of the data, as well as repeated measurements of participants and facilitators.

In the multiple membership structure, each participant was associated with two facilitators, with equal weights assigned to each. This structure allowed us to estimate the influence of facilitators while appropriately accounting for the fact that each facilitator can be associated with multiple participants and each participant was monitored by two facilitators. This is crucial, as it allows us to estimate the influence of each monitor while considering the overlapping roles each monitor plays in multiple sessions. This model is depicted below in *lme4*'s *lmer* function format:

Total MEQ percent max ~ Dose + Session number + Study number + Facilitator 1 sessions monitored + Facilitator 2 sessions monitored + (1|Facilitator) + (1|participant)

In this model, the membership structure is specified through the inclusion of a weight matrix for session facilitators, indicating the degree to which each monitor is associated with each participant across sessions. We calculated the variance partition coefficient (VPC) which indicates the percentage of variance in MEQ scores explained by facilitators and participants after controlling for the fixed effects. To examine the robustness of our results and model choice, we also estimated additional alternative models and repeated our analyses on simulated data (reported in Supporting Information). Simulations demonstrated that this model could, in principle, identify meaningful variance if it existed. We also considered non-multiple-membership analyses but these models did not properly account for the hierarchical structure of the data and often failed to converge. See Supporting Information for more detail.

We next explored whether facilitator-level variance differed between studies in clinical populations versus healthy volunteers. We subset the data by study type, yielding a clinical population dataset and a healthy volunteer dataset. The above model was then fit to each subset and the random effect of facilitator examined. To compare random effect variances between these models, we implemented a non-parametric cluster bootstrap approach. At each bootstrap replicate, participants were resampled with replacement within each group (clinical and healthy), preserving the within-subject structure. For each of 5000 bootstrap replicates, we fit the same multiple-membership multilevel model described above and extracted the variance component attributable to session facilitators. We then computed the difference in facilitator-level variance (clinical minus healthy) across replicates, yielding an empirical distribution of variance differences. This procedure yielded a 95 % confidence interval and p-value, allowing us to assess whether the observed difference in facilitator variance between clinical and healthy samples was greater than would be expected by chance under repeated sampling.

3. Results

The final sample included 298 participants, 670 dosing sessions, and 60 unique session facilitators. The clinical sample included 97 participants, 211 dosing sessions, and 39 session facilitators. The healthy volunteers sample included 201 participants, 459 dosing sessions, and 45 session facilitators.

The variance among the entire dataset for the facilitator random effect was 0.001 (SD = 0.031), indicating an extremely minimal degree of variability in MEQ scores across session facilitators. The VPC (percent variance in MEQ attributable to facilitators after controlling for fixed effects) was 1.6 %. Fig. 1 depicts the individual random effect of each de-identified session facilitator, depicting nil to negligible impact on MEQ scores for each facilitator, with every 95 % confidence interval for each facilitator including 0, indicating no difference from the average MEQ score.

Conversely, variance in MEQ scores among all participants was 0.026 (SD = 0.160), a 26-fold difference from variance explained by facilitator. The VPC of participant was 43.2 % respectively. Full model results are depicted in Table 1. For additional analysis of MEQ subfactors, see Supporting Information.

Finally, we explored whether there was a difference in facilitator-level variance between clinical samples and healthy volunteers. In clinical samples, the estimated variance attributable to facilitators was 0.009 (SD = 0.09), compared to just 0.0005 (SD = 0.02) in healthy volunteer trials. In clinical populations, these corresponded to a VPC (percent variance explained) of 13.6 % for facilitators and 30.4 % for participants. In healthy volunteer trials, these corresponded to a VPC of 0.8 % for facilitators and 41.9 % for participants. A bootstrap test using 5000 resampled datasets indicated that there was significantly greater variance in clinical trials relative to healthy ones (95 % CI[−0.003, 0.058], $p = .012$) (Figs. 2 and 3).

4. Discussion

Across several seminal drug administration trials involving various doses of psilocybin and numerous session facilitators, we found that facilitators explained negligible variation of subjective effects, indexed by the MEQ, in trials of healthy volunteers (0.8 %), but markedly greater variation in clinical populations (13.6 %)—exceeding the average therapist effect size observed in traditional psychotherapy contexts (~8 %; Johns et al., 2019). These results indicate the greater role facilitators may play in clinical contexts, meaningfully impacting psychedelic experiences and treatment outcomes in patient populations. In such settings, participants may come with more psychological complexity, emotional vulnerability, therapeutic expectations, or other factors that may heighten sensitivity to the interpersonal qualities of the facilitator. In contrast, the acute subjective effects of healthy volunteers were less dependent on facilitator input.

These findings are consistent with related work emphasizing the importance of interpersonal dynamics in clinical psychedelic therapy. Inasmuch as facilitator effects on MEQ are a proxy for therapeutic effects, different psychedelic facilitators may exert differential therapeutic

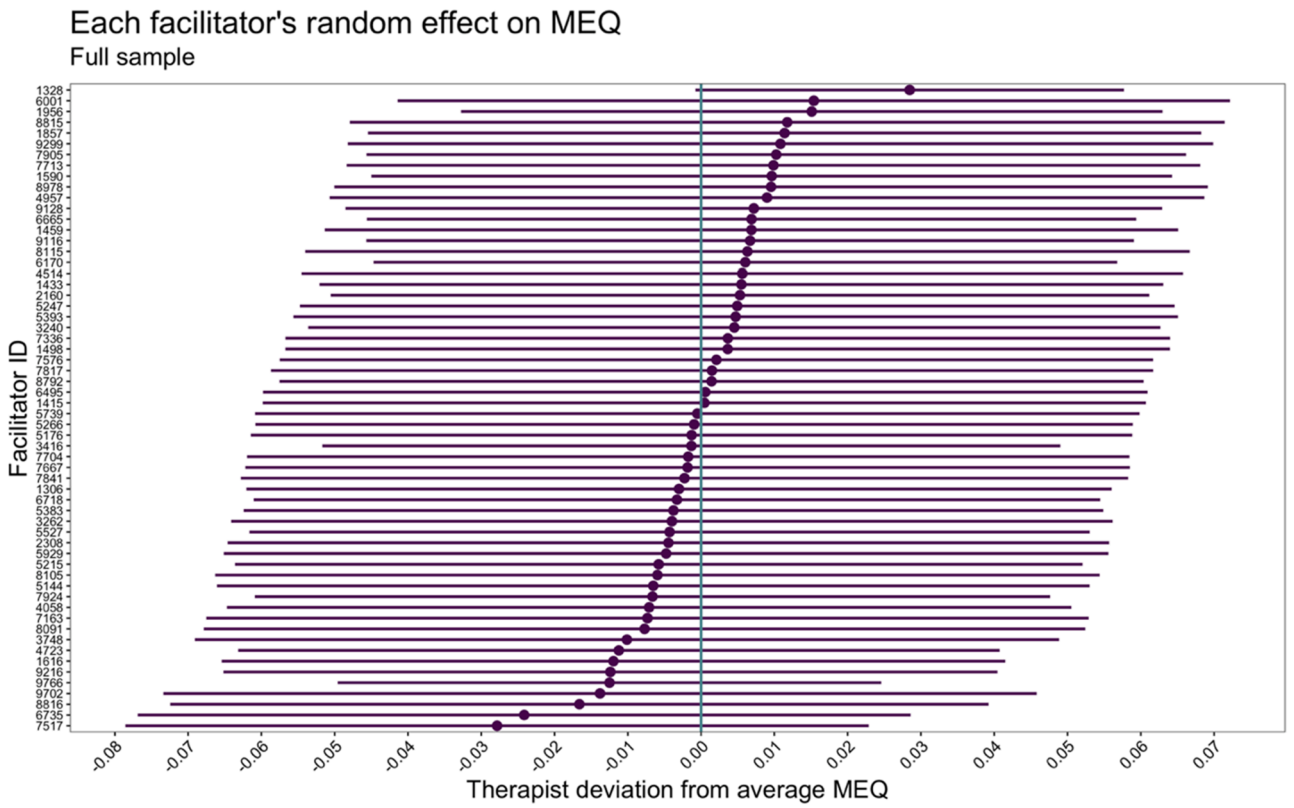

Fig. 1. Individual session facilitator random effects on MEQ scores across the full sample. Each point represents a de-identified facilitator's model-estimated deviation from the mean MEQ score (vertical line) accounting for covariates. Horizontal bars represent 95 % confidence intervals.

Table 1
Full sample multiple-membership multilevel model with total MEQ scores as outcome.

Fixed effects	*Coef.*	*SE*	*t-score*	*95 % Confidence interval*
Intercept	0.3039	0.0603	5.0414	[0.1726, 0.4352]
Dose	0.0154	0.0007	21.5335	[0.0140, 0.0168]
Session number	−0.0133	0.0081	−1.6438	[−0.0292, 0.0026]
Study:				
Griffiths et al. (2011)	0.0589	0.0659	0.8948	[−0.0716, 0.1895]
Griffiths et al. (2016)	−0.0275	0.0628	−0.4381	[−0.1562, 0.1012]
Griffiths et al. (2018)	−0.0162	0.0610	−0.2652	[−0.1456, 0.1132]
Ehrenkranz et al. (in prep)	0.0002	0.0742	0.0024	[−0.1577, 0.1580]
Carbonaro et al. (2018)	−0.0814	0.0778	−1.0455	[−0.2489, 0.0861]
Davis et al. (2021)	−0.0007	0.0801	−0.0084	[−0.1726, 0.1712]
Barrett et al. (2020)	0.0876	0.0965	0.9084	[−0.1087, 0.2840]
Gukasyan et al. (submitted)	−0.1003	0.0809	−1.2392	[−0.2751, 0.0746]
Facilitator 1 number of sessions monitored	0.0000	0.0002	−0.2390	[−0.0005, 0.0004]
Facilitator 2 number of sessions monitored	−0.0003	0.0002	−1.4944	[−0.0008, 0.0001]
Random Effects	*Var.*	*SD*		
ID	0.0256	0.1600		
Facilitator	0.0009	0.0311		
Residual	0.0327	0.1808		

$N = 298$ participants, 670 dosing sessions.
Note: Individual study numbers represent categorical identification numbers for each study. Dose is in units of milligrams.

effects, as is the case in psychotherapy. Indeed, the variance of subjective effects explained by facilitators is on par or greater with that of therapist effects in psychotherapy outcomes, where therapist effects account for an estimated 8 % of variance in participants' outcome (Johns et al., 2019)

While facilitator effects on therapeutic outcomes in psychedelic treatments have never been directly studied before, related evidence suggests that facilitator-participant dynamics do shape both acute subjective effects and therapeutic outcomes. For example, a randomized controlled trial of psilocybin-assisted therapy for moderate-severe depressive disorder found that the therapeutic alliance between facilitators and participants ($N = 30$) was associated with psilocybin's acute subjective effects (specifically, greater emotional-breakthrough and mystical-type experience) and reductions in depression (Murphy et al., 2022). Similarly, a randomized, waitlist-controlled trial of psilocybin-assisted therapy for major depressive disorder ($N = 24$) reported that therapeutic alliance prior to dosing was associated with stronger acute subjective effects (i.e., higher peak ratings of mystical experience and psychological insight), as well as greater reductions in depression severity at 4 weeks, 6 months, and 12 months post-intervention (Levin et al., 2024). Together, these results underscore that facilitator-participant dynamics may be particularly consequential in clinical populations, potentially due to increased psychological complexity, vulnerability, therapeutic motivation, or facilitator actions. In contrast, healthy volunteers may be less sensitive to interpersonal factors due to the relative absence of psychological complications inherent in various mental health conditions, and they may be more influenced by individual traits or pharmacological effects alone. Alternately, it may be that psychedelic facilitators more naturally and effectively apply psychotherapeutic techniques when reviewing life history, preparing participants for psychedelic experiences, and supporting integration after these experiences, especially in the context of a therapeutic clinical trial, whereas the depth and intensity of anything

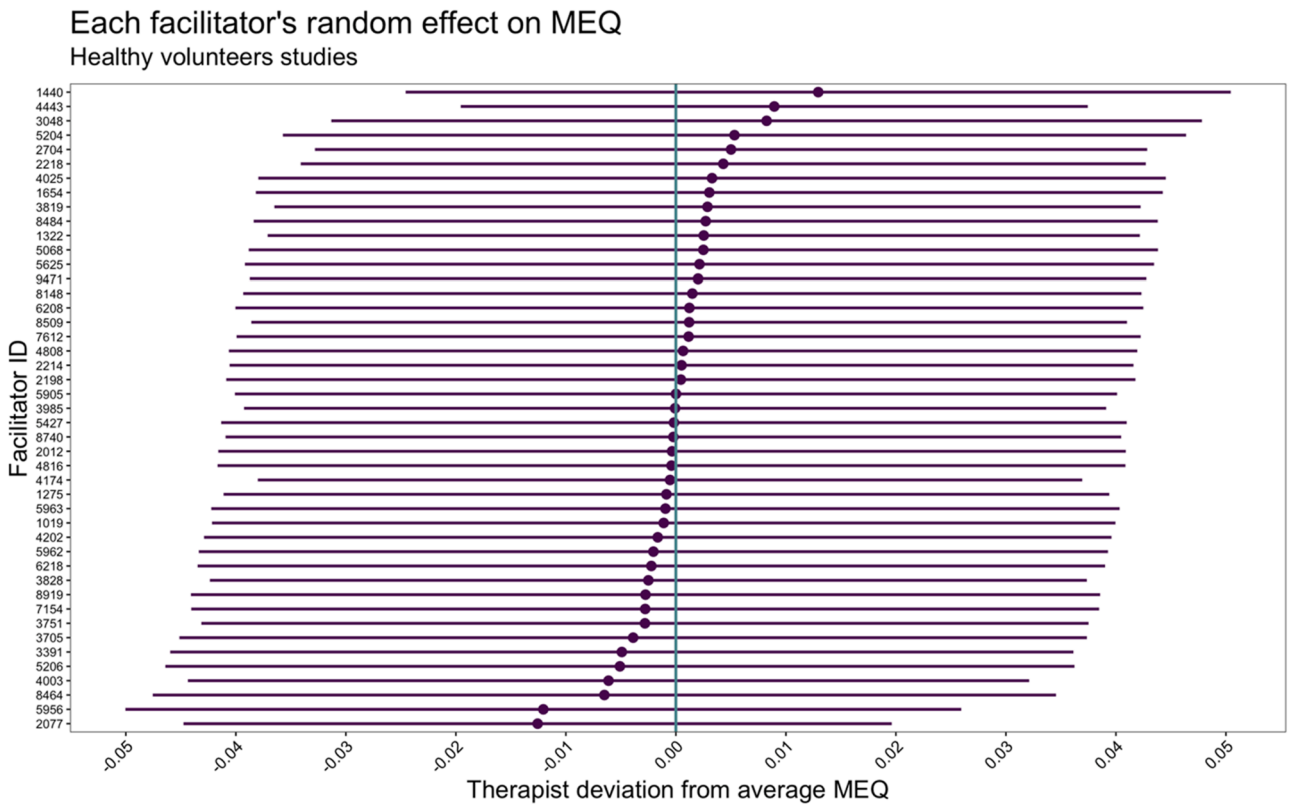

Fig. 2. Individual session facilitator random effects on MEQ scores in healthy volunteers studies. Each point depicts a de-identified facilitator's model-estimated deviation from the average MEQ (vertical line) accounting for covariates. Horizontal bars represent 95 % confidence intervals.

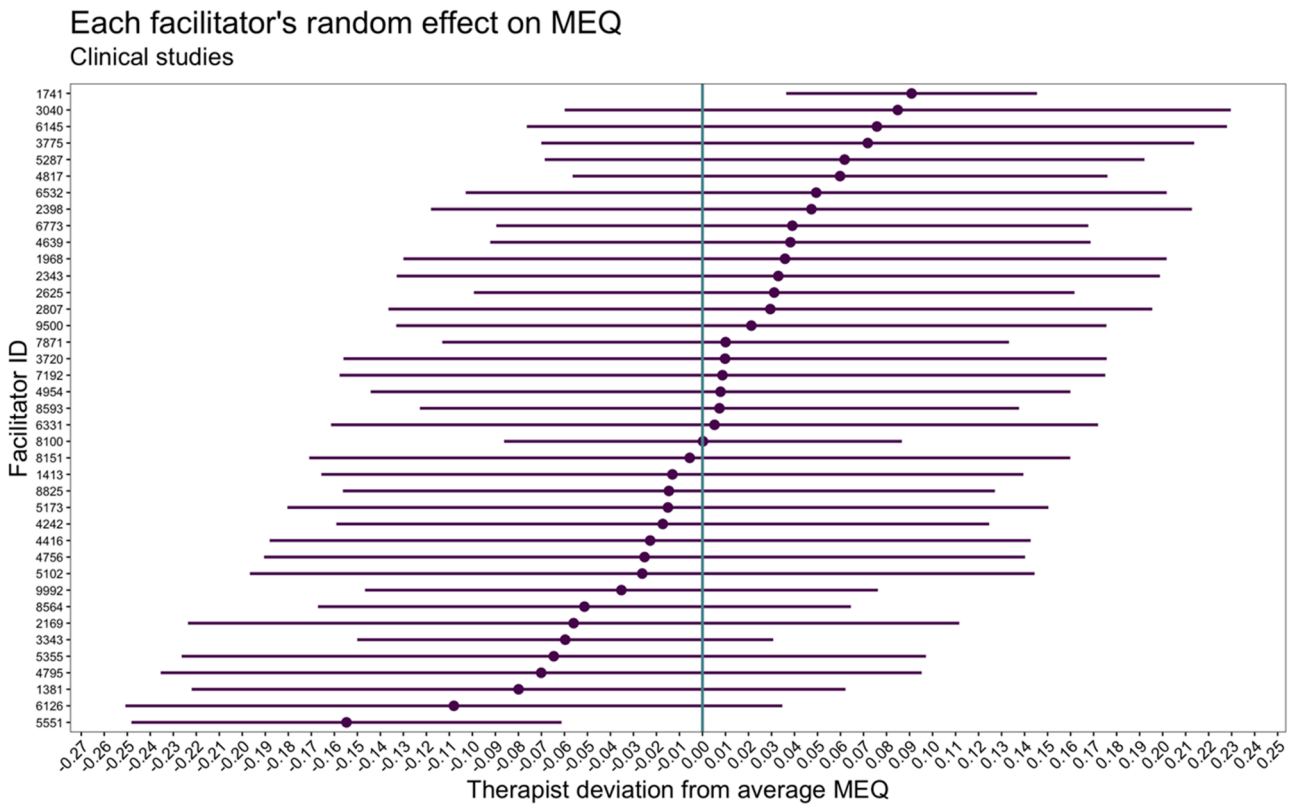

Fig. 3. Individual session facilitator random effects on MEQ scores in clinical studies. Each point depicts a de-identified facilitator's model-estimated deviation from the average MEQ (vertical line) accounting for covariates. Horizontal bars represent 95 % confidence intervals.

that might be like psychotherapy in these processes in healthy participants is necessarily minimal in comparison. As such, these results suggest it may be reasonable to allow trained facilitators without therapeutic licensure to facilitate psychedelic sessions in healthy volunteers, though in patient populations it appears the role of facilitator is not inconsequential and may require clinically trained facilitators, particularly when elements of psychotherapeutic interventions may be involved (Richard and Levine, 2025). It is ultimately unclear what explains this variation in facilitators. Psychotherapists' interpersonal skills can predict therapeutic outcomes in psychotherapy trials, and ability to form a working alliance is one of the most important of these skills (Wampold, 2021). This may also be true in psychedelic-assisted therapy and warrants further investigation. Regardless, the substantial facilitator effects we observed in clinical samples suggest that efforts to standardize and optimize facilitator training could meaningfully improve treatment consistency and efficacy.

4.1. Limitations

These analyses have several limitations. First, our assessment of participants' acute subjective effects focused on only MEQ scores, primarily due to variations in study outcomes and measures used in various trials. Although the MEQ is one of the most widely used methods for assessing psychedelics' acute subjective effects and documenting their positive correlations with therapeutic benefits (Garcia-Romeu et al., 2015; Griffiths et al., 2016; Johnson et al., 2014; Ross et al., 2016; Weiss et al., 2024), there are numerous other scales used to measure psychedelic experiences, all of which have limitations (Yaden et al., 2024). Some of these measures may display conceptual overlap and positively correlate with the MEQ, but more work is needed to rigorously characterize these relationships. Certain measures may be better suited to capture aspects of the psychedelic experience that could be more prone to variation between session facilitators (e.g., feelings of connection, including interpersonal connection, assessed via the Watts Connectedness Scale, (Watts et al., 2022); psychedelic-induced insights via the Psychological Insight Questionnaire, (Davis et al., 2021a); emotional breakthrough, which has also been found to predict therapeutic outcomes using the Emotional Breakthrough Inventory (Roseman et al., 2019); or novel measures to capture changes in distinct emotions (such as awe; e.g., Goldy et al., 2022), rather than broad affect (Goldy et al., 2024). Additionally, rigorous psychometric re-evaluations of existing scales may yield more precise measures: a recent revalidation of the 100-item Psychedelic Experience Scale (from which the MEQ was derived) identified additional factors capturing paradoxicality, connectedness, visual experience, and distressing experience (Stocker et al., 2024). Future research should compare facilitator-moderated variation in psychedelics' acute subjective effects among different measures.

We also note that our data come from a single academic research center; though, they span a period of >10 years and a variety of study protocols involving healthy or clinical samples, with the latter featuring different therapeutic approaches. Results might vary depending on the context and structure of psychedelic administration (e.g., retreat centers, other research centers, outpatient clinics, and other cultures). In particular, the setting in an academic research center is a highly controlled environment, requiring numerous safety precautions in place as dictated at the institutional and federal level. All facilitators in the present dataset received training at Johns Hopkins, had medical oversight from study physicians, adhered to a rapport-building approach, and dosing sessions were audio and video recorded for accountability and safety. Such procedures may constrain the degree to which facilitators differ when interacting with participants. It is likely that greater variation between facilitators might occur outside of clinical and/or research settings, where standards for facilitator training and how psychedelic drug administration sessions are conducted may differ. Indeed, an examination of therapist effects across psychological treatment care sectors in the United Kingdom found the largest therapist effects on therapeutic outcomes in primary care settings (8.4 %; i.e., first points of contact in U.K. health system), which can feature greater variation in therapist skill and training compared to university contexts (2.1 %; Firth et al., 2020).

Nevertheless, this work covers the largest dataset of psychedelic administration trials to date, spanning multiple studies, dozens of facilitators, and hundreds of participants—our findings account for differences between doses, study design, and facilitator experience. Future collaborative efforts between different institutions and non-academic settings will help address the robustness of our findings and improve generalizability.

Another limitation of this work is that these data concern only oral psilocybin. Depending on their subjective effects profile, other psychedelics beyond psilocybin (e.g., DMT, 5-MeO-DMT, LSD) and other routes of administration with more intense or rapid onset (e.g. intravenous, intranasal, or vaporized) might be differentially susceptible to facilitator influence. For example, insofar as one's social context can influence visual phenomena (Larøi et al., 2014), compounds that are associated with highly visual (e.g. DMT; Davis et al., 2020; Lawrence et al., 2022; Timmermann et al., 2019) or entactogenic effects (Wardle and de Wit, 2014), might be especially prone to variation in subjective effects due to facilitator factors. Additionally, drugs or routes of administration with faster onset of effects may elicit greater psychological challenge and/or disorientation, further shifting the involvement of and engagement of skill by the facilitator. Preliminary work suggests some classic psychedelics' subjective effects might be similar—double-blind, randomized, placebo-controlled, crossover studies found minimal differences in acute subjective effects among psilocybin, LSD, and mescaline (Holze et al., 2022; Ley et al., 2023)—but more comparative studies are needed to determine similarities between different psychedelics' subjective effects.

Finally, our data do not include all conditions that may be responsive to psychedelic-assisted interventions. Given prior work finding that larger therapist effects are positively associated with the initial severity of an individual's diagnosis (Johns et al., 2019), it is possible that there might be greater variation in clinical samples not present in our data. Similarly, the degree to which subjective effects differ among facilitators may vary when examining psychedelics' risks (Carbonaro et al., 2016; Goldy et al., 2025; Hinkle et al., 2024; Simonsson et al., 2023) and depending on whether psychedelics are administered with psychotherapy or with minimal psychological support (Goodwin et al., 2024; Gründer et al., 2024; Richard and Levine, 2025). As the psychedelic treatment landscape continues to expand, it will be important to consider whether certain indications might respond differently to facilitator influence during a psychedelic experience.

4.2. Conclusion

As psychedelic-assisted therapies advance toward clinical implementation, understanding sources of treatment variability is essential for optimizing outcomes at scale. In the largest investigation of facilitator effects on psychedelic treatments to date—spanning decades of studies, hundreds of participants, and dozens of facilitators at a major academic medical institution—we found that facilitators meaningfully impact experiences in clinical samples, but not in healthy ones, with effect sizes comparable to or exceeding those in traditional psychotherapy. These findings advance our understanding of the sources of variability in psychedelics' subjective effects and therapeutic benefits, and they inform efforts to optimize facilitator training protocols in clinical settings, suggesting a need for enhancing the consistency of psychotherapy delivery across facilitators to increase the reliability of psychedelic-assisted treatments' efficacy.

As psychedelic's acute subjective effects predict treatment outcomes, understanding where and when facilitator effects may matter most remains a critical direction for future research. Together, our findings

provide a foundation for future studies aiming to disentangle the roles of facilitator, context, and individual differences in shaping therapeutic outcomes.

Author contributions

SPG, NDS, SNH, BAB, SMN designed and performed the research. All authors wrote the paper.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Supplementary materials

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References

Barrett, F.S., Johnson, M.W., Griffiths, R.R., 2015. Validation of the revised mystical experience questionnaire in experimental sessions with psilocybin. J. Psychopharmacol. 29 (11), 1182–1190. SAGE Publications Ltd STM.

Barrett, F.S., Doss, M.K., Sepeda, N.D., et al., 2020. Emotions and brain function are altered up to one month after a single high dose of psilocybin. Sci. Rep. 10 (1), 2214. Nature Publishing Group.

Bates, D., Mächler, M., Bolker, B., et al., 2015. Fitting linear mixed-effects models using lme4. J. Stat. Softw. 67, 1–48.

Bogenschutz, M.P., Forcehimes, A.A., Pommy, J.A., et al., 2015. Psilocybin-assisted treatment for alcohol dependence: a proof-of-concept study. J. Psychopharmacol. 29 (3), 289–299. SAGE Publications Ltd STM.

Bogenschutz, M.P., Ross, S., Bhatt, S., 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 79 (10), 953.

Browne, W.J., Goldstein, H., Rasbash, J., 2001. Multiple membership multiple classification (MMMC) models. Stat. Model. 1 (2), 103–124. SAGE Publications India.

Carbonaro, T.M., Bradstreet, M.P., Barrett, F.S., et al., 2016. Survey study of challenging experiences after ingesting psilocybin mushrooms: acute and enduring positive and negative consequences. J. Psychopharmacol. 30 (12), 1268–1278. SAGE Publications Ltd STM.

Carbonaro, T.M., Johnson, M.W., Hurwitz, E., et al., 2018. Double-blind comparison of the two hallucinogens psilocybin and dextromethorphan: similarities and differences in subjective experiences. Psychopharmacology 235 (2), 521–534.

Carhart-Harris, R.L., Bolstridge, M., Rucker, J., et al., 2016. Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. Lancet Psychiatry 3 (7), 619–627. Elsevier.

Carhart-Harris, R., Giribaldi, B., Watts, R., et al., 2021. Trial of psilocybin versus Escitalopram for depression. N. Engl. J. Med. 384 (15), 1402–1411. Massachusetts Medical Society.

D'Souza, D.C., Syed, S.A., Flynn, L.T., et al., 2022. Exploratory study of the dose-related safety, tolerability, and efficacy of dimethyltryptamine (DMT) in healthy volunteers and major depressive disorder. Neuropsychopharmacology 47 (10), 1854–1862.

Davis, A.K., Clifton, J.M., Weaver, E.G., et al., 2020. Survey of entity encounter experiences occasioned by inhaled N,N-dimethyltryptamine: phenomenology, interpretation, and enduring effects. J. Psychopharmacol. 34 (9), 1008–1020. SAGE Publications Ltd STM.

Davis, A.K., Barrett Frederick, S., So, S., et al., 2021. Development of the psychological insight questionnaire among a sample of people who have consumed psilocybin or LSD. J. Psychopharmacol. 35 (4), 437–446.

Davis, A.K., Barrett Frederick, S., May, D.G., et al., 2021. Effects of psilocybin-assisted therapy on major depressive disorder: a randomized clinical trial. JAMA Psychiatry 78 (5), 481–489.

de Beer, F., Koops, S., Schoevers, R.A., et al., 2024. Psychiatrists effect on positive symptom severity and daily functioning during pharmacotherapy for first-episode psychosis patients. Sci. Rep. 14 (1), 22871. Nature Publishing Group.

Ehrenkranz, R., Sepeda, N.D., Yaden, D.B., Barrett, F.S. (*in prep*). Psilocybin enhances the experience and practice of meditation in long-term meditators.

Firth, N., Saxon, D., Stiles, W.B., et al., 2020. Therapist effects vary significantly across psychological treatment care sectors. Clin. Psychol. Psychother. 27 (5), 770–778.

Garcia-Romeu, A., Griffiths, R.R., Johnson, M.W., 2015. Psilocybin-occasioned mystical experiences in the treatment of tobacco addiction. Curr. Drug Abuse Rev. 7 (3), 157–164.

Goldy, S.P., Jones, N.M., Piff, P.K., 2022. The social effects of an awesome solar eclipse. Psychol. Sci. 33 (9), 1452–1462. SAGE Publications Inc.

Goldy, S.P., Hendricks, P.S., Keltner, D., et al., 2024. Considering distinct positive emotions in psychedelic science. Int. Rev. Psychiatry 1–12.

Goldy, S.P., Du, B.A., Rohde, J.S., et al., 2025. Psychedelic risks and benefits: a cross-sectional survey study. J. Psychopharmacol. https://doi.org/10.1177/02698811241292951. SAGE PublicationsSage UK: London, England. Epub ahead of print 29 November 2025.

Goodwin, G.M., Aaronson Scott, T., Alvarez, O., et al., 2022. Single-dose psilocybin for a treatment-resistant episode of major depression. N. Engl. J. Med. 387 (18), 1637–1648. Massachusetts Medical Society.

Goodwin, G.M., Malievskaia, E., Fonzo, G.A., et al., 2024. Must psilocybin always 'assist psychotherapy'? Am. J. Psychiatry 181 (1), 20–25.

Goodwin, G.M., Aaronson, S.T., Alvarez, O., et al., 2025. The role of the psychedelic experience in psilocybin treatment for treatment-resistant depression. J. Affect. Disord. 372, 523–532.

Gründer, G., Brand, M., Mertens, L.J., et al., 2024. Treatment with psychedelics is psychotherapy: beyond reductionism. Lancet Psychiatry 11 (3), 231–236.

Griffiths, R.R., Richards, W.A., McCann, U., et al., 2006. Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. Psychopharmacology 187 (3), 268–283.

Griffiths, R., Richards, W., Johnson, M., et al., 2008. Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. J. Psychopharmacol. 22 (6), 621–632. SAGE Publications Ltd STM.

Griffiths, R.R., Johnson, M.W., Richards, W.A., et al., 2011. Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects. Psychopharmacology 218 (4), 649–665.

Griffiths, R.R., Johnson, M.W., Carducci, M.A., et al., 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 (12), 1181–1197. SAGE Publications Ltd STM.

Griffiths, R.R., Johnson, M.W., Richards, W.A., et al., 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 (1), 49–69. SAGE Publications Ltd STM.

Grob, C.S., Danforth, A.L., Chopra, G.S., et al., 2011. Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. Arch. Gen. Psychiatry 68 (1), 71–78.

Gukasyan, N., Davis, A.K., Barrett, F.S., et al., 2022. Efficacy and safety of psilocybin-assisted treatment for major depressive disorder: prospective 12-month follow-up. J. Psychopharmacol. 36 (2), 151–158.

Gukasyan N., Schreyer C., Cosimano M.P., et al. (in prep) Psilocybin-assisted therapy for Anorexia Nervosa: a multi-session open-label pilot study. Epub ahead of print in prep.

Hinkle, J., Graziosi, M., Nayak, S., et al., 2024. Adverse events in studies of classic psychedelics: a systematic review and meta-analysis. JAMA Psychiatry. https://doi.org/10.1001/jamapsychiatry.2024.2546. Epub ahead of print 4 September 2024.
Holze, F., Ley, L., Müller, F., et al., 2022. Direct comparison of the acute effects of lysergic acid diethylamide and psilocybin in a double-blind placebo-controlled study in healthy subjects. Neuropsychopharmacology 47 (6), 1180–1187. Nature Publishing Group.
Johns, R.G., Barkham, M., Kellett, S., et al., 2019. A systematic review of therapist effects: a critical narrative update and refinement to Baldwin and Imel's (2013) review. Clin. Psychol. Rev. 67, 78–93.
Johnson, M.W., Garcia-Romeu, A., Cosimano, M.P., et al., 2014. Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction. J. Psychopharmacol. 28 (11), 983–992.
Johnson, M.W., Garcia-Romeu, A., Griffiths, R.R., 2017. Long-term follow-up of psilocybin-facilitated smoking cessation. Am. J. Drug Alcohol Abuse 43 (1), 55–60. Taylor & Francis.
Larøi, F., Luhrmann, T.M., Bell, V., et al., 2014. Culture and hallucinations: overview and Future directions. Schizophr. Bull. 40 (Suppl 4), S213–S220.
Lawrence, D.W., Carhart-Harris, R., Griffiths, R., et al., 2022. Phenomenology and content of the inhaled N, N-dimethyltryptamine (N, N-DMT) experience. Sci. Rep. 12 (1), 8562. Nature Publishing Group.
Levin, A.W., Lancelotta, R., Sepeda, N.D., et al., 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.
Ley, L., Holze, F., Arikci, D., et al., 2023. Comparative acute effects of mescaline, lysergic acid diethylamide, and psilocybin in a randomized, double-blind, placebo-controlled cross-over study in healthy participants. Neuropsychopharmacology 48 (11), 1659–1667. Nature Publishing Group.
Ludwig, A., Levine, J., Stark, L., et al., 1969. A clinical study of LSD treatment in alcoholism. Am. J. Psychiatry 126 (1), 59–69. American Psychiatric Publishing.
Maclean, K.A., Leoutsakos, J.-M.S., Johnson, M.W., et al., 2012. Factor analysis of the mystical experience questionnaire: a study of experiences occasioned by the hallucinogen psilocybin. J. Sci. Study Relig. 51 (4), 721–737.
McKay, K.M., Imel, Z.E., Wampold, B.E., 2006. Psychiatrist effects in the psychopharmacological treatment of depression. J. Affect. Disord. 92 (2), 287–290.
Murphy, R., Kettner, H., Zeifman, R., et al., 2022. Therapeutic Alliance and Rapport modulate responses to psilocybin assisted therapy for depression. Front. Pharmacol. 12. Frontiers.
Muttoni, S., Ardissino, M., John, C., 2019. Classical psychedelics for the treatment of depression and anxiety: a systematic review. J. Affect. Disord. 258, 11–24.
Nayak, S., Johnson, M.W., 2021. Psychedelics and psychotherapy. Pharmacopsychiatry 54 (4), 167–175.
Olson, D.E., 2020. The subjective effects of psychedelics may not Be necessary for their enduring therapeutic effects. ACS Pharmacol. Transl. Sci. 4 (2), 563–567.
Raison, C.L., Sanacora, G., Woolley, J., et al., 2023. Single-dose psilocybin treatment for major depressive disorder: a randomized clinical trial. JAMA 330 (9), 843–853.
Reckweg, J., Leeuwen, C., Henquet, C., et al., 2023. A phase 1/2 trial to assess safety and efficacy of a vaporized 5-methoxy-N,N-dimethyltryptamine formulation (GH001) in patients with treatment-resistant depression. Front. Psychiatry 14.
Richard, J., Levine, M., 2025. What is psychological support in the context of psychedelic clinical trials? Psychedelic Med. https://doi.org/10.1089/psymed.2024.0026. Mary Ann Liebert, Inc., publishers. Epub ahead of print 7 February 2025.
Rieser, N.M., Bitar, R., Halm, S., et al., 2025. Psilocybin-assisted therapy for relapse prevention in alcohol use disorder: a phase 2 randomized clinical trial. eClinicalMedicine 82. Elsevier.
Roseman, L., Demetriou, L., Wall, M.B., et al., 2018. Increased amygdala responses to emotional faces after psilocybin for treatment-resistant depression. Neuropharmacology 142, 263–269. Psychedelics: New Doors, Altered Perceptions.
Roseman, L., Nutt, D.J., Carhart-Harris, R.L., 2018. Quality of acute psychedelic experience predicts therapeutic efficacy of psilocybin for treatment-resistant depression. Front. Pharmacol. 8. Frontiers.
Roseman, L., Haijen, E., Idialu-Ikato, K., et al., 2019. Emotional breakthrough and psychedelics: validation of the Emotional breakthrough inventory. J. Psychopharmacol. 33 (9), 1076–1087.
Ross, S., Bossis, A., Guss, J., Agin-Liebes, G., Malone, T., Cohen, B., Mennenga Sarah, E., et al., 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 (12), 1165–1180. SAGE Publications Ltd STM.
Ross, S., Bossis, A., Guss, J., Agin-Liebes, G., Malone, T., Cohen, B., Mennenga Sarah, E., et al., 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 (12), 1165–1180.
Rotz, R.v., Schindowski, E.M., Jungwirth, J., et al., 2023. Single-dose psilocybin-assisted therapy in major depressive disorder: a placebo-controlled, double-blind, randomised clinical trial. eClinicalMedicine 56. Elsevier.
Saxon, D., Firth, N., Barkham, M., 2017. The relationship between therapist effects and therapy delivery factors: therapy modality, dosage, and non-completion. Adm. Policy Ment. Health 44 (5), 705–715.
Simonsson, O., Hendricks, P.S., Chambers, R., et al., 2023. Prevalence and associations of challenging, difficult or distressing experiences using classic psychedelics. J. Affect. Disord. 326, 105–110.
Stocker, K., Hartmann, M., Ley, L., et al., 2024. The revival of the psychedelic experience scale: revealing its extended-mystical, visual, and distressing experiential spectrum with LSD and psilocybin studies. J. Psychopharmacol. 38 (1), 80–100. SAGE Publications Ltd STM.
Timmermann, C., Roseman, L., Schartner, M., et al., 2019. Neural correlates of the DMT experience assessed with multivariate EEG. Sci. Rep. 9 (1), 16324. Nature Publishing Group.
U.S. Food and Drug Administration, 2023. Psychedelic drugs: considerations for clinical investigations. Available at https://www.fda.gov/media/169694/download.
van Paridon, J., Bolker, B., Alday, P., 2025. lmerMultiMember: multiple membership random effects. R. Available at https://github.com/jvparidon/lmerMultiMember. accessed 4 August 2025.
Wampold, B.E., 2021. Healing in a social context: the importance of clinician and patient relationship. Front. Pain Res. 2, 684768.
Wardle, M.C., de Wit, H., 2014. MDMA alters emotional processing and facilitates positive social interaction. Psychopharmacology 231 (21), 4219–4229.
Watts, R., Kettner, H., Geerts, D., et al., 2022. The Watts connectedness scale: a new scale for measuring a sense of connectedness to self, others, and world. Psychopharmacology 239 (11), 3461–3483.
Weiss, B., Roseman, L., Giribaldi, B., et al., 2024. Unique psychological mechanisms underlying psilocybin therapy versus Escitalopram treatment in the treatment of major depressive disorder. Int. J. Ment. Health Addict. https://doi.org/10.1007/s11469-024-01253-9. Epub ahead of print 7 March 2024.
Yaden, D.B., Griffiths, R.R., 2021. The subjective effects of psychedelics are necessary for their enduring therapeutic effects. ACS Pharmacol. Transl. Sci. 4 (2), 568–572.
Yaden, D.B., Goldy, S.P., Weiss, B., et al., 2024. Clinically relevant acute subjective effects of psychedelics beyond mystical experience. Nat. Rev. Psychol. 1–16. Nature Publishing Group.