Beyond dose. Perceived group support as a person-level predictor of emotional breakthrough and psychological insight during DMT–harmine administration

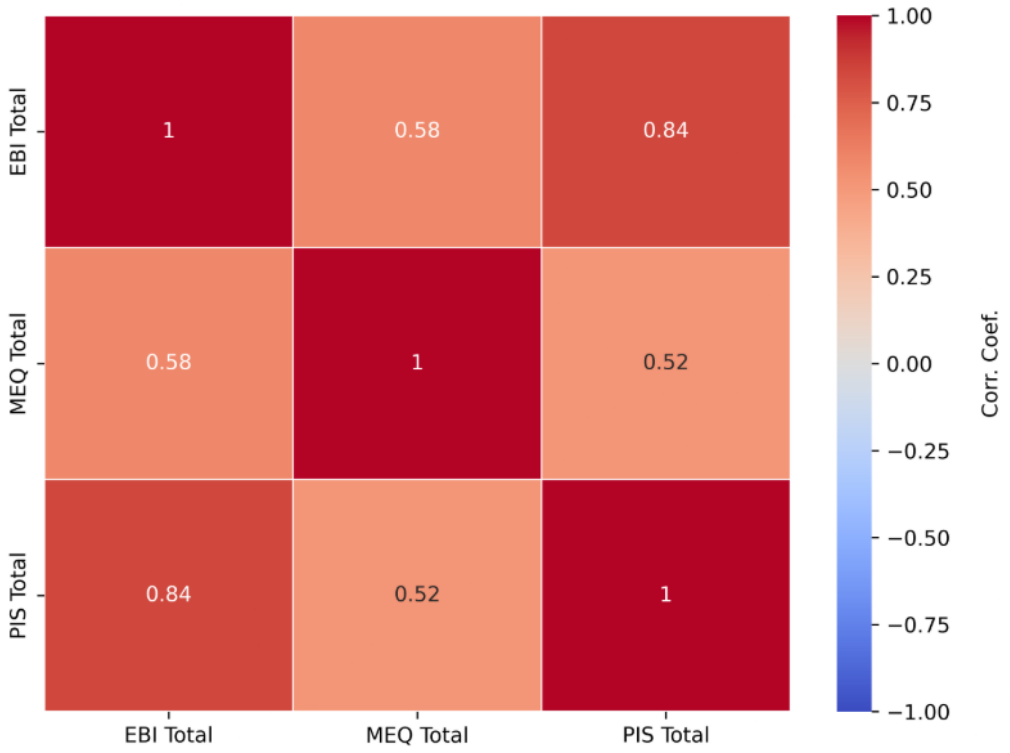


Figure S1. Intercorrelations among the three subjective outcome measures. Pearson correlation coefficients among total scores on the Emotional Breakthrough Inventory (EBI), Mystical Experience Questionnaire (MEQ), and Psychological Insight Scale (PIS), computed at the observation level across all 96 dosing sessions (16 participants × 6 sessions). Cell shading indicates the strength and direction of each correlation (see color bar). EBI and PIS were the most strongly correlated pair (r = 0.84), whereas MEQ was more moderately correlated with both EBI (r = 0.58) and PIS (r = 0.52).

Table S1: Participant demographics

Participants	**N = 16**
Age in years (mean (SD))	35 (5.4)
Sex (frequency (%))	
male	9 (56%)
female	7 (44%)
Gender (frequency (%))	
man	9 (56%)
woman	6 (38%)
other	1 (6%)
Weight in kg (mean (SD))	73.7 (12.7)
BMI (mean (SD))	22.9 (2.1)
Highest degree (frequency (%))	
high school degree	3 (19%)
university degree	11 (69%)
other school degree	1 (6%)
Years of education (mean (SD))	16.8 (3.3)
Ethnicity (frequency (%))	
White	16 (100%)
Previous psychedelic experiences (frequency (%))	
1 – 5	1 (6%)
6 – 10	7 (44%)
11 – 20	5 (31%)
20 – 50	1 (6%)
> 50	2 (13%)

Note: Values are presented either as mean + standard deviation or as frequency.

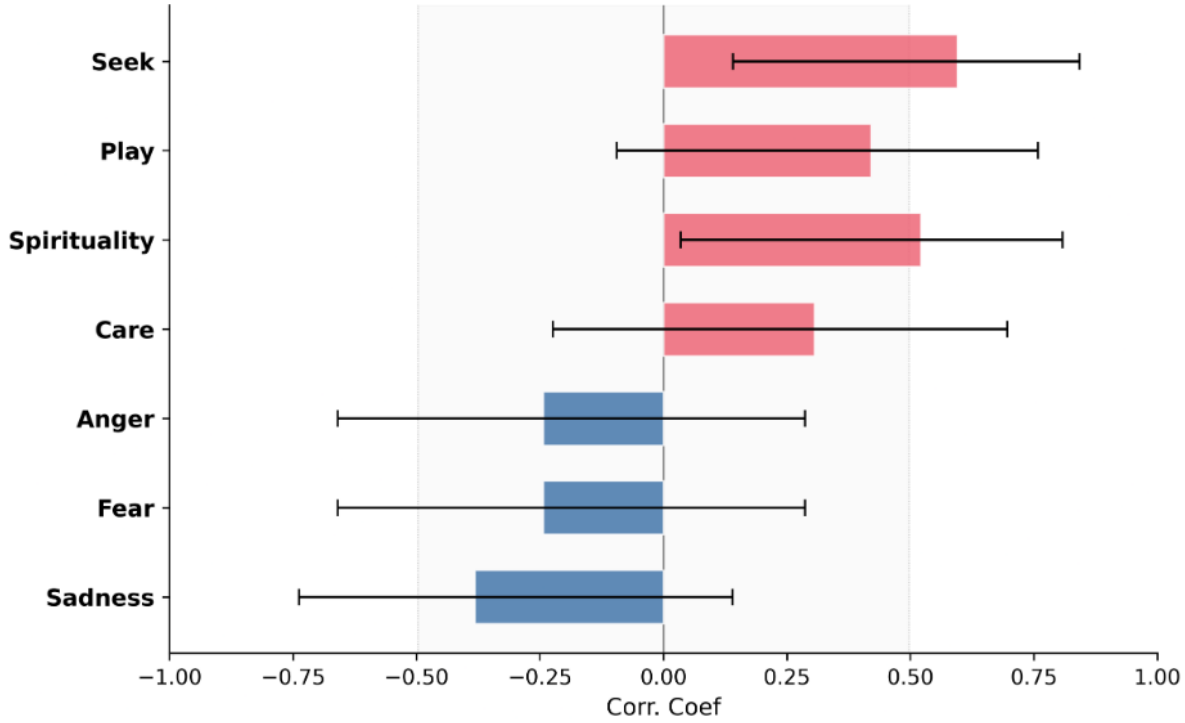


Figure S2. Per-dimension correlations between baseline ANPS dimensions and perceived group support. Pearson correlation coefficients between each of the seven ANPS dimensions and participant-mean PGS trait score (N = 16). Error bars indicate 95% confidence intervals. Approach-related dimensions (Seeking, Play, Care) and Spirituality show positive correlations, whereas withdrawal-related dimensions (Fear, Sadness, Anger) show negative correlations. Seeking (r = 0.60) and Spirituality (r = 0.52) reached statistical significance at α = .05.

Table S2. Model fit and comparison statistics.

Model	Metric	EBI	PIS	MEQ
Baseline (dose only)	AIC	864.0	886.5	918.1
	ICC	.44	.47	.36
Combined model	ΔAIC vs baseline	−1.1	−1.3	−0.9
	Between-subj. variance absorbed	24.9%	19.3%	16.0%
	LR vs baseline	$\chi^2(1) = 0.93$, $p = .33$	$\chi^2(1) = 0.68$, $p = .41$	$\chi^2(1) = 1.11$, $p = .29$
	ΔAIC vs baseline	+11.0	+9.8	+0.5

Decomposed model	Between-subj. variance absorbed	71.9%	66.8%	31.2%
	LR vs baseline (omnibus)	$\chi^2(2) = 14.98$, $p < .001$	$\chi^2(2) = 13.77$, $p = .001$	$\chi^2(2) = 4.51$, $p = .105$
Between-subject model	ΔAIC vs baseline	+12.6	+11.3	+2.5
	Between-subj. variance absorbed	72.5%	67.3%	31.2%
	LR vs baseline	$\chi^2(1) = 14.59$, $p < .001$	$\chi^2(1) = 13.34$, $p < .001$	$\chi^2(1) = 4.51$, $p = .03$
	LR vs decomposed (parsimony check)	$\chi^2(1) = 0.39$, $p = .53$	$\chi^2(1) = 0.44$, $p = .51$	$\chi^2(1) = 0.00$, $p = .99$

Note: AIC = Akaike Information Criterion; ICC = intraclass correlation coefficient from the baseline (dose-only) model, representing the proportion of outcome variance attributable to stable between-subject differences after accounting for dose. ΔAIC = change in AIC relative to baseline, where positive values favor the more complex model. Between-subject variance absorbed = percentage reduction in the random intercept variance ($\sigma^2 u$) relative to baseline, quantifying how much of the stable between-subject variability in outcomes is accounted for by perceived group support. LR = likelihood ratio test. The omnibus LR test of the decomposed model vs baseline (2 df) is the primary inferential test of the scientific question. The parsimony check (bottom row) confirms that removing the within-subject component does not significantly worsen fit, justifying the between-subject model as the primary model reported in Panel A. All models estimated with maximum likelihood (ML).

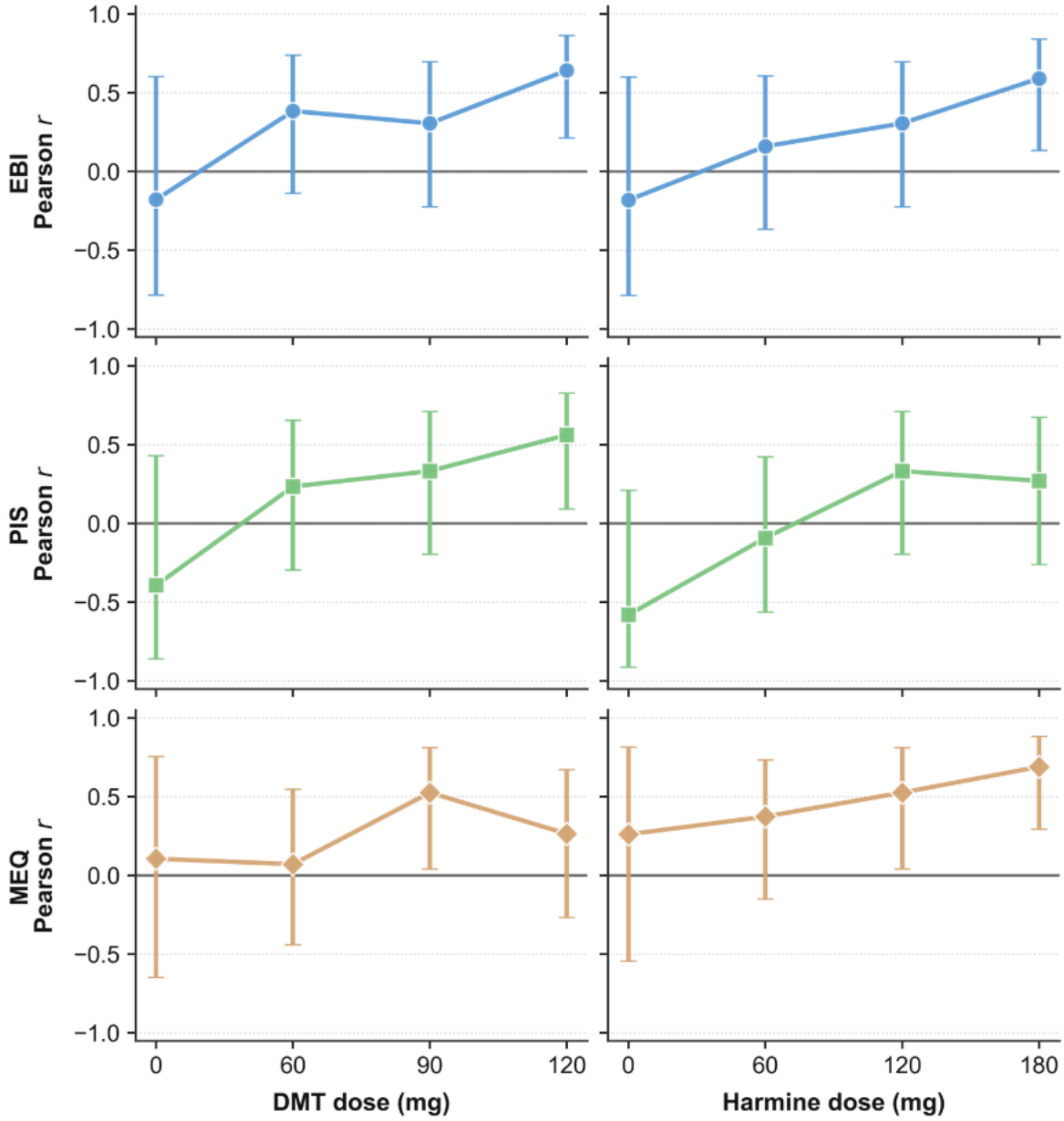


Figure S3. Dose-dependence of the association between approach-oriented personality (AWI⁺) and session-level subjective outcomes. Each panel plots the Pearson correlation between participants' extended Approach-Withdrawal Index (AWI⁺) and session-level outcome scores, computed separately at each dose level along a titration axis. Rows correspond to the three outcome measures (EBI, top; PIS, middle; MEQ, bottom). Left column: DMT dose escalation with harmine held at 120 mg. Right column: harmine dose escalation with DMT held at 90 mg. Points show the correlation coefficient at each dose level; error bars indicate 95% confidence intervals (Fisher z-transformation). N ≈ 16 per active dose level; the zero-dose endpoints (0 mg DMT; 0 mg harmine) comprise N ≈ 8. For EBI and PIS, the correlation is near zero or negative at the lowest doses and strengthens with escalating dose along both axes, reaching its most positive values at the highest dose conditions (120 mg DMT; 180 mg harmine). For MEQ, correlations are weaker and less systematic.

Table S3. Baseline ANPS dimension scores in participants with higher versus lower trait-level perceived group support.

ANPS dimension	Low PGS group, M (SD)	High PGS group, M (SD)	Cohen's *d*
Approach-related			
Seeking	31.88 (3.27)	35.75 (3.11)	1.22
Play	32.25 (3.28)	36.00 (2.88)	1.21
Care	33.38 (3.62)	34.38 (4.21)	0.26
Spirituality[a]	25.50 (6.57)	29.63 (4.47)	0.73
Withdrawal-related			
Fear	25.13 (6.33)	21.00 (4.24)	−0.77
Sadness	27.25 (5.57)	22.13 (4.16)	−1.04
Anger	24.50 (2.83)	23.13 (7.94)	−0.23

Note: Participants were split at the median of their participant-mean perceived group support (PGS) rating across the six dosing sessions (n = 8 per group). Values are means (SDs) of raw ANPS dimension scores; Figure 5A displays the same profiles z-standardized. Cohen's *d* = standardized mean difference (higher-PGS minus lower-PGS group); positive values indicate higher scores in the higher-PGS group. ANPS = Affective Neuroscience Personality Scales. [a]Spirituality is not part of the approach component of the original Approach–Withdrawal Index (AWI; approach = Seeking, Play, Care; withdrawal = Fear, Sadness, Anger) but is included as an approach dimension in the extended index (AWI+).

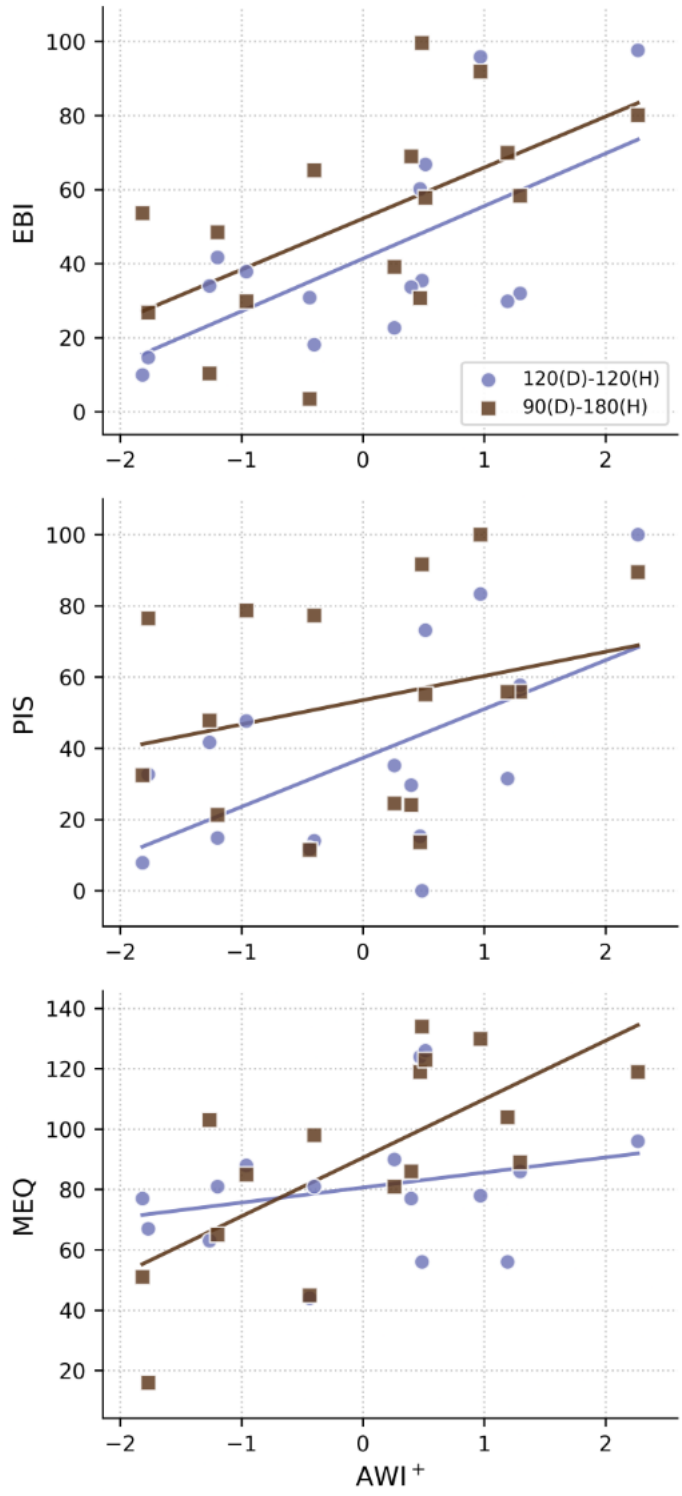


Figure S4. Baseline affective personality (AWI⁺) and session-level subjective outcomes at the two highest-dose conditions. Session-level EBI (top), PIS (middle), and MEQ (bottom) scores plotted against the extended Approach-Withdrawal Index (AWI⁺) for the two escalation maxima: 120(D)-120(H) (top of the DMT-escalation series; blue circles) and 90(D)-180(H) (top of the harmine-escalation series; brown squares). AWI⁺ is defined as mean z(Seeking, Play, Care, Spirituality) minus mean z(Fear, Sadness, Anger). Each point represents one participant in the corresponding dosing session (n = 16 per condition); solid lines show ordinary least-squares regression fits for each condition. For PIS, the correlation was positive in both cases but stronger in the DMT-escalation maximum (120(D)-120(H): r = 0.56, 95% CI [0.09, 0.83]; 90(D)-180(H): r =

0.27, 95% CI [-0.26, 0.68]). For MEQ, the pattern was reversed, with the larger correlation in the harmine-escalation maximum (90(D)-180(H): r = 0.69, 95% CI [0.30, 0.88]; 120(D)-120(H): r = 0.26, 95% CI [-0.27, 0.67]). All correlations were based on n = 16, with 95% confidence intervals computed via Fisher z-transformation.



Picture S1. Setup of the treatment room.

Beyond dose. Perceived group support as a person-level predictor of emotional breakthrough and psychological insight during DMT–harmine administration.

Supplement 1: Study Setting on dosing days

The dosing sessions were conducted in a spacious room decorated like a comfortable living room and located in a quiet and detached space at the University Hospital of Psychiatry Zurich. The setup included light installations, plants, carpets on the floor, and bright-colored cloths hung up on the wall. Lighting of the room was adjustable; bright-white ceiling lighting was turned off during the time of acute substance effects, and indirect lighting was used instead to create a warm and visually less stimulating atmosphere. One of three standardized playlists of background music was randomly played throughout the study day. Participants were lying comfortably on a mattress for most of the sessions. They were provided with blankets, pillows, and eye shades. Dosing sessions were held in a group setting with three to four participants being tested simultaneously. However, one dosing session of pilot day 4 and one of pilot day 5 were performed with only two participants due to logistical reasons. Each participant had their individual sitter, who stayed with them throughout the whole study day. At least one study physician and 4–6 experimenters, all with basic formal training, were always present in the room during the study days. They monitored participants for adverse effects and vital signs and offered emotional/psychological support if needed. A board-certified psychotherapist or psychiatrist was either present during dosing sessions or on-call duty. Participants were invited to focus on their own process and internal experience. We provided nature themed picture books and arts material for creative expression. Study days began at 8:30 AM and ended at around 7:30 PM, after which participants were discharged upon medical evaluation through a physician. Upon arrival at the study site, a drug urine test (Drug-Screen Multi 12Q Test, Nal von Minden GmbH, Regensburg, Germany), an alcohol breath test (Lion Alcolmeter® 500, Lion Laboratories Limited, Wales, UK), and a pregnancy test for women, were carried out to verify drug abstinence and exclude pregnancy. The participants then underwent baseline measurements. For the duration of the 9 hours of a study day, if possible, but always for the time of acute drug effects, participants stayed in the treatment

room. They could use the bathroom, located roughly 10m away from the experiment room, accompanied by their sitter. If necessary and advised, after the acute effects subsided, a participant could individually leave the experiment room to walk in nature on campus of the psychiatric hospital, always accompanied by one experimenter. Participants undertook each study day in a fasted state and were provided with a light lunch from 3:00 PM onwards, during which they were also invited to share about their experience from the given study day. Participants were asked not to drink alcohol the day before study days and not to consume caffeinated products on study days. There were no separate formal preparation or integration session included in the study design. Each study day started with an informal "check-in", with each person in the treatment room (including study staff) getting the space to share about their inner emotional/ psychological state or their intention for today's session. This was followed by a guided mindfulness practice. Participants were informed that they could seek support or advise from study physicians or therapist or contact the study team, even after the final active study day.

Beyond dose. Perceived group support as a person-level predictor of emotional breakthrough and psychological insight during DMT–harmine administration.

Supplement 2: Eligibility criteria for participating in the trial

Inclusion criteria

- Age between 25–45 years
- Willing and capable to give informed consent for the participation in the study after it has been thoroughly explained
- Willing to refrain from drinking alcohol one day before testing days and caffeinated drinks at the testing days and from consuming psychoactive substances or other medications for 2 weeks before testing days and for the duration of the study
- Already experienced with psychedelic substances (at least 5 prior experiences - microdoses do not count)
- Able and willing to comply with all study requirements
- Informed consent form was signed
- Good knowledge of the German language
- Participant informs study physicians / project scientists about simultaneous treatment or therapy with other physicians and about current intake of psychotropic substances or medication
- Women of childbearing potential are required to use effective, established contraception, such as oral, injected or implanted hormonal methods of contraception, placement of an intrauterine device (IUD) or intrauterine system (IUS), barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository

Exclusion Criteria

- Previous significant adverse response to a hallucinogenic drug
- Participation in another study where pharmaceutical compounds will be given
- Presence of Axis I affective, anxiety, or dissociative disorders
- Present or antecedent diagnosis of bipolar disorder (I, II, not otherwise specified), schizophrenia, schizoaffective disorder, psychosis, or other disorders from the psychotic spectrum
- First-degree relatives with present or antecedent schizophrenia, schizoaffective disorder, or bipolar disorder type I
- History of head trauma, seizures, cancer, or cerebrovascular accidents
- Recent cardiac or brain surgery
- Current addiction of medication or psychotropic substances (including nicotine addiction) according to SCID I criteria
- Presence of major internal or neurological disorders (including sepsis, pheochromocytoma, thyrotoxicosis, drug-induced fibrosis, familiar or basilar artery migraine)

- Cardiovascular disease (hypertonia, coronary artery disease, heart insufficiency, myocardical infarction, coronary spastic angina)
- Peripheral vascular disease (thromboangiitis obliterans, luetic arteritis, severe arteriosclerosis, thrombophlebitis, Raynaud's disease)
- Cerebrovascular disease (e.g. stroke, intracranial bleeding / hemorrhage, intracranial aneurysm)
- Serious abnormalities in ECG or blood count/chemistry
- Liver or renal or pulmonary disease
- Pregnant or breastfeeding women (a urine pregnancy test will be done for all women capable of bearing children), occurrence of premenstrual dysphoric disorder (PMDD)
- Current use of medications with significant interaction potential with MAOI (e.g. antidepressants, antipsychotics, psychostimulants, dopaminergic/serotonergic agents, anticonvulsants)
- high risk of adverse emotional or behavioral reaction based on investigator's clinical evaluation (e.g. evidence of serious personality disorder, serious current stressors, lack of social support)

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Supplement 3: Description of Psychometric Instruments

Below are brief descriptions of the three retrospective self-report instruments used to assess subjective psychedelic effects on the six dosing days.

Emotional Breakthrough Inventory (EBI)

Construct assessed	Degree of emotional release, confrontation, and resolution ('emotional breakthrough') experienced during a psychedelic session
Number of items	6
Item response format	Visual analogue scale (VAS), 0-100 ("no, not more than usually" to "yes, entirely or completely")
Subscales	None — unidimensional, single-factor structure (Cronbach's α = 0.93)
Scoring	Total/mean score computed by averaging the 6 items; range 0-100
Direction of effect	Higher scores indicate greater emotional breakthrough

Psychological Insight Scale (PIS)

Construct assessed	Psychological insight gained during/following a psychedelic experience, and associated behavioral change
Number of items	7 total: a 6-item core scale (PIS-6) plus 1 additional single item on behavioral change (PIS item 7), scored separately
Item response format	7-point Likert scale, 1 ("strongly disagree") to 7 ("strongly agree")
Subscales	None — PIS-6 is unidimensional (single-factor structure, α = 0.94); item 7 is a standalone behavioral-change item not included in the PIS-6 average
Scoring	PIS-6 Average = mean of the 6 core items; range 1-7. Item 7 reported separately
Direction of effect	Higher scores indicate greater psychological insight (and, for item 7, greater likelihood of resulting behavioral change)

Mystical Experience Questionnaire (MEQ30)

Construct assessed	Intensity of mystical-type phenomena occasioned by a psychedelic experience
Number of items	30
Item response format	6-point Likert scale, 0 ("none; not at all") to 5 ("extreme (more than any other time in my life and stronger than 4)")
Subscales (4)	Mystical (unity, noetic quality, sacredness) Positive mood Transcendence of time and space Ineffability
Scoring	Total score range 0-150, typically expressed as a percentage of the maximum possible score (0-100%); subscale scores computed and expressed the same way. A "complete mystical experience" is defined as ≥60% of the maximum possible score on all four subscales
Direction of effect	Higher scores indicate more intense mystical-type experience

References

Barrett, F. S., Johnson, M. W., & Griffiths, R. R. (2015). Validation of the revised Mystical Experience Questionnaire in experimental sessions with psilocybin. Journal of Psychopharmacology, 29(11), 1182-1190.

Peill, J. M., Trinci, K. E., Kettner, H., Mertens, L. J., Roseman, L., Timmermann, C., Rosas, F. E., Lyons, T., & Carhart-Harris, R. L. (2022). Validation of the Psychological Insight Scale: A new scale to assess psychological insight following a psychedelic experience. Journal of Psychopharmacology, 36(1), 31-45.

Roseman, L., Haijen, E., Idialu-Ikato, K., Kaelen, M., Watts, R., & Carhart-Harris, R. (2019). Emotional breakthrough and psychedelics: Validation of the Emotional Breakthrough Inventory. Journal of Psychopharmacology, 33(9), 1076-1087.

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Supplement 4: Participant Feedback Form (PFF) – Group Setting and Environment Subscales

Group Setting

The following questions relate to the group setting:

	Strongly Disagree [-3]	Disagree [-2]	Slightly Disagree [-1]	Neither [0]	Slightly Agree [1]	Agree [2]	Strongly Agree [3]
12. I often felt distracted by the other group participants and would probably have been better able to engage with my personal experience without them.	○	○	○	○	○	○	○
13. I often felt distracted by the other group participants and would probably have been better able to engage with my personal experience without them.	○	○	○	○	○	○	○
14. I believe the group setting supported me in having a meaningful experience.	○	○	○	○	○	○	○

15. Comments:	

Environment

These questions relate to the setting on the study day:

	Strongly Disagree [-3]	Disagree [-2]	Slightly Disagree [-1]	Neither [0]	Slightly Agree [1]	Agree [2]	Strongly Agree [3]
16. The music was appropriate for my experience:	○	○	○	○	○	○	○
17. The ambience of the group room was appropriate:	○	○	○	○	○	○	○
18. I felt physically comfortable in the group room:	○	○	○	○	○	○	○
19. I was able to relax in the group room:	○	○	○	○	○	○	○

20. Comments:	

CONSORT 2025 checklist of information to include when reporting a randomised trial*

Section / Topic	No	CONSORT 2025 checklist item description	Reported on page no.
Title and abstract			
Title and structured abstract	1a	Identification as a randomised trial	2
	1b	Structured summary of the trial design, methods, results, and conclusions	2
Open science			
Trial registration	2	Name of trial registry, identifying number (with URL) and date of registration	7
Protocol and statistical analysis plan	3	Where the trial protocol and statistical analysis plan can be accessed	7
Data sharing	4	Where and how the individual de-identified participant data (including data dictionary), statistical code and any other materials can be accessed	25
Funding and conflicts of interest	5a	Sources of funding and other support (e.g., supply of drugs), and role of funders in the design, conduct, analysis and reporting of the trial	8, 32
	5b	Financial and other conflicts of interest of the manuscript authors	33
Introduction			
Background and rationale	6	Scientific background and rationale	2-5
Objectives	7	Specific objectives related to benefits and harms	4-5
Methods			
Patient and public involvement	8	Details of patient or public involvement in the design, conduct and reporting of the trial	Not applicable
Trial design	9	Description of trial design including type of trial (e.g., parallel group, crossover), allocation ratio, and framework (e.g., superiority, equivalence, non-inferiority, exploratory)	5-6
Changes to trial protocol	10	Important changes to the trial after it commenced including any outcomes or analyses that were not prespecified, with reason	Not applicable
Trial setting	11	Settings (e.g., community, hospital) and locations (e.g., countries, sites) where the trial was conducted	6-7, supplement 1
Eligibility criteria	12a	Eligibility criteria for participants	Supplement 2

	12b	If applicable, eligibility criteria for sites and for individuals delivering the interventions (e.g., surgeons, physiotherapists)	Not applicable
Intervention and comparator	13	Intervention and comparator with sufficient details to allow replication. If relevant, where additional materials describing the intervention and comparator (e.g., intervention manual) can be accessed	5-6,8 + Egger et al. (2025)
Outcomes	14	Pre-specified primary and secondary outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change from baseline, final value, time to event), method of aggregation (e.g., median, proportion), and time point for each outcome	8,9
Harms	15	How harms were defined and assessed (e.g., systematically, non-systematically)	Parent publication Egger et al. (2025)
Sample size	16a	How sample size was determined, including all assumptions supporting the sample size calculation	7 + ClinicalTrials.gov (NCT05829603)
	16b	Explanation of any interim analyses and stopping guidelines	Not applicable
Randomisation:			
Sequence generation	17a	Who generated the random allocation sequence and the method used	8
	17b	Type of randomisation and details of any restriction (e.g., stratification, blocking and block size)	8
Allocation concealment mechanism	18	Mechanism used to implement the random allocation sequence (e.g., central computer/telephone; sequentially numbered, opaque, sealed containers), describing any steps to conceal the sequence until interventions were assigned	8
Implementation	19	Whether the personnel who enrolled and those who assigned participants to the interventions had access to the random allocation sequence	8
Blinding	20a	Who was blinded after assignment to interventions (e.g., participants, care providers, outcome assessors, data analysts)	5
	20b	If blinded, how blinding was achieved and description of the similarity of interventions	5,6
Statistical methods	21a	Statistical methods used to compare groups for primary and secondary outcomes, including harms	10-12
	21b	Definition of who is included in each analysis (e.g., all randomised participants), and in which group	7
	21c	How missing data were handled in the analysis	7

	21d	Methods for any additional analyses (e.g., subgroup and sensitivity analyses), distinguishing prespecified from post-hoc	10-12
Results			
Participant flow, including flow diagram	22a	For each group, the numbers of participants who were randomly assigned, received intended intervention, and were analysed for the primary outcome	5-7
	22b	For each group, losses and exclusions after randomisation, together with reasons	7
Recruitment	23a	Dates defining the periods of recruitment and follow-up for outcomes of benefits and harms	Egger et al. (2025)
	23b	If relevant, why the trial ended or was stopped	Not applicable
Intervention and comparator delivery	24a	Intervention and comparator as they were actually administered (e.g., where appropriate, who delivered the intervention/comparator, how participants adhered, whether they were delivered as intended [fidelity])	6-8, Supplement 1 + Egger et al. (2025)
	24b	Concomitant care received during the trial for each group	6,7, Supplement 1
Baseline data	25	A table showing baseline demographic and clinical characteristics for each group	Table S1
Numbers analysed, outcomes and estimation	26	For each primary and secondary outcome, by group: ● the number of participants included in the analysis ● the number of participants with available data at the outcome time point ● result for each group, and the estimated effect size and its precision (such as 95% confidence interval) ● for binary outcomes, presentation of both absolute and relative effect size	5,6,12-21
Harms	27	All harms or unintended events in each group	Egger et al. (2025)
Ancillary analyses	28	Any other analyses performed, including subgroup and sensitivity analyses, distinguishing pre-specified from post-hoc	21,21
Discussion			
Interpretation	29	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	21-24

Limitations	30	Trial limitations, addressing sources of potential bias, imprecision, generalisability, and, if relevant, multiplicity of analyses	24

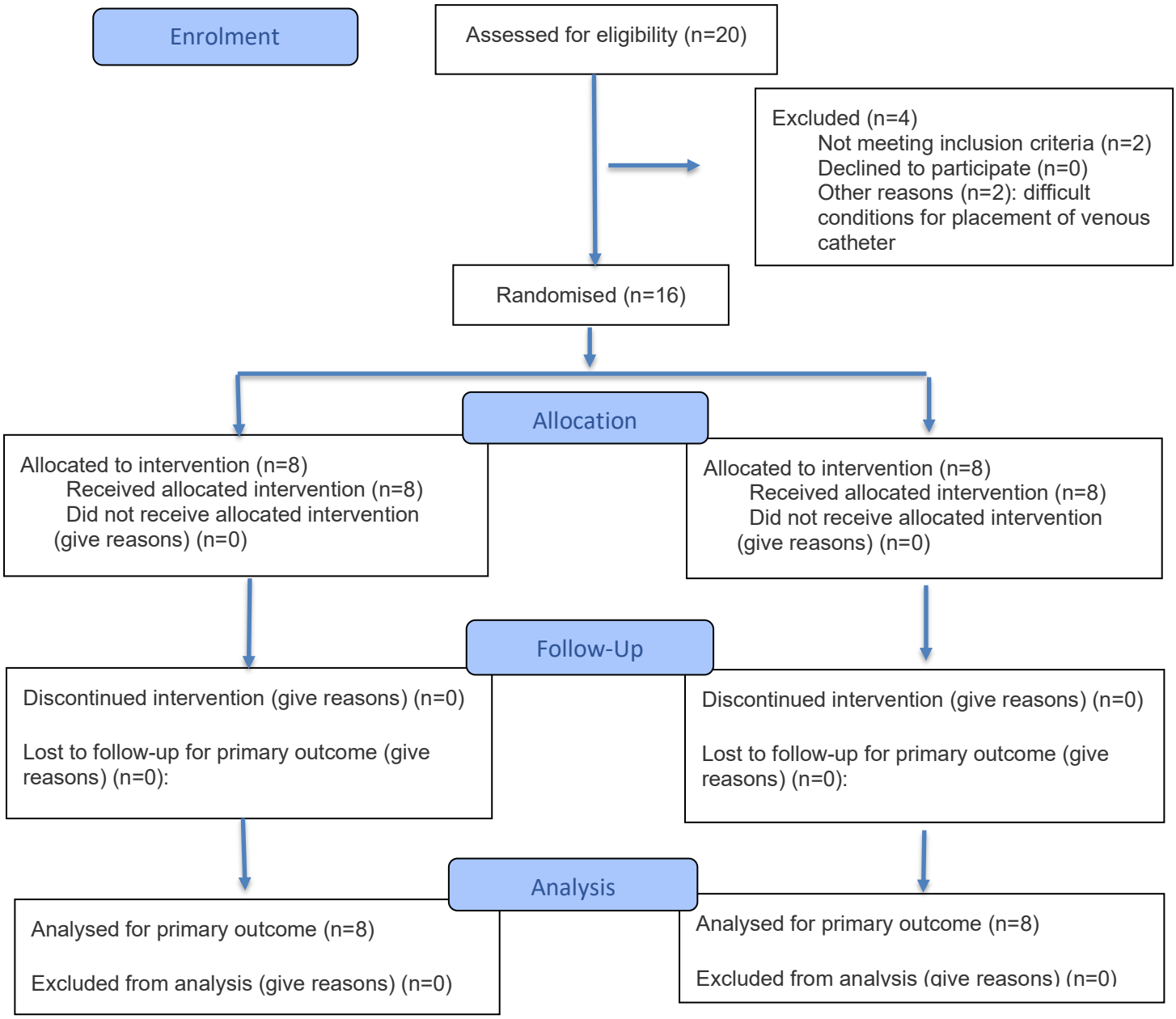
*We strongly recommend reading this statement in conjunction with the CONSORT 2025 Explanation and Elaboration and/or the CONSORT 2025 Expanded Checklist for important clarifications on all the items. We also recommend reading relevant CONSORT extensions. See www.consort-spirit.org.

Citation: Hopewell S, Chan AW, Collins GS, Hróbjartsson A, Moher D, Schulz KF, et al. CONSORT 2025 Statement: updated guideline for reporting randomised trials. BMJ. 2025; 388:e081123. https://dx.doi.org/10.1136/bmj-2024-081123.

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Figure 1: CONSORT 2025 Flow Diagram

Flow diagram of the progress through the phases of a randomised trial of two groups (that is, enrolment, intervention allocation, follow-up, and data analysis)



Citation: Hopewell S, Chan AW, Collins GS, Hróbjartsson A, Moher D, Schulz KF, et al. CONSORT 2025 Statement: updated guideline for reporting randomised trials. BMJ. 2025; 388:e081123. https://dx.doi.org/10.1136/bmj-2024-081123
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