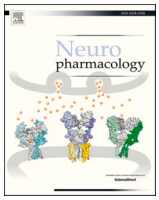
Neuropharmacology 284 (2026) 110732

Contents lists available at ScienceDirect

Neuropharmacology

journal homepage: www.elsevier.com/locate/neuropharm



Microdosing psilocybin and its effect on creativity: Lessons learned from three double-blind placebo controlled longitudinal trials

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ARTICLE INFO

Keywords:
Microdosing
Psychedelics
Double-blind
Placebo-controlled
Convergent thinking
Divergent thinking
Creativity

ABSTRACT

Background: Taking very small doses of psychedelics (LSD, truffles) over an extended period became prevalent in Western societies for its alleged cognitive benefit, including enhanced creativity. However, in the absence of robust, double-blind-controlled quantitative studies, such claims remain anecdotal.
Methods: Here we present results from 3 double-blind placebo-controlled longitudinal trials *(one* of which pre-registered) assessing the effects of microdosing psilocybin on convergent and divergent creativity in a well-controlled semi-naturalistic setting. To enhance statistical power and generalizability, data from all trials (N = 171) were pooled in a mega-analysis, resulting in one of the most robust laboratory-based studies on microdosing to date.
Results: We found that active microdosing increased the ratio of original responses (originality/fluency), indicating higher quality of divergent thinking in the active microdosing condition. The unadjusted originality score was significantly more pronounced in the active microdosing condition, but only when relative dosage (dose/weight of participants) was considered. Importantly, these effects survived controlling for dose guess and demographic biases. No effects of active microdosing were found for other divergent-thinking scores or convergent thinking.
Conclusion: The results suggest that the effects of truffle mirodosing are limited to the quality of divergent thinking. Moreover, our findings highlight the importance of controlling for placebo effects and prior psychedelic experience in assessing the impact of microdosing.

1. Introduction

Art, metaphors, and poetry are all expressions of creativity that rely on linking remote concepts through uncommon or unexpected associations (Zabelina and Robinson, 2010). High doses of psychedelics have been shown to stimulate hyper-associative thinking, enhance mental imagery, intensify emotional experiences, and alter the perception of meaning (Baggott, 2015; Carhart-Harris, 2018F; Nichols, 2016). These effects raise the question of whether psychedelics can promote creativity (Girn et al., 2020; Sessa, 2008).

Creativity is not a unitary construct or a single process (Sadler-Smith, 2015). Rather, it encompasses a multi-layered set of dissociable—and to some extent, opposing—subprocesses, most notably convergent and divergent thinking (Guilford, 1967). Convergent thinking refers to the

This article is part of a special issue entitled: Microdosing published in Neuropharmacology.

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https://doi.org/10.1016/j.neuropharm.2025.110732
Received 22 June 2025; Received in revised form 18 September 2025; Accepted 22 October 2025
Available online 2 November 2025

ability to integrate disparate ideas to arrive at a single logical solution. This process can be assessed using the Remote Associates Task (RAT; Mednick, 1968), which asks participants to identify the common link between three seemingly unrelated words (e.g., "Cottage," "Swiss," and "Cake," with the correct answer being "Cheese"; see Bowden and Jung-Beeman, 2003). In contrast, divergent thinking refers to the ability to generate multiple, loosely associated ideas in response to an open-ended question. This is typically assessed using the Alternate Uses Task (AUT), which prompts individuals to list as many creative uses as possible for a common object (e.g., a bottle or towel) within a limited time (Guilford, 1967).

Mechanistically, divergent thinking is associated with cognitive flexibility and reduced top-down control, which allows for the parallel co-activation of diverse mental representations (Boot et al., 2017; Cools and D'Esposito, 2011; Dreisbach and Goschke, 2004; Hommel, 2015). In contrast, convergent thinking requires greater top-down control, promoting mutual competition among ideas and guiding cognitive search toward a single optimal answer. These distinct modes of thought are supported by different cognitive control mechanisms and neural networks (Prochazkova and Hommel, 2020), and are likely influenced by different neuropharmacological processes (Akbari Chermahini and Hommel, 2010). Psychedelics have been hypothesized to enhance cognitive flexibility (Carhart-Harris and Nutt, 2017), and thus may primarily impact divergent thinking, rather than creativity as a broad, undifferentiated construct. Accordingly, in this paper, we systematically distinguish between convergent and divergent thinking.

Psilocybin (the active compound in so-called "magic truffles") belongs to the tryptamine class of compounds and exerts its psychedelic effects primarily through agonism of the serotonergic 5-HT2A receptor (Kraehenmann et al., 2017; Nichols, 2016; Vollenweider and Geyer, 2001). Notably, activation of 5-HT2A receptors has been associated with enhanced cognitive flexibility (Carhart-Harris and Nutt, 2017), improved associative and reversal learning (Aloyo et al., 2001; Boulougouris et al., 2008, 2008; Zhang and Stackman, 2015), and increased neuroplasticity (Catlow et al., 2013; Hutten et al., 2020)—all of which may theoretically contribute to improved divergent thinking and creative output.

Studying the acute effects of psychedelics on creativity poses significant challenges. Moderate to high doses are known to induce cognitive disorganization (Carhart-Harris, 2018). In such states, participants often struggle with task compliance due to impairments in memory and executive functioning (Pokorny et al., 2020). For example, a study by Mason et al. (2021) showed that acute effects of moderate doses of psilocybin decrease task-dependent creativity (convergent thinking and divergent fluency), while seven days after treatment performance in generating novel ideas significantly increased. Recently, however, microdosing—the repeated administration of very low psychedelic doses—has gained popularity as a more sustainable and subtle method of enhancing cognition (Fadiman and Korb, 2019).

1.1. Previous research

Surveys and anecdotal reports from community members who engage in psychedelic microdosing often describe enhanced creativity as a perceived benefit (Anderson et al., 2019a; Fadiman and Korb, 2019; Lea et al., 2020; Ona and Bouso, 2020). Retrospective research comparing individuals who microdose to those who do not has revealed higher performance in divergent thinking tasks among microdosers (Anderson et al., 2019b), though such findings may be influenced by inherent differences at baseline between the conditions.

Double-blind, placebo-controlled designs are the gold standard in clinical research, but regulatory and financial constraints make such trials with psilocybin especially difficult—particularly for microdosing, which requires repeated administration over time.

To date, only few double-blind placebo-controlled studies have examined microdosing's impact on creativity. In one of the earliest placebo-controlled investigations, Bershad et al. (2019) administered LSD microdoses (0, 6.5, 13, 26 μg) in 20 healthy adults using the Remote Associates Test (RAT) to assess convergent thinking. (Note: Doses are reported as LSD tartrate; approximately 6.5/13/26 μg tartrate correspond to ~5/10/20 μg LSD base for cross-study comparisons). LSD did not enhance performance but slightly increased the number of attempted trials, suggesting a possible motivational effect. However, the study's small sample and the lack of divergent thinking measures limits the strength of its conclusions. Similarly, Cavanna et al. (2022) employed a double-blind, placebo-controlled design (N = 34) using 0.5 g of dried *Psilocybe cubensis* and found no effects on divergent or convergent thinking. The study was constrained by its short duration (2 dosing days) with reliance on a single tasks administration which may have been insufficient to capture cumulative or behavioral changes reported in naturalistic microdosing practices. More recently, Molla et al. (2023) examined the effects of a single 26 μg dose of LSD in individuals with varying levels of depressive symptoms (N = 24). While subjective effects were more pronounced in those with higher symptomatology, no improvements were found in creativity tasks. Again, the study was limited by its sample size and single-dose design, where lack of repeated dosing limits its generalizability to longitudinal microdosing context.

Murphy et al. (2024) conducted a six-week, randomized, placebo-controlled trial in which 40 participants received 10 μg of LSD and 40 received placebo every third day and completed a multimodal creativity battery (Alternate Uses Task, Remote Associates Test, and Consensual Assessment Technique) at baseline, after the first week of dosing (240 min post-administration), and at a final visit 48 h after the final dose. While participants reported feeling more creative on dose days, objective measures revealed no significant improvements at either the acute or post-treatment assessments. However, participants were given only 2 min to complete the Alternative Uses Task (AUT), which is problematic due to the well-documented serial-order effect in creativity. This effect refers to the tendency for individuals to produce more conventional ideas early in the response sequence (drawn from memory), with more original and less accessible ideas typically emerging later, even as overall fluency declines (Shaw et al., 2024; Beaty and Silvia, 2012). As such, the brief duration likely limited the opportunity to capture more original responses, potentially underestimating the effects of microdosing. Furthermore, the creativity tasks were administered 4 h post-dose—after EEG recordings—at a time when participants may have been cognitively fatigued.

Together, these studies suggest that microdosing may enhance the subjective perception of creativity. However, methodological limitations—such as the absence of longitudinal designs, reliance on suboptimal assessment tools, and underpowered samples—continue to constrain definitive conclusions about its cognitive benefits.

1.2. Current study

To critically assess the cognitive effects of microdosing psilocybin, we conducted three placebo-controlled experiments employing slide variations in microdosing protocols, each designed to evaluate convergent and divergent thinking. While individual trials yield informative findings, their relatively modest sample sizes limit generalizability and more advanced analyses (Pan et al., 2018). To overcome this, we performed a mega-analysis combining individual-level data across all three studies (N = 171). Unlike a meta-analysis, which combines published summary statistics, a mega-analysis pools raw individual participant data across studies, allowing for standardized preprocessing, improved statistical power, and finer control over covariates (Stewart and Tierney, 2002; Riley et al., 2010). This approach was particularly appropriate here considering the uniform design at given time point, yielding more reliable estimates of microdosing's effects on creativityby enhancing statistical power. Importantly, we were able to control for dose guess and demographic biases. Concise descriptions of each experiment are included in the main text, while full methodological and statistical

details as well as exploratory analyses are provided in the Supplementary Materials. Given the statistical advantages of the mega-analysis, it serves as the primary basis for evaluating our hypotheses.

2. General method

2.1. General design

Three randomized, double-blind, placebo-controlled longitudinal trials took place at two experimental testing sites at Leiden University (Experiment 1 and Experiment 2) and the University of Amsterdam (Experiment 3). The protocols were approved by the local ethics committees of Leiden University and University of Amsterdam. The experimental procedure complies with ethical standards from the Helsinki Declaration of 1975, as revised in 2008. The doses were post-hoc analyzed for psychedelic content. Subjective drug effects and dose-guess effects were systematically assessed throughout all trials. Experiments 1 (Fig. 1a) and 2 (Fig. 1b) employed between-subject, placebo-controlled designs in which approximately half of the participants self-administered active doses and the other half placebos, all within a naturalistic setting. These trials lasted approximately three and four weeks, respectively. Experiment 3 (Fig. 1c), which was pre-registered on the Open Science Framework, used a within-subject crossover design spanning approximately eight weeks.

Finally, data from all three trials (N = 171) were combined in a mega-analysis using both frequentist and Bayesian approaches. This analysis was conducted to increase statistical power, account for sampling variation, and control for differences in study design (e.g., dose size, trial duration) across experiments, while adjusting for dose guess and demographic factors.

2.2. General procedure

All three trials were organized around public microdosing workshop events organized by the Microdosing Institute and Psychedelic Society of Netherlands (MI & PSN) - an external organization promoting psychedelic education. Participants who passed PSN's initial screening of mental health were invited to attend the microdosing workshop and could volunteer in a placebo-controlled study organized by university researchers. Workshop participants interested in taking part in the experimental trials were asked to fill in an additional screening form created by the university researchers and to attend a baseline testing session at the university labs (in Experiment 1 and 2). Only healthy applicants free from contra-indications, including a prior diagnosis or family problems with schizophrenia, psychosis, mania, or borderline disorder, were invited to take part in the microdosing event and related study.

After screening and baseline measures, participants attended the MI & PSN workshops. The public workshops always consisted of the same program, involving a short lecture, dose preparation, randomization to placebo and control conditions, and first dose self-administration. During each workshop, participants put precisely pre-determined amounts and packed psilocybin-containing truffles into opaque capsules. Participants were then randomly assigned by members of the PSN to receive

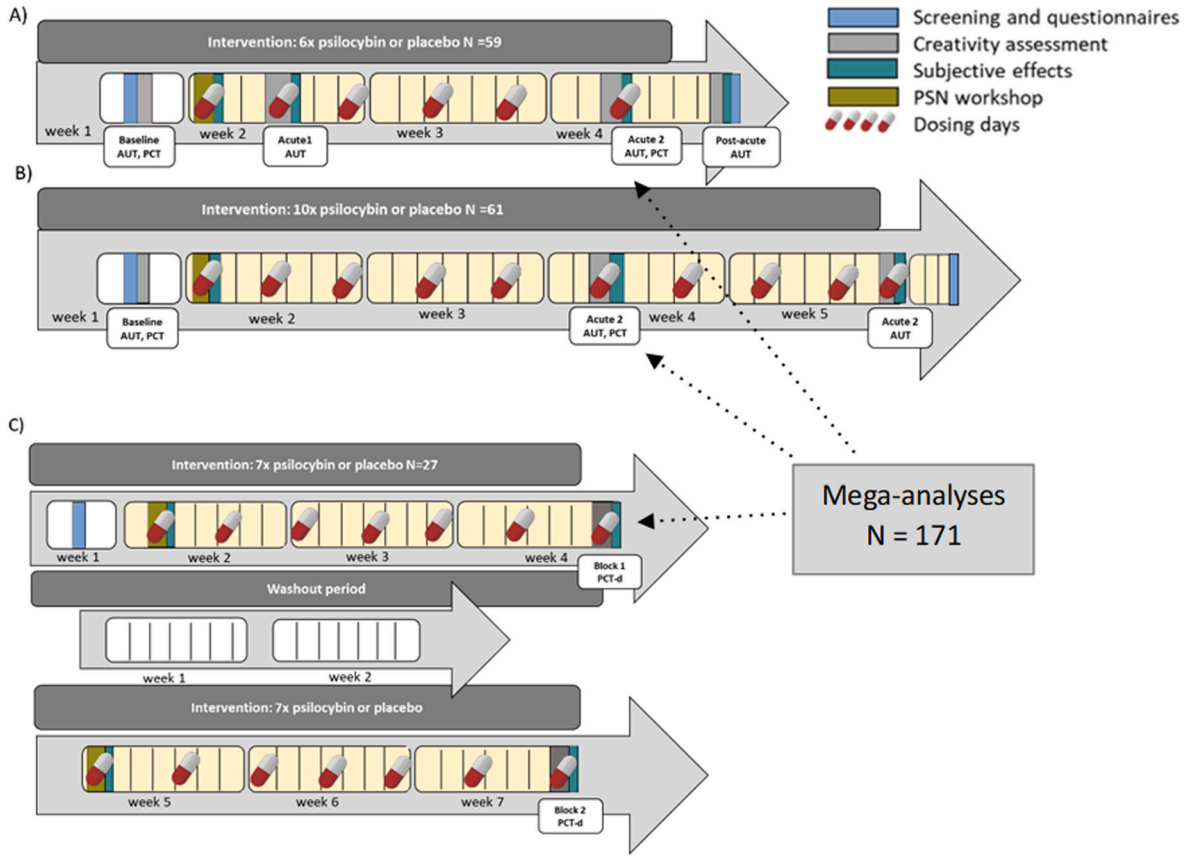

Fig. 1. Overview of Experimental Designs: (A) Experiment 1: Between-subject design, six psilocybin or placebo doses (N = 59), B) Experiment 2: Between-subject design, ten psilocybin or placebo doses (N = 61), (C) Experiment 3: Within-subject cross-over design, 2 blocks of seven doses each (N = 27). The combined mega-analysis (N = 171) was performed using data from the first 4 weeks of dosing across all studies. Red/gray capsules indicate active psilocybin or placebo microdoses. *Note:*The pooled mega-analysis includes additional participants who completed the relevant acute time point but did not complete later sessions, hence the larger pooled counts (E1 = 61; E2 = 71; E3 = 43; total = 175 pre-screening; 171 post-screening). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

either active microdoses or non-psychoactive placebos. Before the workshops, participants were informed that they might receive either a placebo or an active compound. Condition allocation was concealed by the PSN team to both participants and researchers until the analyses were finalized.

Participants were asked to follow a regular microdosing schedule approximately every 3 days, which is an interval that has been recommended by previous, qualitative research (Fadiman and Korb, 2019). To ensure regular dosing, participants received a dosing schedule with prescribed dosing days (see Fig. 2a), where they could also note any changes, they may have made in their dosing throughout the trial. Participants were reminded to self-administer their doses on the dosing days by MI & PSN through reminders sent online. The dosing schedules were collected at the end of the trial by the researchers to provide additional screening information. Participants were requested to take their microdoses up to 1 h before every testing session, since the effects of psilocybin contained in the truffles are reported to peak approximately 60–90 min after ingestion with a plateau phase lasting 2–4 h (Tylš et al., 2014).

Participants were tested 2 to 3 times in the university labs under the acute effects of the microdose. The test battery was always kept short-lasting (up to ~ 1 h and 45 min) to prevent fatigue and creativity tasks were assessed at the peak effect of microdosing and were contrabalanced. Participants were scheduled to attend testing sessions at similar times across the three testing moments to control for possible fluctuations in arousal in a day. For the overview of dependent variables at each testing session see (Fig. 1). All tasks were administered within this time limit, yet creativity tasks were consistently performed as one of the first tasks, to avoid fatigue and potential priming effects after prolonged cognitive testing. Experimental sessions took place in front of a computer screen in a university laboratory (in Experiment 1 and 2) and participants were free to take a short break between tasks. During every experimental session in the university lab, participants were asked to reflect on their subjective experience and guess which condition they believed to be ('placebo', 'not sure', 'active'). Participants found out their condition allocation (placebo/active) after the last online assessment from a PSN representative. However, participants' blinding stayed concealed to the researchers until the analyses were finalized. Due to the heterogeneity of experimental questions posed by each researcher, the limited scope of this paper and our primary goal of the current trial to replicate the pilot effect of microdosing on creativity (Prochazkova et al., 2018), results of other tasks will be reported elsewhere.

In this manuscript, we report participants' dose allocation guesses (active/placebo/not sure) collected at each acute session as indices of blinding. We did not collect a priori expectancy at baseline (cf. Muthukumaraswamy et al., 2021). Accordingly, where we adjusted for 'expectancy' in earlier drafts, we now refer to 'dose guess' and report blinding (or breaking blind) accordingly; analyses control for dose guess rather than pre-dose expectancy.

Safety protocols were in place across all experiments. Participants were screened for psychiatric vulnerability, instructed to abstain from concomitant psychoactive substance use, and tested under supervision in university laboratories. During the dosing period, participants were asked to promptly report any adverse effects to the research team; if a dose felt too strong, they were instructed to contact a PSN staff member, who could adjust subsequent capsules to a lower dose. Notably, across the three trials, two participants—both later revealed to be in the placebo condition—reported very strong effects and requested a lower dose, consistent with salient placebo responses and effective blinding. No other adverse psychological or physiological events were reported.

2.3. Exclusion criteria

Across all three experiments, participants were excluded if they missed more than two scheduled doses or reported concomitant psychoactive drug use during the trial. Also, participants who self-administered microdoses longer than 2.5 h before testing were excluded. In addition, only participants who completed the baseline session and all acute follow-up laboratory sessions were included in the primary analyses. Experiment 3 spanned 8 weeks and given the study length and crossover structure, a higher attrition rate was anticipated a priori. For the pooled mega-analysis, we analyzed outcomes from the first 3 weeks of dosing across all three trials (i.e., the 6th/7th dose time point). Consequently, participants who dropped out after this window did not need to be excluded, which increased the pooled sample by 24 additional participants whose data had not been included in the individual trial analyses. Full exclusion criteria are detailed in the Supplementary Materials (Sections S3–S5)."

2.4. Measures

Divergent thinking was assessed using the *Alternate Uses Task* (AUT; Guilford, 1967) in Experiments 1 and 2. Participants had 5 min per item to think of as many possible uses for an object (e.g., towel, pen). Different items were used for each session, but the order of items presented across time was consistent. By keeping the order consistent we eliminated possible co-founding factors of item difficulty (e.g., availability heuristics) to interact with the result. Responses were scored by two independent raters on fluency, flexibility, elaboration, originality and the ratio between originality and fluency (originality/fluency) as an additional index of divergent thinking that was previously suggested as a more parsimonious measure of divergent quality (Hocevar and Michael, 1979; Runco and Albert, 1985) and was shown to be affected by psychedelics in previous research (Kuypers et al., 2016; Mason et al., 2019).

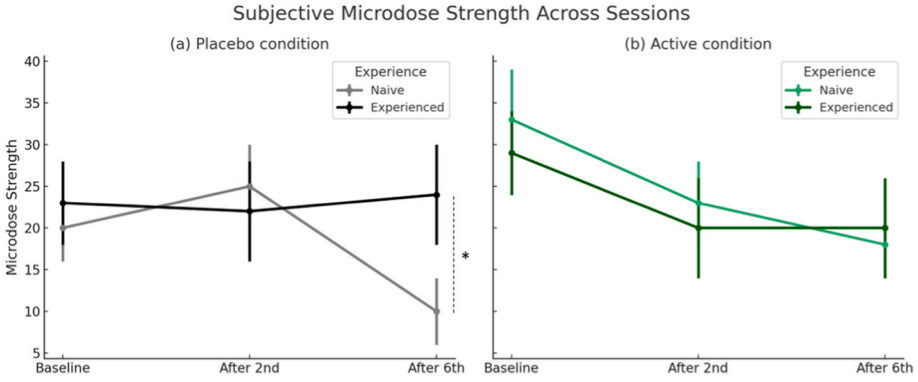

Fig. 2. *Subjective microdose strength ratings across sessions for naïve and experienced microdosers.* Mean ratings (±SEM) are shown separately for the placebo condition (a) and active condition (b) across three time points: Baseline, after the 2nd dose, and after the 6th dose. The result indicates that participants with previous psychedelic experience rated the microdosing strength significantly more salient in placebo condition at acute 2 compared to naive participants.

Convergent thinking was measured using the *Picture Concept Task* (PCT; Wechsler, 1991), in which participants identified a single shared association across rows of images. Accuracy-based scoring was used, and timing followed prior work (Mason et al., 2021). Task format and scoring details are provided in Supplementary Section S3.1. Experiment 3 used adapted version of PCT with divergent component. *PCT-d* including convergent score, fluency score, originality score and originality-to-fluency ratio (for details see Supplementary Section S5.1.) This task was validated for its comparability with the AUT (Zhang et al., 2025). To ensure equivalent block difficulty across counterbalanced conditions, we conducted a pilot (N = 20) with Item Response Theory (IRT) to assemble matched-difficulty item sets per block. In the main study, all participants received the same PCT-d items within a block, with different items across blocks to limit practice effects. Final PCT-d scores were z-scored within block to adjust for any residual difficulty differences. Full details regarding power analyses, pre-processing, scoring procedures and inter-rater reliability are detailed in Supplementary Materials.

2.5. The truffe dosing

The microdosing dose size was up-tiered at every experimental trial to explore possible dose-dependent effects on outcome measures in the final mega-analyses. Specifically, in Experiment 1 participants microdosed with ~0.65 g of fresh truffles equivalent lower range microdose ~1/15th, in the Experiment 2 participants microdosed with ~1 g of fresh truffles equivalent mid-range microdose ~1/10th and in Experiment 3 participants microdosed with ~1.5 g of fresh truffles equivalent higher-range microdose ~1/7th. For details regarding dosing please see Supplementary Section S2.

2.6. Analyses

2.6.1. Experiment 1 and Experiment 2

Baseline comparability between placebo and active conditions was checked with independent-samples *t*-tests and χ^2 tests on demographics. To assess subjective effects beliefs about condition allocation (i.e., dose guess) were compared between conditions at each session with χ^2 tests. Perceived psychoactive strength was analyzed with mixed-design *rm*ANOVA: Session (baseline, acute 1, acute 2; within subject factor) × Condition (placebo, active; between subject factor). Furthermore, we explored to what degree previous psychedelic experience (naïve vs. experienced) played a role in the ratings of the subjective effects. To this end, differences in subjective ratings of psychedelic strength between psychedelically naïve and experienced participants were analyzed with independent samples *t*-tests at every session.

Table 1
Demographic and baseline characteristics by treatment condition (randomized sample) across all three experiments. Data are presented as mean (standard deviation) unless otherwise specified.

Experiment 1							
	Mean	SD	Mean	SD	*t*	p	Cohen's d
	Placebo (n = 30)		Active (n = 29)				
Age	23.8	5.24	23.72	4.52	0.06	0.95	0.02
Weight	69.66	10.21	68.25	11.06	0.5	0.62	0.13
BMI	22.16	2.09	21.88	2.72	0.46	0.65	0.12
Time dose S1	1.72	0.35	1.74	0.09	0.37	0.71	0.1
Time dose S2	1.57	0.99	1.36	0.38	1.02	0.31	0.27
Sleep hours	7.5	0.24	7.21	1.48	0.93	0.36	0.191
	Placebo (n = 27)		Active (n = 26)		*X2*	p	Cramer's V
Gender % (Non-bin/F/M)	3.3/46.7/50		0/44.4/55.6		1.05	0.59	0.134
Psych. Exp % (yes/no/missing)	36.6/53.3		34.5/55.2		0.03	0.98	0.023
Experiment 2							
	Mean	SD	Mean	SD	*t*	p	Cohen's d
	Placebo (n = 30)		Active (n = 31)				
Age	27.87	5.32	27.65	7.32	0.14	0.89	0.035
Weight	69.22	11.35	70.44	11.94	0.41	0.69	0.104
BMI	22.75	3.22	23.84	3.88	1.2	0.24	0.307
Time dose S1	1.15	0.3	1.22	0.26	0.85	0.53	0.08
Time dose S2	1.22	0.12	1.15	0.23	1.6	0.24	0.21
Sleep hours	7.14	1.45	7.76	1.57	1.4	0.17	0.31
	Placebo (n = 30)		Active (n= 31)		*X2*	p	Cramer's V
Gender % (F/M)	53.3/46.6		54.8/45.2		0.014	0.91	0.015
Psych. Exp % (yes/no/missing)	92.3/7.6/0		85.7/14.2/0		0.59	0.44	0.593
Experiment 3							
	Mean	SD	Mean	SD	*t*	p	Cohen's d
	Placebo (n = 13)		Active (n= 14)				
Age	28.39	9.465	34	10.69	1.44	0.16	0.56
Weight	73	12.356	68.57	13.15	−0.9	0.38	−0.35
BMI	23.16	2.661	31.22	33.17	0.87	0.39	0.34
Time dose Block1	1.27	0.109	1.3	0.06	1.04	0.31	0.4
Time dose Block 2	1.19	0.259	1.33	0.09	1.81	0.18	0.71
Sleep hours Block 1	7.29	0.722	7.04	0.72	−0.9	0.38	−0.36
Sleep hours Block 2	7.23	1.367	7.59	1.28	0.64	0.53	0.28
	Placebo (n = 30)		Active (n = 31)		*X2*	p	Cramer's V
Gender % (F/M)	53.3/46.6		50/50		0.04	0.84	0.04

Note: Time dose – refer to the time (in hours) between ingestion of the microdose and task administration.

Creativity outcomes of AUT and PCT were analyzed with mixed-design *rm*ANOVAs (assumptions checked; appropriate corrections or non-parametric alternatives applied if violated). For AUT, acute effects were tested with 2 × 3 *rm*ANOVAs on each divergent index (fluency, flexibility, originality, elaboration, originality ratio). The session (e.g., baseline, acute 1, acute 2) was entered as the within-participant factor and condition (placebo vs active) as the between-participant factor. Post-acute effects were tested with 2 × 2 *rm*ANOVAs [Session (baseline, post-acute) × Condition]. Because five AUT indices were tested, we applied Bonferroni correction (α = .01). PCT was tested with a 2 × 2 *rm*ANOVA [Session (baseline, acute 2) × Condition]. The primary tests of interest were Session × Condition interactions. Significant omnibus effects were followed by Bonferroni-corrected simple effects/contrasts.

In exploratory analyses, we re-ran the AUT and PCT mixed-design rmANOVAs, first including guessed allocation (active/unsure/placebo) and next prior psychedelic use as between-participant factors. We also computed Pearson correlations between perceived psychoactive strength and baseline-corrected changes in creativity indices. These analyses assessed whether perceived strength/dose guess moderated effects beyond pharmacology. Only significant, interpretable findings are reported in the main text; nonsignificant results are in the Supplement.

2.6.2. Experiment 3

Involved cross-sectional design with two experimental blocks (i.e., active vs. placebo), subjective beliefs about one's allocation were compared between conditions with χ^2 tests. Perceived microdose strength was compared conditions at each block using independent-samples *t*-tests. Following the preregistered plan, we analyzed PCT-d (involving one convergent score; three divergent indices). First, we ran a 2 × 4 repeated-measures ANOVA with within-participant factors: Condition (placebo, active) and Score Type (convergent, fluency, originality, originality ratio). To control for order effects, we then fit a mixed 2 × 4 × 2 ANOVA adding Block Order (placebo in block 1 vs block 2) as a between-participant factor. Post-hoc tests for four planned contrasts were Bonferroni-adjusted (α_adj ≈ 0.013) according to the four comparisons of interests. Final PCT-d scores were z-scored within block to adjust for any residual difficulty differences.

3. Experiment 1

3.1. Rationale and method

This experiment aimed to test whether microdosing psychedelics enhances creative cognition. We hypothesized that microdosing would either (a) increase divergent thinking and impair convergent thinking, suggesting competitive cognitive processes, or (b) enhance both, through improved metacontrol (Hommel, 2015a). Participants completed the AUT and PCT tasks. A between-subjects, double-blind design was used with two conditions (placebo vs. microdose). Participants were assessed at baseline, and after the 2nd (Acute 1) and 6th (Acute 2) doses. A sub-acute session was also conducted two days after the final dose.

3.2. Participants

The final AUT sample consisted of 59 participants (30 placebo, 29 microdose; M_age = 27.75, SD = 6.32) who completed all sessions. The

Table 2
Dose guess regarding condition allocation. Participants' subjective estimation regarding their own condition allocation by treatment condition for all three experiments. Total N indicates total sample size for each cell. Truffles microdose amounts across experiments: Experiment 1 (~0.65 g; ~1/15th dose, lower range), Experiment 2 (~1.0 g; ~1/10th dose, mid-range), and Experiment 3 (~1.5 g; ~1/7th dose, higher range).

Experiment 1				
	Acute 1			
	Guess Active	*Not sure*	*Guess Placebo*	Total *n*
Placebo	20.00 %	53.33 %	26.66 %	30
Active	27.58 %	51.73 %	20.69 %	29
	Acute 2			
	Guess Active	*Not sure*	*Guess Placebo*	
Placebo	26.67 %	23.33 %	50 %	30
Active	31.03 %	41.38 %	23 %	29
Experiment 2				
	Acute 1			
	Guess Active	*Not sure*	*Guess Placebo*	Total *n*
Placebo	25.80 %	48.38 %	25.80 %	30
Active	30.00 %	40.00 %	30.00 %	31
	Acute 2			
	Guess Active	*Not sure*	*Guess Placebo*	
Placebo	26.66 %	30.00 %	43.33 %	30
Active	29.03 %	38.71 %	32.25 %	31
Experiment 3				
	Block1			
	Guess Active	*Not sure*	*Guess Placebo*	Total *n*
Placebo	8.33 %	83.33 %	8.33 %	9
Active	44.44 %	33.33 %	22.22 %	12
	Block 2			
	Guess Active	*Not sure*	*Guess Placebo*	
Placebo	0.000 %	85.71 %	14.29 %	8
Active	76.92 %	15.38 %	7.69 % **	13

Note: * = p < .05; ** = p < .01, p-values refer to t-tests.

final PCT sample included 57 participants (28 placebo, 29 microdose), with two excluded for incorrect task interpretation. The post-acute AUT session was completed by 62, but three were excluded due to missing prior sessions. Further details on inclusion criteria and dosing compliance are in Supplement S3.2.

3.3. Results

3.3.1. Demographics and subjective effects

Conditions did not differ in age, gender, BMI, prior psychedelic use, or timing of sessions (Table 1).

Participants in the active psilocybin and placebo conditions did not

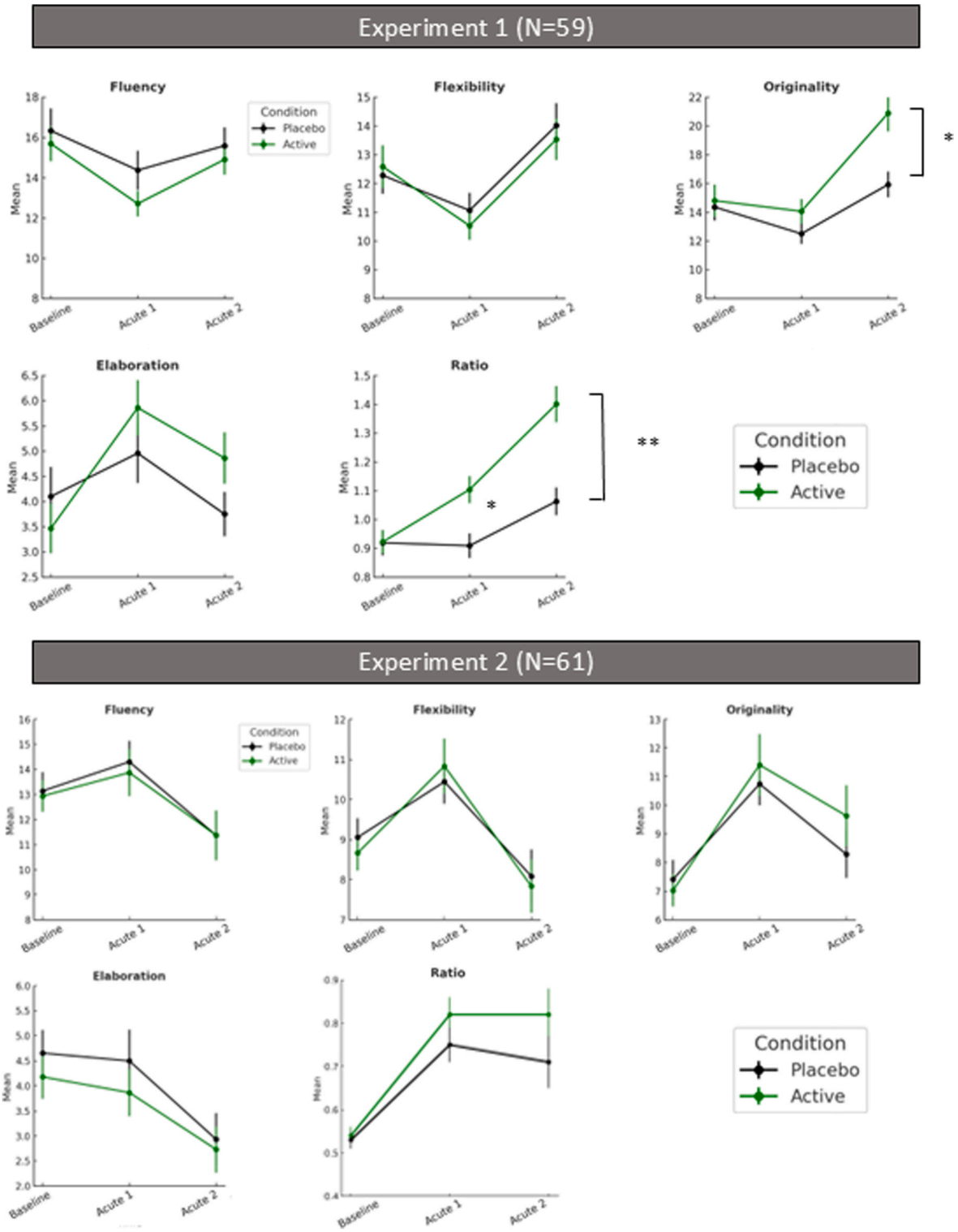

Fig. 3. *Results of Experiment 1 and Experiment 2*, show mean scores for the four divergent scores measured by AUT as a function of condition (Placebo vs. Active psilocybin) across the three testing sessions. Vertical capped lines indicate standard error of the mean. Asterisks indicate significant differences between active and placebo sessions (*$p < .005$, **$p < .001$).

differ in guessed allocation at the first session (χ^2 (3, N = 59) = 0.587, p = .746, Cramér's V = 0.10) or the second follow-up (χ^2 (3, N = 59) = 6.21, p = .10, Cramér's V = 0.324). Most participants reported being unsure, with similar rates of false positives/negatives (Table 2, Exp. 1). Notably, 26.6 % of the placebo condition believed they were in the active condition after two weeks.

A mixed RM-ANOVA showed a main effect of Session, F (2, 110) = 4.499, p = .013, ηp^2 = 0.08, indicating perceived strength changed over time, collapsing across Condition. Follow-up t-tests showed diminishing effects from the initial workshop (M = 23.77, SD = 21.82) to the last session (M = 15.68, SD = 16.86), t (56) = 2.91, p = .005, in both conditions. The main effect of Condition (F (1, 55) = 0.97, p = .75, ηp^2 = 0.002) and the Session × Condition interaction (F (2, 110) = 0.94, p = .39, ηp^2 = 0.017) were non-significant, indicating no difference in perceived strength between active and placebo. On average, ratings were ~20 % of "maximal psychedelic effects" and decreased over time (Table 2, Exp. 1), supporting successful blinding.

Using independent-samples t-tests with Welch's correction, participants with prior psychedelic experience reported stronger effects at Acute 2 (M = 19.87, SD = 10.56) than naïve participants (M = 8.81, SD = 10.56), t (49.74) = 2.69, p = .01, d = 0.713, irrespective of Condition. No differences emerged at baseline or Acute 1 ($|ts| \leq 1.13$, $ps \geq 0.28$). Follow-ups indicated this was driven by the placebo condition: experienced participants reported higher perceived strength at Acute 2 (M = 22.6, SD = 21.5) than naïve participants (M = 6.9, SD = 8.9), t (21.44) = 2.6, p = .016, d = 0.951. No experience-related differences appeared in the active condition ($|ts| \leq 1.08$, $ps \geq 0.29$) (see Fig. 2).

3.3.2. Divergent thinking

We ran 2 × 3 mixed RM-ANOVAs (Greenhouse–Geisser as needed) for each divergent index (Fig. 3, Exp. 1). Session main effects were significant for all measures (minimum $F \geq 16.3$, $p \leq .001$, $\eta p^2 \geq 0.22$), reflecting practice/item-difficulty changes. Condition main effects were significant for originality (F (1, 57) = 4.26, p = .044, ηp^2 = 0.070) and originality ratio (F (1, 57) = 12.87, p < .001, ηp^2 = 0.184), but not for fluency, flexibility, or elaboration (maximum $F \leq 0.747$, $p \geq .391$, $\eta p^2 \leq$ 0.013).

Session × Condition interactions were significant for elaboration (F (2, 114) = 4.924, p = .009, ηp^2 = 0.080), originality (F (1.64, 93.8) = 5.741, p = .007, ηp^2 = 0.092), and originality ratio (F (1.63, 93) = 8.907, p = .001, ηp^2 = 0.135). Between-condition contrasts at Acute 1 and Acute 2 showed higher originality for active vs placebo at Acute 2 (p = .002, d = 0.837) but not Acute 1 (p = .162, d = 0.369); higher originality/fluency at both Acute 1 (p = .003, d = 0.804) and Acute 2 (p < .001, d = 1.11). Elaboration did not differ between conditions at either follow-up ($ps \geq 0.104$, $ds \leq 0.43$); the interaction reflected a baseline →Acute 1 increase in the active condition (p = .009, d = 0.520), which was not central to our hypotheses (see Fig. 3) Dose guess and perceived strength did not significantly moderate AUT changes (Supplement S3.4). Post-acute AUT effects (days later) were also non-significant (Supplement S3.5).

3.3.3. Convergent thinking (PCT)

Baseline PCT did not differ between conditions (t (55) = 0.76, p = .88). RM-ANOVA showed a main effect of Session, F (1, 55) = 0.35, p = .040, ηp^2 = 0.075, consistent with a small practice effect. There was no main effect of Condition (F (1, 55) = 0.426, p = .517, ηp^2 = 0.008) and no Session × Condition interaction (F (1, 55) = 0.35, p = .556, ηp^2 = 0.006), indicating no microdosing effect on convergent thinking (Fig. 3). Results were unchanged after controlling for dose guess.

3.4. Discussion Experiment 1

The results of Experiment 1 suggest that the cognitive effects of microdosing psilocybin are more subtle and selective than initially expected. While we anticipated broader enhancements in creative thinking, improvements were limited to measures of originality and originality-to-fluency ratio, particularly after repeated dosing. Other aspects of divergent thinking—such as fluency, flexibility, and elaboration—remained unaffected. Suggesting that microdosing may selectively enhance idea novelty without broader cognitive benefits and highlighting the need for further research into its mechanisms and their selectivity. No effects were observed on convergent thinking, and a slight improvement across sessions likely reflected practice. Sub-acute effects, measured two days post-intervention, were also absent. Subjective reports of perceived drug effects were comparable across conditions, confirming successful blinding. However, interestingly participants with prior psychedelic experience reported stronger placebo responses, underscoring the potential influence of expectancy effects in those who were experienced (Muthukumaraswamy et al., 2021).

Please note, session-wise fluctuations in AUT means (e.g., a decrease–increase pattern in Exp. 1 versus the reverse in Exp. 2) do reflect item-set differences rather than pharmacological effects, as distinct prompt sets were administered at each session to limit practice. As such they are not experimentally informative and we base interpretation on between-condition contrasts.

4. Experiment 2

4.1. Rationale and method

Experiment 2 was designed to replicate and extend the findings of Experiment 1 by exploring potential dose-dependent and cumulative effects of microdosing. The study used a between-subjects design with three assessment points: baseline, Acute 1 (after the 6th dose), and Acute 2 (after the 10th dose). The procedure mirrored that of Experiment 1, using the same creativity and subjective measures (AUT, PCT), but incorporated two key modifications: (1) the psychedelic dose was increased to ~1 g of fresh truffles, and (2) the microdosing period was extended to four weeks (10 doses total; see Fig. 1b). These changes aimed to increase pharmacological impact and allow for cumulative neuroadaptive effects, as suggested by prior literature (Fadiman & Korb, 2017; Carhart-Harris et al., 2016).

4.2. Participants

Of the 83 participants who completed baseline testing, 71 attended the Acute 1 session and 66 completed Acute 2. Five were excluded for missing sessions or psychoactive drug use. The final AUT sample included 61 participants (31 microdose, 30 placebo; M_age = 27.75, SD = 6.32) who completed all key sessions. For the PCT, six additional participants were excluded due to task misinterpretation, resulting in a final sample of 55 (29 microdose, 26 placebo; M_age = 28.1, SD = 6.1). Further details are provided in Supplementary Section S4.

4.3. Results

4.3.1. Demographics and subjective effects

Conditions did not differ in demographics or prior psychedelic use (Table 1). Compared to Experiment 1, participants in Experiment 2 were significantly older (t (118) = 3.85, p < .001) and more likely to have prior psychedelic experience (88.9 % vs. 60.4 %). Despite the higher dose, blinding remained effective: condition allocation estimates did not differ from chance at either follow-up (ps > 0.65), and perceived microdosing strength was comparable across conditions and time points (F (2,118) = 0.133, p = .876, $\eta 2p$ = .002; see Tables 2 and 3.

4.3.2. Divergent thinking (AUT)

Five 2 x 3 mixed-design ANOVAs were conducted for each AUT metric with alpha adjusted to p < .01. Session effects were significant across all measures ($Fs \geq 17.8$, $Ps \leq 0.001$, $\eta 2p \geq .23$), reflecting learning or task familiarity. No main effects of condition emerged ($Fs \leq$

1.37, $Ps \geq 0.25$, $\eta 2p \leq .028$), and all interaction terms were also non-significant: fluency (F (1.6,99) = 0.115, p = .857, $\eta 2p$ = .002), flexibility (F (2,118) = 0.643, p = .527, $\eta 2p$ = .011), elaboration (F (2,118) = 0.290, p = .749, $\eta 2p$ = .005), originality (F (2,118) = 1.315, p = .272, $\eta 2p$ = .022), and originality/fluency (F (2,118) = 1.674, p = .192, $\eta 2p$ = .028). Although the effect directions for originality and originality/fluency were consistent with Experiment 1, the findings did not reach significance, and no post hoc tests were conducted.

4.3.3. Convergent thinking (PCT)

Baseline performance on the PCT did not differ between conditions (t (49) = 0.037, p = .848). ANOVA showed no main effect of session (F (1,53) < 0.001, p = .995, $\eta 2p$ < .001), condition (F (1,53) = 0.280, p = .599, $\eta 2p$ = .005), or their interaction (F (1,53) = 0.021, p = .913, $\eta 2p$ < .001), indicating no influence of microdosing on convergent thinking (see Fig. 3). Dose guess also did not moderate these outcomes. Please see Supplement S4 for further details on the analyses and results.

4.4. Discussion Experiment 2

Experiment 2 failed to replicate the significant effects observed in Experiment 1. While the active microdosing condition showed similar trends in originality-based measures (e.g., originality ratio), these were not significante. Moreover, as in Experiment 1, no benefits of microdosing were observed for convergent thinking.

Importantly, even with increased dose and trial duration, participants remained effectively blinded, and subjective drug effects declined over time in both conditions. The null results raise questions about the robustness of the effects observed in Experiment 1 and call attention to several methodological differences between the two studies. Participants in Experiment 2 were older, more experienced with psychedelics, and drawn from the general public rather than a university setting, possibly contributing to variability in baseline performance and task familiarity. Differences in study duration (6 vs. 10 doses), dose, condition composition, and psychological training may have further influenced outcomes. For instance while a linear dose-response would be anticipated to predict progressively greater improvements in divergent thinking, prior findings point to possible non-linear effects, with lower doses at times yielding stronger outcomes (Hutten et al., 2020). These findings suggest that the cognitive effects of microdosing—if present—may be unstable, small, or highly context-dependent.

Table 3
Ratings of subjective microdosing strength. Shows three experiments divided by treatment (placebo vs active) measured at different time points. Data are presented in mean (SD). The intensity was measured on the Likert-type scale, zero referred to "no effects" and hundred referred to "extremely strong psychedelic effects". Truffles microdose amounts across experiments: Experiment 1 (~0.65 g; ~1/15th dose, lower range), Experiment 2 (~1.0 g; ~1/10th dose, mid-range), and Experiment 3 (~1.5 g; ~1/7th dose, higher range).

Experiment 1			
Condition	*Workshop*	*Dose 2*	*Dose 6*
Placebo	21,1 (21,35)	20,5 (21,23)	16,2 (18,53)
Active	26,74 (22,36)	19,7 (17,55)	15,11 (15,13)
Experiment 2			
Condition	*Workshop*	*Dose 6*	*Dose 10*
Placebo	35,6 (32,07)	21,17 (28,02)	17,1 (19,95)
Active	38,61 (32,17)	20,77 (24,8)	16,6 (21,6)
Experiment 3			
Condition	*Workshop*	*Dose 7*	*Dose 14*
Placebo	19,38 (18,22)	10,75 (13,38)	4,28 (8,01)
Active	36,7 (19,28)	25,6 (27,77)	33,23 (30,09) **

Note: * = p < .05; ** = p < .01, p-values refer to chi-square tests.

5. Experiment 3

5.1. Rationale and method

Given these limitations and the inconsistent pattern of results, a third study was conducted using a within-subjects, cross-over design to control for between-subject variability. Experiment 3 aimed to replicate previous findings while improving statistical power. The dose was increased to 1.5 g of fresh truffles. All procedures and hypotheses were pre-registered (https://osf.io/cn8z4/).

5.2. Methods

5.2.1. Design

Participants self-administered 14 microdoses across two counterbalanced blocks (active vs placebo), each lasting three weeks, separated by a two-week washout period (Fig. 1C). Testing was conducted at the University of Amsterdam. Condition allocation was blinded from researchers and participants. A divergent adaptation of the PCT task (PCT-d) was employed to assess both convergent and divergent creativity (Zhang et al., 2025). The PCT-d was administered once per dosing block (i.e., week 3 of active vs. placebo). The PCT-d, included one convergent and three divergent scores (fluency, originality, originality/fluency). Given the crossover design of Experiment 3 and counterbalancing across participants, block difficulty needed to be equivalent. A pilot study (N = 20) using item response theory (IRT) was conducted to create test sets of matched difficulty. To further control for residual difficulty differences, final scores were Z-standardized within each block minimizing block-level confounds.Task details are in Supplement S5. Subjective effects and condition allocation guesses were collected at each block. Prior psychedelic use was not formally recorded, though considering the study was advertised via Psychedelic Society we assume participants were experienced.

5.2.2. Participants

Initially 75 participants started out with our study and filled in the initial research screening information. Twenty-five participants dropped out after the first block and additional 16 participants dropped out during the second block of testing (i.e., approximately eight weeks after the first dose). Furthermore, 5 participants were excluded as they took other psychoactive drugs and 2 participants self-administered microdoses longer than 2.5 h before testing. This yields a final sample of 27 healthy participants (13 females) between the age of 20–48 with mean age 31.3 years (SD = 10.00) from which 14 participants started with the active doses. For further details on screening please see Supplementary Materials (S5.2).

5.3. Results

5.3.1. Demographics and subjective effects

Randomization was successful (Table 1, Exp. 3). The Exp. 3 sample was older (M = 31.25, SD = 9.79) than Exp. 1 (M = 23.96, SD = 5.10), t (99) = 4.49, p < .001, and Exp. 2 (M = 27.75, SD = 6.32), t (111) = 2.45, p = .016. Blinding held at Block 1 (7th dose): χ^2 (2, N = 21) = 5.588, p = .061, Cramér's V = 0.516; but broke at Block 2 (14th dose): χ^2 (2, N = 20) = 11.209, p = .004, V = 0.749 (Table 2). Perceived strength did not differ by condition at Block 1, t (32) = 1.40, p = .173, d = 0.541, but was higher in the active condition at Block 2 (active: M = 33.23, SD = 30.09; placebo: M = 4.28, SD = 8.01), t (32) = 3.23, p = .002, d = 1.33 (Table 3). Strength ratings decreased from workshop to the first follow-up across conditions, t (34) = 2.74, p = .011, d = 0.52.

5.3.2. Divergent thinking (PCT-d) and convergent thinking

A 2 × 4 *rm*ANOVA revealed no main effect of condition (F (1,26) = 1.54, p = .225, η_p^2 = .056), but a significant condition × score interaction (F (3,78) = 2.80, p = .045, η_p^2 = .097), suggesting that microdosing

Table 4
Comparison of creativity scores between active and placebo conditions in Experiment 3. Means Z-scores, standard errors (SE), and results from paired-sample t-tests (including Cohen's *d*) are reported for each creativity measure (*$p < .005$).

Experiment 3								
Active				Placebo				
Creativity	N	Mean	SE	Mean	SE	*t*	*p*	*Cohen's d*
Convergent	27	0.050	0.177	0.103	0.192	0.29	0.773	0.056
Fluency	27	−0.031	0.194	0.163	0.170	1.32	0.198	0.254
Originality	27	0.187	0.161	0.009	0.204	1.35	0.189	0.259
Ratio	27	0.316	0.152	−0.100	0.185	2.68	0.012*	0.518

Note: * = p < .05.

differentially influenced specific creativity components. Post hoc comparisons indicated that participants in the active condition scored significantly higher on the originality/fluency ratio ($M = 0.316$, $SD = 0.78$) than those in the placebo condition ($M = -0.100$, $SD = 0.95$), $t(26) = 2.68$, $p = .012$, $d = 0.52$. No significant differences emerged for fluency, unweighted originality, or convergent thinking ($ps > 0.18$). These results replicate the null effects for convergent thinking observed in Experiments 1 and 2. Descriptive statistics of Z-scores and full test results are presented in Table 4.

Dose guess (active/placebo/not sure) showed no main or interaction effects in 2 × 4 × 3 RM-ANOVAs: $Fs \leq 1.149$, $ps \geq 0.340$ (details in Supplement). Controlling for dose guess reduced the Condition × Score-type effect to non-significance, consistent with overlap between condition and expectancy once blinding broke at Block 2. Correlations between originality-ratio change (placebo – active) and perceived strength were non-significant ($|rs| \leq .212$, $ps \geq 0.228$).

5.3.3. Order effects

Adding Block Order (active first vs. second) in a 2 × 2 × 4 mixed RM-ANOVA: no main effect of Block, $F(1, 25) = 0.052$, $p = .821$, $\eta p^2 = 0.002$; no Condition × Block, $F(1, 25) = 0.194$, $p = .663$, $\eta p^2 = 0.008$; no three-way interaction, $F(3, 25) = 0.066$, $p = .978$, $\eta p^2 = 0.003$. The Condition × Score-type effect was marginal, $F(3, 78) = 2.679$, $p = .053$, $\eta p^2 = 0.097$, likely underpowered given the small *n* and added factor.

5.4. Discussion Experiment 3

Experiment 3 aimed to clarify inconsistencies between Experiments 1 and 2 using a within-subject cross-over design with adequate statistical power (N = 27, based on a priori power analysis for medium effects). The results partially replicated earlier findings: originality-to-fluency ratio was significantly higher in the microdosing condition, aligning with effects observed in Experiment 1. This consistency across studies and task paradigms suggests a potential, albeit selective, impact of microdosing on the *quality* of creative responses rather than their quantity. Importantly, the effect did not appear to be driven by participants' beliefs about their condition allocation.

However, other key findings from Experiment 1—such as effects on unweighted originality—were not replicated, and convergent thinking remained unaffected. This again points to the possibility that microdosing's influence on creativity is narrow and unreliable. Moreover, blinding broke down during the second block, and participants reported significantly stronger subjective effects under the active condition, raising concerns about blinding efficacy —particularly in the later sessions (see Supplement S5.6). However, the non-significant interaction is unsurprising: once blinding deteriorated at Block 2, participants' condition and dose-guess became highly aligned, leaving little unique variance to detect moderation. This mirrors findings from the self-blinding microdosing trial by Szigeti et al. (2021), where effects attenuated after controlling for dose guess. To probe subjective influences further, we correlated change in the originality ratio (placebo–active) with perceived drug-strength ratings at each block; correlations were non-significant, suggesting subjective strength did not drive the creativity results, although small residual biases cannot be ruled out.

The sample in Experiment 3 also differed demographically: participants were older, mostly working professionals, and nearly all had prior psychedelic experience. These factors, combined with the small sample size and task variation, may have influenced both sensitivity to the drug and outcome variability. Together, the results suggest that microdosing may produce modest, specific effects under certain conditions, but these are not robust across samples, doses, or creativity metrics.

To address the limitations of small sample sizes, inconsistent findings, and possible confounding variables, we next conducted a pooled mega-analysis across all three experiments to examine the overall pattern of results with increased statistical power and more precise control over moderating factors.

6. Mega-analysis

6.1. Rationale

Given the inconsistencies and modest effect sizes observed across Experiments 1–3, we conducted a pooled mega-analysis to increase statistical power and reduce heterogeneity. This exploratory approach allowed us to re-examine the central hypothesis—that microdosing enhances creative performance—using a combined dataset with improved sensitivity to subtle effects.

Creativity measures that overlapped across the experiments and were collected at comparable time points were aggregated and re-analyzed using both frequentist and Bayesian frameworks. This enabled a more robust assessment of potential effects while accounting for key covariates such as age, gender, weight, relative dose size, prior psychedelic experience, subjective drug strength, and participants' dose guess regarding their condition assignment.

The aim of the mega-analysis was to test the overall effect of microdosing on creativity with greater statistical confidence, it also allowed us to explore whether individual differences and contextual factors may moderate these effects—offering insight into the conditions under which microdosing might exert cognitive benefits.

6.2. Method

6.2.1. Data overview and preprocessing

To increase power and assess consistency, we pooled data from corresponding time points across the three experiments: the 6th dose (Acute 2) in Experiment 1, the 6th dose (Acute 1) in Experiment 2, and the 7th dose (block 1) in Experiment 3. This allowed for a between-subjects comparison across all datasets. Only overlapping creativity metrics—fluency, originality, originality-to-fluency ratio, and convergent thinking—were included. Prior to integration, all dependent variables were z-scored within each study to address scaling differences.

6.2.2. Participants

For the mega-analysis, we pooled individual-level data from the first 3 weeks of dosing across all three studies (i.e., the acute time point closest to the 6th/7th dose: Acute 2 in Experiment 1, Acute 1 in

Experiment 2, and Block 1 in Experiment 3). This approach allowed inclusion of participants who completed the relevant acute assessment even if they did not attend later sessions, thereby reducing attrition bias relative to previous designs. In total, we pooled N = 175 participants prior to screening (Experiment 1: n = 61; Experiment 2: n = 71; Experiment 3: n = 43). After pre-specified exclusions—3 participants reported concomitant psychoactive drug use and 1 missed more than two scheduled doses—the final mega-analysis sample comprised N = 171 for the divergent-thinking outcomes (86 active psilocybin; 85 placebo). This pooled dataset includes 24 additional participants who were not part of the individual trial analyses because their subsequent sessions were incomplete but their acute-time-point data met inclusion criteria. The sample included 88 females. The mean age was M = 27.22 years (SD = 7.40). Participants had a mean weight of M = 70.20 kg (SD = 7.45) and a mean BMI of M = 23.55 (SD = 10.35). The same sample was used to examine the subjective drug effects. Convergent-thinking measures were available for a subset of n = 138 participants (71 females). Their mean age was M = 27.30 years (SD = 7.60), mean weight M = 60.68 kg (SD = 11.26), and mean BMI M = 23.56 (SD = 11.54).

6.2.3. Main analyses

First, the subjective microdosing effects were analyzed with $\chi 2$ test and independent sample t-tests. Since psychedelic effects are thought to be highly dose-dependent, we examined to what extent increments in dose across trials interacted with subjective microdosing effects. The subjective strength of microdosing in the active condition was examined across the 3 trials with a one-way ANOVA. The experimental trial was entered as the between-participant factor and subjective dose strength as the dependent variable. The main goal of the mega-analyses was to assess possible differences in the four creativity scores (e.g., a convergent thinking, fluency, originality, and the originality ratio) between the two conditions (e.g., placebo vs active microdose) at a single time point (after the 6th/7th dose). The data was analyzed using four independent sample t-tests corrected for multiple comparisons (Bonferroni correction $p \leq .013$). In addition to standard statistical methods, we calculated Bayesian (posterior) probabilities associated with the occurrence of the null [p (H0|D)] and alternative [p (H1|D)] hypotheses for each analysis. To estimate Bayesian probabilities, we implemented the procedure previously implemented by Masson (2011).

6.2.4. Exploratory analyses

To determine to what degree subjective effects and demographic factors interact with the creativity scores, we performed a set of exploratory analyses. First, we explored the effect of relative dose size on outcome measures considering that most existing psychedelic trials administered psilocybin on a weight-adjusted basis (Garcia-Romeu et al., 2021). To do so, regression analysis was run between the adjusted dose size (dose size/weight of participant) and each of the four dependent measures. Secondly, we assessed effect of subjective and demographic factors on outcome measures. The data were entered in a linear hierarchical regression with each of the four creativity scores entered separately as the modeled variable. In the first step, nuisance variables were entered in order to control for their variance (i.e. *Creativity index* = b_0 + (b_1 × *age*) + (b_2 × *gender*) + (b_3 × *weight*) + (b_4 × *experimental trial number*) + (b_5 × *drug strength*) + (b_6 × *dose guess*). In the second step the condition (active vs. placebo) was included as a regressor.

6.3. Results

6.3.1. Subjective effects

First, the differences in subjective drug effects were examined. Independent samples t-tests showed that the active condition (M = 22.29, SD = 25.64) and placebo condition (M = 20.9, SD = 25.32), t (169) = 0.355, p = .723), had comparable ratings of microdosing strength at this point of experimental procedures. The chi-square analysis of dose guess regarding condition allocation was also not significant (X^2 (3, N = 158) = 4.302, p = .231). The null result suggests that the blinding procedure was successful at this time point (6th/7th dose) even after increasing statistical power. Next, the subjective strength of microdosing was examined across the three experiments. As could be anticipated the one-way ANOVA was significant (F (2,83) = 1.034, p = .029), indicating that subjective drug effects increased with higher dose.

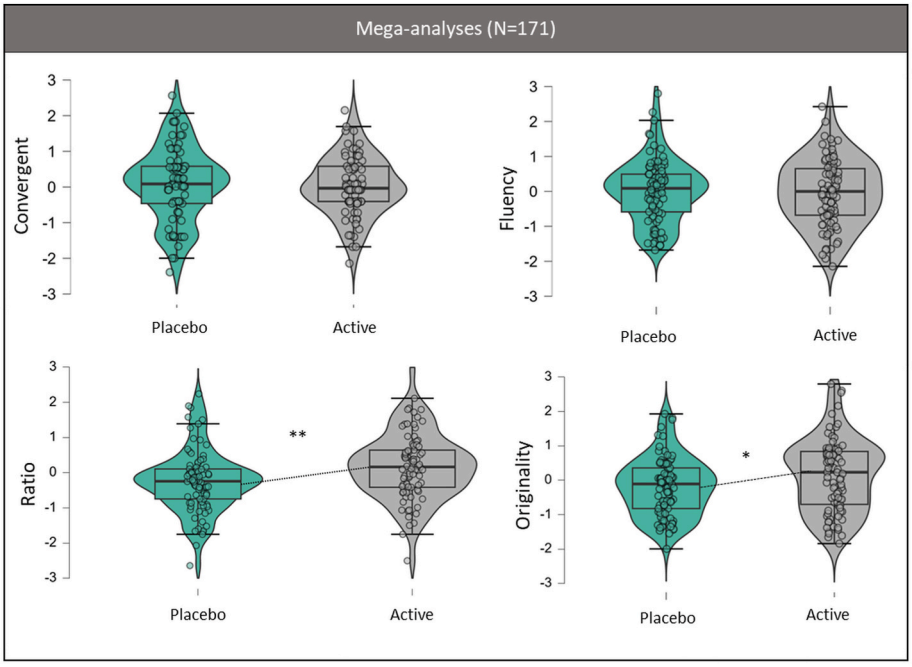

Fig. 4. *Mega-analyses.* Mean standardized (Z) scores for divergent and convergent thinking measures in Experiment 3 and the mega-analysis, *plotted by condition (active psilocybin vs. placebo).* Scores include fluency, flexibility, originality (PCT-d), originality ratio (AUT), and convergent thinking. Error bars represent standard errors of the mean. Asterisks denote statistically significant differences between conditions based on Bonferroni-adjusted thresholds ($p < .0125$*, $p < .001$**).

6.3.2. Divergent and convergent thinking

Independent-samples t-tests showed non-significant differences between the active (M = - 0.074, SD = 1.01) and placebo (M = 0.056, SD = 0.97) condition for the fluency score, t (168) = 0.864, p = .389, with Bayes factor indicating moderate evidence towards the null effect, BF01 = 4.722). The originality score in active condition (M = 0.15, SD = 1.07) and placebo condition (M = −0.19, SD = 0.85) was initially significant, t (169) = 2.28, p = .024, d = 0.349, *but* Bayes factor indicated only anecdotal evidence for the effect, BF10 = 1.25). Finally, the condition difference for the originality ratio was significant even after correcting for multiple comparisons, t (166) = 0.723, p = .002, d = 0.483, with participants in the active microdosing condition scoring higher (M = 0.22, SD = 1.03) than participants in the placebo condition (M = −0.245, SD = 0.89) and Bayes factor showed relatively strong evidence for the effect, BF10 = 9.902). The result for convergent scores showed that there was not a significant difference between the active microdosing condition (M = 0.024, SD = 0.852) and placebo (M = 0.056, SD = 1.05), t (136) = 0.197, p = .844, d = 0.034). Bayes factor indicated moderate evidence towards the null effect, BF01 = 5.46 (Fig. 4).

6.3.3. Exploratory analyses

The regression with adjusted dose size replicated previous analyses and showed that relative dose size (dose/participant's weight) predicted the originality ratio (F (1, 159) = 9.24, p = .003, R^2 = 0.055) with Bayes factor indicating strong evidence for the alternative hypothesis, BF10 = 11.24. Yet, as compared to the previous analyses the result indicated that relative dose size significantly predicted the unweighted originality score, (F (1, 159) = 7.39, p = .007, R^2 = 0.04), even after Bonferroni correction with Bayes factor indicating moderate evidence for the effect, BF10 = 4.91). This result suggested that a higher microdose may be required for heavier participants to show effects for unweighted originality. The result for the fluency score was not significant (F (1, 159) = 0.07, p = .78, R^2 < 0.001), with moderate evidence for the null hypothesis, BF01 = 5.69; as well as result for convergent score (F (1, 138) = 0.01, p = .78, R^2 < 0.001) with moderate evidence for null effect, BF01 = 5.39.

Furthermore, the hierarchical linear regressions indicated that demographic and subjective drug effects did not significantly predict any of the four creativity scores in the first step of the analyses, R^2s < 0.049, Ps > 0.062. These results indicate that drug effects and demographic variables did not significantly predict creativity scores alone. When the drug condition was added as a predictor, the full model became marginally statistically significant for unweighted originality, (R^2 = 0.117, p = .015) and originality ratio (R^2 = 0.178, p < .001) but did not improve the model for convergent score and fluency score, R^2s < 0.095, Ps > 0.593. These results overall corroborate previous t-test and regression analyses, see Supplementary materials for the complete output (S.6.2 and S6.3).

7. Discussion

This study aimed to systematically investigate the effects of psilocybin microdosing on creativity, using standard measures of divergent and convergent thinking. While initial evidence from Experiment 1 suggested that microdosing might enhance aspects of divergent creativity—specifically originality and the originality ratio—these findings were not consistently replicated in Experiment 2. In Experiment 3, which employed a more statistically powerful within-subject crossover design, partially replicated the effect on the originality ratio but failed to reproduce effects on unweighted originality. While the individual trials showed mixed results, the pooled analysis revealed reliable effect of microdosing on the originality ratio—a metric reflecting the quality of creative responses relative to their quantity. These effects were present even after controlling for dose-guess and subjective strength biases and demographic factors, suggesting that subjective effects did not account for these results alone. No effects were found on fluency, unweighted originality, or convergent thinking.

7.1. Effect of microdosing on divergent creativity

The effect of microdosing on originality ratio appears particularly relevant to the hypothesis that psychedelic states enhance cognitive flexibility (Carhart-Harris and Nutt, 2017; Prochazkova and Hommel, 2020). During divergent thinking tasks, common responses are typically generated first, with more original ideas emerging later in the process (Beaty and Silvia, 2012; Johns et al., 2001; Phillips and Torrance, 1977). This phenomenon, known as the serial-order effect in creativity, is thought to reflect a broader spread of activation within semantic networks (Kenett, 2018; Mekern et al., 2019). Common associations are more readily accessible in the semantic hierarchy because they are familiar and easily retrieved from long-term memory. In contrast, generating original responses often requires a novel, symbolic recombination of existing knowledge. Accessing such remote associations relies more heavily on executive functions to navigate less obvious links within the semantic space (Gilhooly et al., 2007; Vartanian et al., 2020). Computational models of creativity suggest that original ideas are formed through the deconstruction of objects into sub-components, or object feature maps (Mekern et al., 2019). For example, identifying "roundness" as a shared feature among apples, balls, and balloons enables novel associations across distinct categories. These overlapping features facilitate connections between seemingly unrelated concepts. As such, retrieval from long-term memory plays a vital role in generating divergent but relatively common ideas (e.g., using a brick as a chair, using a brick as a weapon) which are represented by the fluency and flexibility scores in AUT. On the other hand, generating original ideas requires a higher spread of activation within the semantic networks (e.g., using a crushed brick powder as a sunblock; using a brick as a prisoner's anchor). Such ideas indicate high cognitive flexibility, wherein broader networks of feature representations are activated simultaneously (Hommel, 2015).

Given that psychedelics have been theorized to relax high-level priors and broaden associative thinking (Carhart-Harris and Friston, 2019), the originality ratio may be especially sensitive to subtle cognitive shifts induced by microdosing. These effects can be understood within the REBUS framework, which posits that psychedelics loosen hierarchical constraints, enabling bottom-up sensory inputs and unconventional associations to influence cognition. Increased network flexibility and disruption of canonical functional hierarchies may enhance access to abstract or remote ideas (Mason et al., 2019). Unlike higher doses that can impair task engagement, microdosing may induce a mild cognitive disinhibition that facilitates creativity without overwhelming executive control.

7.2. Previous studies

Such findings are congruent with previous studies indicating positive yet limited effects of high doses of psychedelics on divergent thinking (Mason et al., 2021; Mason et al., 2019). For instance, Zegans and colleagues (1967) conducted a placebo-controlled study with a low dose of LSD and observed that participants in the LSD condition showed more original responses as compared to participants in the placebo condition. Similarly, Frecska et al. (2012) compared the performance on the Torrance task (divergent thinking task) between ayahuasca users and participants without recent psychedelic use and reported that Ayahuasca increased the number of highly original solutions, while other aspects of creativity (fluency and flexibility) were unaffected.

On the other hand, the current findings partially diverge from previous double-blind microdosing studies, which have largely failed to detect objective cognitive benefits (e.g., Cavanna et al., 2022; Murphy et al., 2024). The differences may stem from key methodological advancements in our study, including timing of the measurements of divergent creativity, larger sample (N = 171) and longitudinal design.

As mentioned, lack of power may lie behind the absence of creativity effects seen in the laboratory studies as subtle microdosing-induced effects may require larger sample sizes to be detectable (Murphy et al., 2024). Moreover, the originality ratio was proposed to be a more robust indicator of cognitive flexibility than raw fluency or flexibility, which was not captured in previous microdosing research. Finally, as shown in the mega-analysis, relative dose (dose/weight) predicted the originality/fluency ratio and unweighted originality suggesting that heavier participants may require a larger microdose to see effects. Thus, controlling for dose guess and demographic confounds, and factoring in relative dose, our results provide a more nuanced understanding of when and how microdosing may selectively enhance creative thinking.

7.3. Ecological validity of creativity measures

Our creativity outcomes rely on tasks that target complementary pieces of the creative process—divergent idea generation (AUT) and convergent/insight problem solving (RAT-like/PCT)—rather than "creativity" as a single ability. This separation is useful because real projects often require both modes at different moments (e.g., exploring many options, then homing in on a workable solution), and it lets us test which component a manipulation like psilocybin microdosing might actually shift (Guilford, 1967; Mednick, 1968; Prochazkova and Hommel, 2020).

An open question is how well these lab-based tasks translate to everyday creativity. Meta-analytic studies typically report small-to-moderate associations (about $r \approx 0.20–0.35$), however some measures perform better than others (Jauk et al., 2013; Kim, 2008; Said-Metwaly et al., 2022). For example, in a comparison of three commonly used tests (RAT, AUT, and TTCT), only AUT scores predicted expert-rated creativity in a product-design context (Kwon et al., 2017). Crucially, quality-focused indices—such as originality ratings, weighted originality, or semantic-distance approaches—tend to show stronger ecological validity than raw fluency or flexibility counts (Silvia et al., 2008; Jauk et al., 2013; Beaty & Johnson, 2021). In line with this pattern, our effects emerged on originality-weighted metrics (originality/fluency ratio; dose-adjusted originality), suggesting potential real-world relevance while underscoring that laboratory tasks capture components—not the entirety—of everyday creativity. Future studies should triangulate lab scores with ecologically grounded outcomes (e.g., the Creative Achievement Questionnaire, Inventory of Creative Activities and Achievements, the Biographical Inventory of Creative Behaviors) to assess transfer to real-life creativity more directly.

7.4. Subjective effects

Regarding the results on subjective effects we found that repeated microdosing was overall well-tolerated. No adverse psychological or physical effects were reported. Subjective drug effects were shown to be dose dependent and diminished over dosing period, independently of experimental condition. Prominent placebo effects were found in all three trials and placebo effects were especially pronounced for those with previous drug experience (in Experiment 1). These effects could be interpreted as a by-product of state-conditioning account of placebo effects (for review please see Schwarz et al., 2016). Effective drugs can be considered a stimulus that creates a particular internal state that researchers consider responsible for the impact of the drug on personal experience and behavior (Büchel et al., 2014). Through accumulating experience with a drug and its effects, the intake of the drug will be accompanied by particular expectations of these effects, which through response conditioning may induce the same or a similar psychopharmacological state to the one that intake of the actual drug would create. In other words, expectations need not be interpreted as creating artifacts, but they may come as potent as the real drug effects.

7.5. Risks associated

Moreover, it is important to weigh potential risks alongside the modest benefits observed here. Although no major adverse effects were reported in our trials, prior work documents some negative psychological side-effects in microdosing, such are nervousness/anxiety, occasional jitters/overstimulation, and tension and some trials note confusion at higher "micro" doses (Bershad et al., 2019; Hutten et al., 2020; Molla et al., 2023; Ona and Bouso, 2020). While our findings indicate selective and small effects on creativity, this risk–benefit balance still warrants particular caution outside controlled research settings.

Further consideration should be given to the task in hand and where people sit on the flexibility–stability continuum at baseline. Theories of cognitive control and creativity emphasize an inverted-U relation: too little flexibility yields rigidity, whereas too much can erode goal maintenance, increase distractibility, and impair performance (Cools and D'Esposito, 2011; Hommel, 2015). Tipping the balance on the flexibility–stability continuum may occasion symptoms in vulnerable individuals (e.g., personal or family history of psychosis) (Johnson et al., 2008; Schenberg, 2018). If so, individuals already high in baseline flexibility (e.g., high absorption or schizotypy) may be pushed beyond the optimal zone even at low doses—a possibility consistent with trait-based moderation of psilocybin responses (Studerus et al., 2012). Based on these model, heightened flexibility at the extreme could manifest as apophenia or referential thinking—perceiving meaningful connections in unrelated events Kapur, 2003; Eckblad and Chapman, 1983) and if intensified, this can foster excessive superstition, megical thinking or suspiciousness. While such cases are rarely documented even at large-doses, in practice, careful screening (e.g., for personal/family psychosis risk) are advisable when evaluating putative cognitive benefits (Hartogsohn, 2016; Johnson et al., 2008).

7.6. Limitations and future directions

This study has several limitations. First, although the studies were double-blind, the semi-naturalistic administration of microdoses limited control over timing and dosing accuracy. While fresh truffle doses were post-hoc analyzed, we could not control for alkaloid degradation over time or confirm participant compliance beyond self-report. Moreover, our results pertain specifically to psilocybin microdosing and should not be generalized to other agents without direct evidence. Future work should test whether effects on divergent and convergent thinking generalize or dissociate across compounds with different pharmacology—e.g., serotonergic psychedelics such as LSD, which differs from psilocybin in binding kinetics and potency (Nichols, 2016). Extension to non-classical agents sometimes "microdosed" in the community (e.g., MDMA) should be treated as a separate empirical question given distinct mechanisms and safety considerations Lea et al. (2020); Nichols (2016); Ona and Bouso (2020) Secondly, the sample predominantly included individuals with prior psychedelic experience and we lacked consistent measurements of years of education, race/ethnicity, and IQ (or validated proxies) across studies, limiting assessment of representativeness and moderation by sociocultural or cognitive factors. Although Experiments 2 and 3 broadened age range and backgrounds beyond a student sample, future trials should pre-register and collect standardized demographic/cognitive measures, oversample underrepresented conditions, and formally test moderation by education, culture, and baseline cognitive ability. Future research should aim for fully lab-controlled dosing protocols with chemically standardized substances and consider pre-selecting naïve participants to minimize conditioning biases. Neuroimaging studies could help uncover whether observed behavioral effects correspond to changes in functional connectivity, particularly within the default mode and executive control networks. Finally, larger, pre-registered replications are needed to determine the robustness and boundary conditions of the effects reported here.

CRediT authorship contribution statement

Luisa Prochazkova: Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Josephine Marschall:** Investigation. **Michiel van Elk:** Writing – review & editing, Supervision, Project administration. **Ben D. Rifkin:** Project administration, Data curation. **Neil R. Schon:** Investigation, Data curation. **George Fejer:** Project administration, Investigation. **Martin Kuchar:** Validation, Formal analysis, Data curation. **Bernhard Hommel:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of generative AI and AI-assisted technologies in the writing process

Statement: During the preparation of this work the author(s) used ChatGPT in order to improve grammar and readability. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to thank the Microdosing Institute and Psychedelic Society of The Netherlands for providing us with the opportunity to run the experiments at several of their events as well as MagicTruffles.com for donating the truffles to participants. Furthermore, we would like to give a special acknowledgment to Dr. Zsuzsika Sjoerds for her invaluable help and advice through-out the study and Donatella Fiacchino for her valuable assistance with data collection. Finally, we would like to acknowledge Katerina Hajokova, Pascal Lempe, Maria J. Maraver, Dominique P. Lippelt, Lorenza S. Colzato, Samo Zilinicik, Archisman Dash, Eliska Prochazkova and Kenny Elteren for their help in carrying out the experiment. This research was partly funded by an Advanced Grant of the European Research Council (ERC-2015-AdG-694722) to BH, and by the MICR (grant no. VI20172020056) to MK.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuropharm.2025.110732.

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