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Mapping the phenomenology of intranasal 5-MeO-DMT in psychedelic-naïve healthy adults

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5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT) is a naturally occurring psychedelic tryptamine. Plants containing 5-MeO-DMT have been used throughout history, and in recent years both synthetic and toad-derived 5-MeO-DMT use is being increasingly reported in naturalistic settings as well as clinical research. However, its subjective effects are not well characterised, and no qualitative research studies have been published to date. In this study, 32 psychedelic-naïve healthy participants from a double-blind, randomised, placebo-controlled, phase 1 trial of the escalating doses of a proprietary formulation of intranasal 5-MeO-DMT (BPL-003) were interviewed using the microphenomenology method shortly after dosing sessions. Microphenomenology is a qualitative research method well-suited to elucidating how subjective effects of this short-acting psychedelic unfold over time. Detailed qualitative and quantitative analysis of interview transcripts revealed a generic time-course of subjective effects, with rapid onset peaking at 8–15 min and gradual return to baseline over 45–60 min. The overall intensity of effects increased with dose and the doses tested were generally well tolerated. 5-MeO-DMT has a distinctive profile of subjective effects relative to published reports of other psychedelics, with a short duration of action, relative lack of visual effects, strong emotional or bodily experiences and the potential to elicit therapeutically relevant content, such as emotional breakthroughs and personal insights. These findings inform therapeutic applications, participant preparation, and future research on 5-MeO-DMT.

Keywords 5-MeO-DMT, Microphenomenology, Subjective experience, Psychedelics, Qualitative interview, Natural language processing

5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) is a short-acting serotonergic psychedelic of the tryptamine class. It occurs naturally in the glands of the Sonoran Desert toad (*Incilius alvarius*), and in trace amounts in a numerous plant species[1]. 5-MeO-DMT is a serotonin (5-HT) receptor agonist with affinity for a variety of serotonin receptors, particularly 5-HT1A and 5-HT2A receptors[2,3]. Characterised by its rapid onset and short duration of action, 5-MeO-DMT is currently undergoing clinical development as a potential treatment for depression, substance use disorders and bipolar disorder[4,5].

Reports from epidemiological studies on individuals who use 5-MeO-DMT in ceremonial and recreational settings suggest that this substance possesses a unique pharmacological profile with distinctive subjective effects, such as rapid onset, short duration and profound alterations in consciousness, including mystical experiences and higher rates of non-dual experiences compared to other psychedelics, while producing minimal visual effects[6–10]. However, to date, no published studies have systematically investigated the subjective experiences elicited by 5-MeO-DMT in either clinical or non-clinical settings.

Psychedelic experiences are highly individual and personal, and quantitative measures often fail to fully capture the spectrum of people's experiences. Qualitative research methods, particularly those grounded in phenomenology, are well-suited for capturing the dynamic and temporal nature of subjective experiences. These approaches can provide valuable insights into the contents of altered states of consciousness elicited during psychedelic drug sessions. Growing evidence suggests that the quality and content of psychedelic-induced subjective experiences may contribute to their potential therapeutic effects[11–13], thus, a nuanced understanding of the phenomenology of psychedelic experiences is important[14]. Insight into the subject's lived experience can help identify factors that contribute to positive or adverse outcomes in psychedelic studies, as well as elucidate potential underlying psychological mechanisms[15–17]. Moreover, qualitative results can complement quantitative

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research by generating novel hypotheses to inform and improve future research and psychological support. Although the majority of psychedelic research to date has relied on quantitative measures and questionnaires, a few qualitative studies have yielded important insights into the therapeutic mechanisms of psilocybin[18–24], ayahuasca[25,26], LSD[27], ibogaine[28] and MDMA[29,30].

A large part of our subjective experience often remains below the threshold of what we spontaneously notice and recall[31]. Under the influence of psychedelics, subjects can experience radically altered thoughts, emotions, and sensations, which have been described as unusual but meaningful, and often partly ineffable or difficult to articulate verbally[32]. Therefore, techniques that enable subjects to become aware of multiple aspects of their subjective experience and facilitate more precise descriptions can contribute to a more comprehensive understanding of their experience. Microphenomenology is a qualitative method of semi-structured interview and analysis particularly well-suited for this purpose[1][33,34]. This method has been successfully applied to investigate subjective experiences elicited by another short-lasting psychedelic, DMT[35]. The microphenomenology interview technique employs careful prompts and questions to help subjects become aware of previously unrecognised details of their experience. This approach is thought to reduce subjective biases that commonly affect first-person reports[33]. By identifying common themes across participants, microphenomenology enables the construction of a general structure of the 5-MeO-DMT experience, which can be contrasted with other psychedelics.

This study is part of a double-blind, placebo-controlled, Phase 1, single ascending dose trial in psychedelic-naïve healthy participants, which characterised the pharmacokinetic and pharmacodynamic effects of 5-MeO-DMT (NCT05347849, registered 26/04/2022)[36,37]. The study aims to understand subjects' experience of 5-MeO-DMT's psychoactive effects, focusing on the phenomenology of the acute, inner experience. This report is limited to describing the 5-MeO-DMT experience; the findings of the placebo experiences will be reported elsewhere. The goal is to provide a comprehensive summary of 5-MeO-DMT effects in clinical settings, describing participants' experiences and the impact on them. We combine qualitative analysis of the interview transcript with quantitative analysis using unsupervised and supervised topic modelling.

Methods

Compliance with ethical standards

This trial was conducted in accordance with International Council for Harmonisation Good Clinical Practice guidelines and ethical principles that have their origin in the Declaration of Helsinki. Protocols were approved by the Medicines and Healthcare Products Regulatory Agency and an independent recognised NHS research ethics committee before eligibility screening. Written informed consent was obtained from each participant before any trial-related procedures were performed. Microphenomenology interviews were optional and required separate consent.

Trial participants

Fifty healthy adult volunteers, aged 25 to 55 years and naïve to psychedelics (i.e. subjects without prior lifetime experience of using psychedelics), were enrolled in the trial. Participants included both males and females and were recruited through online advertisements. Inclusion and exclusion criteria are listed in the Supplementary Information.

Trial design

This Phase I, double-blind, randomised, placebo-controlled, single ascending dose trial evaluated the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of intranasal BPL-003 (5-MeO-DMT benzoate salt, dry powder formulation; Beckley Psytech Ltd, Oxford, UK) at doses ranging from 1 to 12 mg in healthy participants who were psychedelic-naïve. For a detailed description of the study design see Rucker et al.[36,37]. Additionally, this article includes qualitative data from an extra open-label cohort of participants who received 12 mg of 5-MeO-DMT in a modified formulation (see Table 1).

Dosing day

During dosing sessions, a nurse and one psychedelic monitor were present to provide non-directive support and reassurance for participants. To ensure an optimal setting, dosing took place in a decorated room with a prepared playlist of relaxing music. Prior to dosing, participants were instructed to perform breathing exercises to facilitate relaxation.

For up to 90 min post-dose, participants and the psychedelic monitor rated overall subjective drug intensity. As soon as possible after the dosing session (usually approximately 2 h after dosing), consented participants took part in a one-on-one guided interview with one of two independent researchers trained in microphenomenology methods to discuss their psychedelic experience. After the interview, psychometric scales were administered to provide quantitative measures of the participant's psychedelic experience.

[1] Microphenomenology is a method developed by Claire Petitmengin and directly inspired by philosophical phenomenology. Petitmengin was herself a student of Francisco Varela, whose program of naturalized phenomenology explicitly sought to integrate rigorous first-person experiential investigation inspired by philosophical phenomenology with third-person scientific methods. Our use of "phenomenology" aligns with its meaning in the context of naturalized phenomenology and contemporary cognitive science, as exemplified by leading phenomenologists like Dan Zahavi and Shaun Gallagher who bridge philosophical and empirical work. It refers to the systematic study of subjective experience using methods specifically designed for that purpose and grounded in phenomenological principles.

Dose level (mg, or placebo equivalent)	Dose category	Number of participants dosed (BPL-003:placebo)	Number of participants consented for the interview	No interview	Interview in-person:online
1 mg	low	6 (4:2)	6 (4:2)	0	4:2
2.5 mg	low	6 (4:2)	0	6 (no interviewers available)	0:0
4 mg	low	7 (5:2)	7 (5:2)	0	3:4
6 mg	medium	6 (4:2)	5 (3:2)	1 (not consented)	5:0
8 mg	medium	7 (5:2)	6 (5:1)	1 (not consented)	4:2
10 mg	high	7 (5:2)	5 (5:0)	2 (not consented)	4:1
12 mg	high	6 (5:1)	6 (5:1)	0	3:3
12 mg (s)	high	5 (5:0)	5 (5:0)	0	5:0
Total		50 (37:13)	40 (32:8)	10	28:12

Table 1. Participants by dose level Interview was optional, 1 participant who had an active dose did not consent to it. The 12 mg (s) cohort was a modified formulation of 5-MeO-DMT, and was open-label.

Subjective drug intensity (SDI)

Participants and the psychedelic monitor rated the intensity of BPL-003 subjective effects using a Likert scale of 0–10, where 0 was 'definitely no effect' and 10 was 'the strongest effect imaginable'. The assessment was performed every 2 min for up to 90 min post-dose. If the trial participants were not responsive, a rating of 10 was recorded.

Microphenomenological interviews

The interviews were conducted either in person or via online video conferencing and audio recorded. Participants were asked about their personal experience during the dosing session, with the focus not limited to the effects of the drug itself, but open to any aspects of their experience that emerged. To facilitate recollection, interviewers had access to the participants' ratings of drug intensity over time on a Likert scale.

The interviews lasted for up to 60 min, but could be shorter if subjects felt they had fully described their experience. Microphenomenology is a semi-structured interview method that enables the collection of detailed subjective reports through guided recall and targeted questioning. The method is designed to guide subjects to mentally revisit a specific experience by reconstructing its sensory context, achieving a state of engaged recall indicated by observable markers such as present-tense speech, slowed verbal pace, and unfocused gaze. Interviewers' direct attention to the temporal sequence and process of the experience using questions focused on "how" rather than "what" ("How did you first notice that?", "How did that change develop?"), breaking down the experience into fine-grained sequential components ("What happened just before?", "And then?"). The interview explores experiential qualities through non-suggestive structural probes ("Can you describe that sensation?", "Where did you perceive that?"), avoiding leading questions while systematically mapping different dimensions of the experience. This method enables participants to describe subtle aspects of their experience that might otherwise elude questionnaires or remain unarticulated in open-ended self-reports. This method is described in detail by Petitmengin et al.[33].

Qualitative analysis

Audio recordings from the interviews were transcribed verbatim and any personally identifiable information was removed to protect participant confidentiality.

Microphenomenological analysis is described in detail by Petitmengin and colleagues[34,38]. The method is conceptually similar to other qualitative approaches in so far as it follows the stages of data reduction, data display and conclusion drawing/verification as described by Miles and Huberman[39], however is usually applied for very short experiences. Given that 5-MeO-DMT experience was 60–90 min, we used a microphenomenology-inspired method of analysis adapted to a longer duration experience. Pre-determined coding was not used in order to not constrain the rich subjective experience and to allow for the emergence of unexpected findings. Instead, an inductive approach was taken, where codes arise from the data in an open coding process. The analysis focuses on two key dimensions: synchronic and diachronic. The synchronic analysis explores particular features or aspects of the experience regardless of their temporal evolution. By contrast, the diachronic dimension relates to the progression or change of the experience as it unfolds over time.

Two researchers conducted a within-participant analysis to identify structures and categories emerging from the interview transcripts. The analysis involved chronologically re-organising the transcripts and identifying 'descriptemes', which are structural statements that capture minimal units of meaning. Related 'descriptemes' were then clustered together to form categories. Both researchers independently read all the transcripts and discussed the emerging structures and categories iteratively to ensure that no category was over- or under-represented. Any disagreements were resolved through discussion until consensus was reached. Finally, all authors reviewed and agreed upon the overall map of categories that emerged across all study participants.

Quantitative analysis

In addition to qualitative analysis, a quantitative analysis of the interview transcripts was performed using natural language processing (NLP) methods. The aim was to complement the qualitative insights with objective, data-driven findings about the prevalent themes and their temporal dynamics in the 5-MeO-DMT experience.

Data preparation
As a first step, all utterances spoken by participants were extracted from the interview transcripts, excluding interviewer speech. This yielded a corpus of 9,774 participant utterances across all interviews.

Sentence embedding
To convert the raw text data into a format suitable for computational analysis, the sentences were embedded into a high-dimensional vector space using a pre-trained Transformer language model. Specifically, we used NV-Embed-v2, a Transformer model that produces 4096-dimensional sentence embeddings[40,41]. As of October 2024, this model achieves state-of-the-art performance for open-source models of its size class on the Massive Text Embedding Benchmark (MTEB)[42]. The sentence embeddings capture high-level semantic content that enables meaningful comparisons and clustering of sentences by their meaning.

Topic modelling
Two complementary topic modelling approaches were applied to the sentence embeddings to extract key themes in the reported experiences: unsupervised topic modelling using dimensionality reduction, hierarchical clustering, and natural language labelling, and supervised topic modelling using semantic similarity to hypothesis-driven reference sentences. For each approach, both static modelling of participant sentences and dynamic modelling of the temporal evolution of topics were performed.

Unsupervised topic modelling
For unsupervised topic modelling, the high-dimensional sentence embeddings were first reduced to a 5-dimensional space using Uniform Manifold Approximation and Projection (UMAP), a non-linear dimensionality reduction algorithm that preserves local and global structure to facilitate effective clustering[43]. To identify meaningful clusters of semantically related sentences in UMAP-reduced embeddings, we then applied the Hierarchical Density-Based Spatial Clustering of Applications with Noise (HDBSCAN) algorithm, computing cluster membership probabilities for all sentences. The topic model was fit on the full 9,774 sentence corpus. Following a manual curation step to remove non-phenomenological clusters (e.g., conversational fillers), this process resulted in the identification of 28 distinct, content-relevant topics. Utterances not assigned to any cluster (outliers) were excluded from subsequent topic-level quantitative analyses. A detailed explanation of model parameters is provided in the Supplementary Information.

To create human-interpretable representations of the topics, both extractive and abstractive techniques were used. First, the c-TF-IDF algorithm was applied to a bag-of-words representation of the sentences (removing stop words, including only words in $>=2$ sentences, and including bigrams) to identify the most distinctive terms for each topic. Second, the Llama 3 70B large language model was used to generate concise natural language labels of $<=5$ words for each topic based on both the top c-TF-IDF terms and a set of representative sentences.

To investigate the temporal dynamics of different aspects of the 5-MeO-DMT experience, we leveraged the fact that participants rated the subjective intensity of drug effects every 2 min during dosing sessions. During interviews, participants recalled at which intensity level they experienced specific subjective effects. We checked the veracity of these recollections against the ground truth of their recorded intensity ratings. When the recollections were accurate, we used the recalled intensity ratings as temporal anchors to link the subjective effects described to specific time points in the dosing session, at 2 min resolution. Using this approach, a substantial portion of participants' utterances were linked to specific timestamps over the time course of drug effects. This enabled modelling the evolution of topic prevalence over time, providing insight into which aspects of the 5-MeO-DMT experience tend to occur in different phases.

Supervised topic modelling
Supervised topic modelling was performed by computing the semantic similarity (cosine similarity) between the sentence embedding of each participant utterance and the embedding of each predefined reference sentence. These reference sentences corresponded to key themes identified in the qualitative analysis (see the full list of reference sentences in Supplementary Materials). To quantify the expression of each theme per participant, the following steps were taken: (1) Cosine similarities between a participant's utterances and a given reference sentence were calculated. (2) Similarities below a threshold of 0.50 were discarded as irrelevant. (3) The remaining similarities (≥ 0.50) were normalised to a 0–1 scale (where 0.50 maps to 0 and 1.0 maps to 1). (4) The mean of these normalised, above-threshold similarities was calculated, yielding a single score per participant per reference theme. If a participant had no utterances above the threshold for a theme, their score was 0. To assess dose-dependency (as shown in Figs. S3 and 6), these participant-level scores were averaged across all participants within defined dose ranges (Low: 1–4 mg, Medium: 6–8 mg, High: 10–12 mg). These dose-dependent trends are presented descriptively to illustrate potential patterns.

Results

Baseline characteristics

40/50 (80%) of study participants were interviewed, 32 of which received 5-MeO-DMT, and 8 received placebo. 4 participants did not consent to the interview (3 placebo and one 6 mg 5-MeO-DMT) and no interviewer was available for the 2.5 mg cohort (see Table 1). Participants' demographics are in Table 2.

Qualitative analysis

The sample was stratified into low (1–4 mg), medium (6–8 mg), and high (10–12 mg) dose groups. Although the intensity of subjective effects generally increased with the dose across all experiential modalities, some participants who received low doses reported intense effects while some participants who received high or

Group/BPL-003 dose	Sex (N [%])		Race (N [%])				Age, years (mean [SD])
	Male	Female	Asian	Black/AA	White	Other	
Placebo (N = 13)	10 (77)	3 (23)	0	2 (15)	7 (54)	4 (31)	34 (8.0)
1 mg (N = 4)	4 (100)	0	0	1 (25)	3 (75)	0	34 (9.5)
2.5 mg (N = 4)	1 (25)	3 (75)	0	1 (25)	2 (50)	1 (25)	33 (10.1)
4 mg (N = 5)	4 (80)	1 (20)	0	1 (20)	4 (80)	0	30 (3.1)
6 mg (N = 4)	4 (100)	0	2 (50)	1 (25)	1 (25)	0	38 (7.4)
8 mg (N = 5)	4 (80)	1 (20)	1 (20)	0	4 (80)	0	40 (6.9)
10 mg (N = 5)	4 (80)	1 (20)	1 (20)	1 (20)	2 (40)	1 (20)	39 (9.3)
12 mg (N = 5)	2 (40)	3 (60)	0	1 (20)	4 (80)	0	31 (8.8)
12 mg (s) (N = 5)	1 (20)	4 (80)	0	1 (20)	4 (80)	0	37.8 (8.7)

Table 2. Demographics AA, African American; BMI, body mass index; N, number of participants; SD, standard deviation. 12(s) is a modified formulation of 5-MeO-DMT, but with an identical profile of subjective effects.

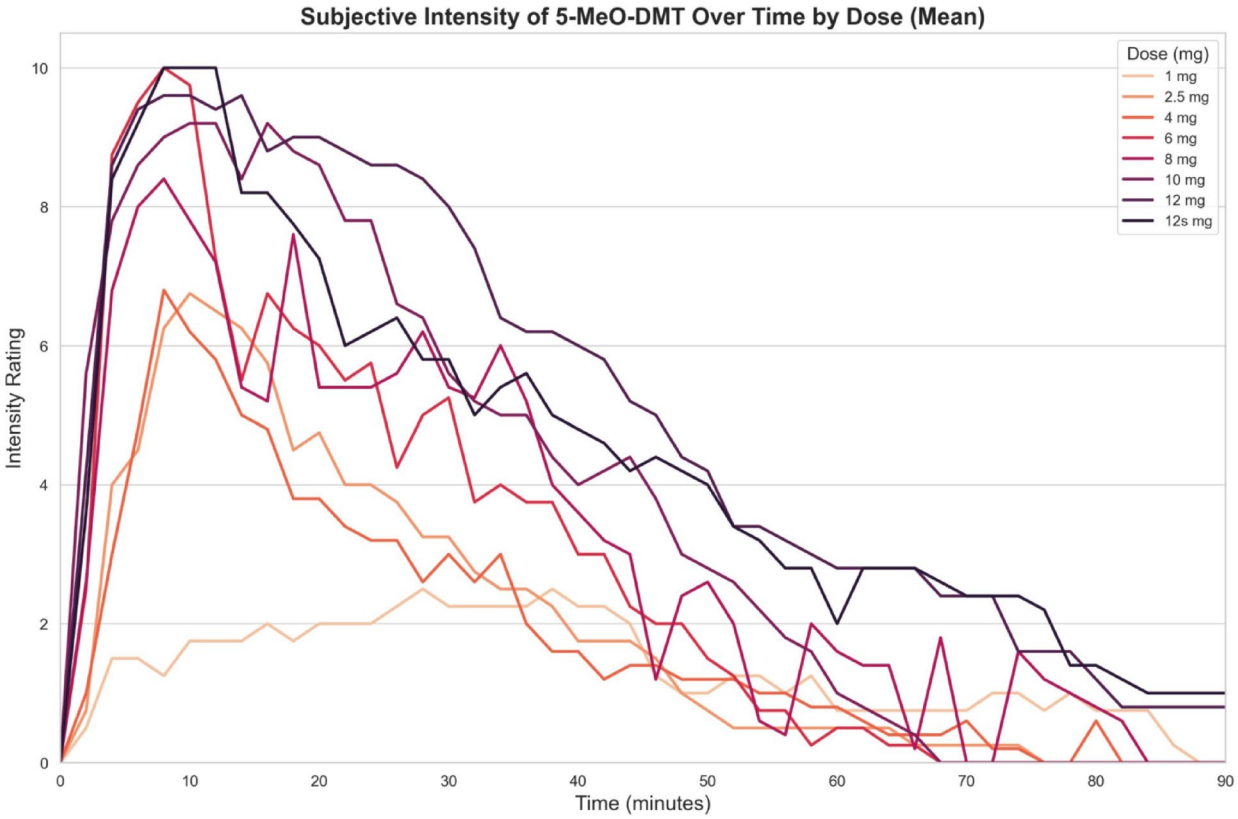

Fig. 1. Perceived drug intensity by dose of 5-MeO-DMT.

medium doses reported mild effects. Selected quotes from study participants illustrating these results, especially related to key elements relevant to improving the support of participants in future clinical studies, are included here and in the supplementary material (Tables S1–S5).

Time-course

The subjective effects reported using the SDI scale closely matched the sequence and cadence of effects described in the qualitative interviews. The time-course of experiences generally followed a consistent pattern, with initial effects noticed within 0–2 min, followed by rapidly increasing intensity from 2 to 8 min, peaking at 8–15 min. This was followed by a plateau of variable length, then dissipation of effects from 15 to 40 min, with some lingering effects for 40–90 min. Higher doses were associated with a slightly longer peak and more prolonged dissipation (Fig. 1). Consciousness-altering effects typically ended after 45–60 min, and individuals were lucid during the interview.

Themes

Several key domains were identified, including alterations in sensory and emotional experience, cognition, metacognition, arousal, and perceived relationships between self, others, and the environment (Fig. 2). Fig. 3 delineates how these themes unfold over time.

Onset of effects (typically within 0–2 min post-administration)

The first effects were sensations related to the administration of BPL-003, dissipating as psychedelic effects became salient. These sensations ranged in intensity across dose levels, most common was burning or stinging sensation, while some participants compared it to sensations of a salt spray, others described a blocked nose analogous to a cold.

> I felt the substance go into my nose and I felt it in the back of my nose. I didn't taste any chemical smell, there was no chemical taste or the smell or anything like that. It was just the feeling of a slight burning, just in the back of the nose… It was, I could notice it, but it wasn't painful… when I started to come up on to the experience, I didn't notice, I had no awareness of it. So, it only lasted until I was off of the experience… It was gone by the time I was coming down. -P4, 12 mg.

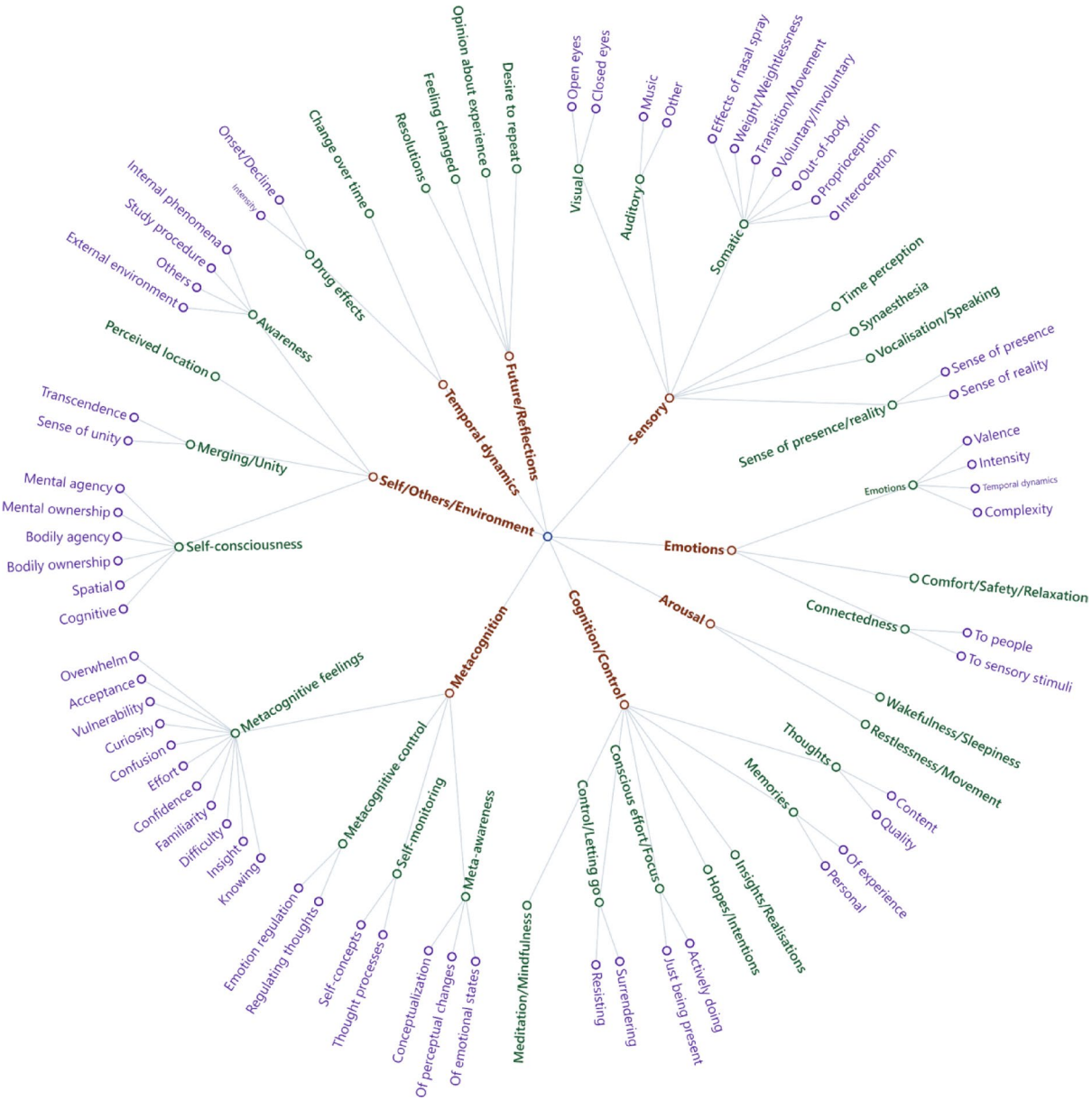

Fig. 2. Dendrogram of the themes extracted from qualitative analysis of interview transcripts.

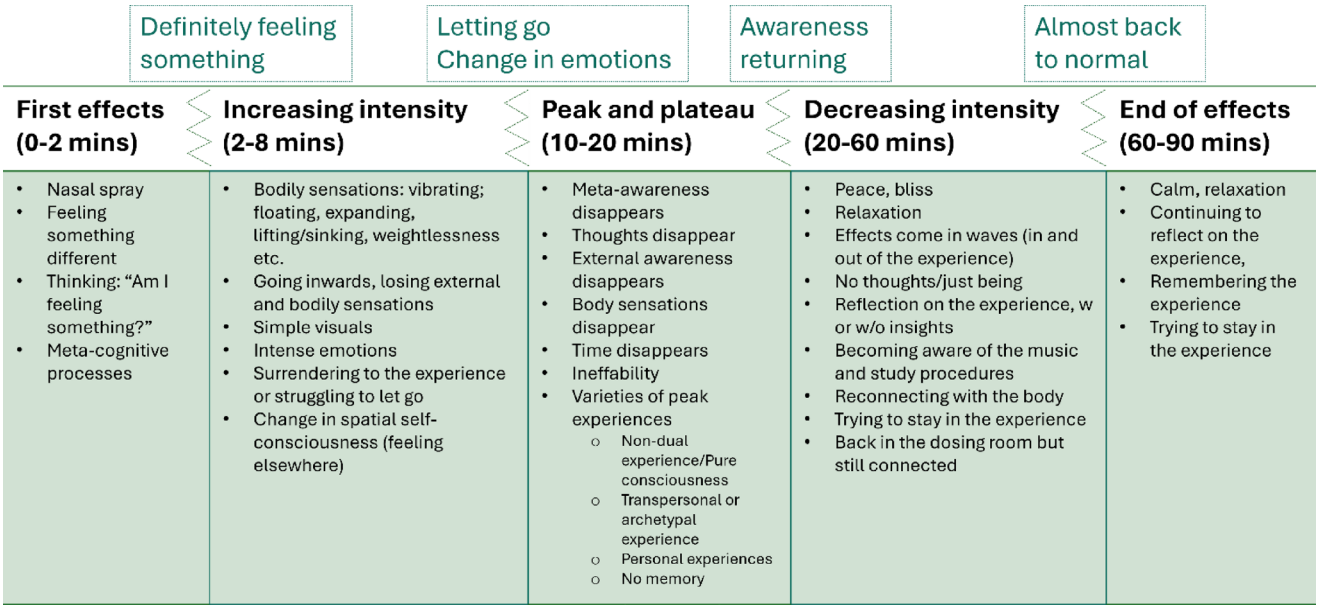

Fig. 3. Generic diachronic structure of 5-MeO-DMT experience.

> I felt a burning sensation in my nose, and it went quickly to my head. On the left part of the nose. Left part of the head, and it was burning as well inside. It lasted for a bit… I forgot to think about it when it kicked in. But still, I feel a bit uneasy on the nose. It's not bothers you, it's like something there. -P6, 8 mg.

For many participants, the first psychedelic effects were changes in bodily sensations, both interoceptive and proprioceptive, often more prominent at higher doses. Examples include sensations of floating, falling, drifting, loss of body strength, tingling, numbness, and waves of unusual sensations, such as warm feelings spreading through their bodies. Some participants experienced visual effects at high and medium doses, including changes in colour brightness or darkness, perceived movement of objects, and closed-eye geometric visuals or memories. Many noted the rapid onset of effects, which often took them by surprise.

> I instantly felt different. -P2, 12 mg.

> It was really fast. I started to feel really intense, and I saw the first part, it was the strongest part, the intense part. -P3, 12 mg.

Intensity increasing (2–8 min post-administration)

Most participants maintained awareness of their external environment, body, and perceptual changes, with some reporting heightened sensory perception. As psychedelic intensity increased, awareness of the external and internal generally diminished. Some felt transported elsewhere, like inside their body, a dark void, or the ocean. Changes in perceptions of bodily control were a prominent theme. A few participants described the sensations as if their mind, spirit or soul was separating from their body. For some, the experience of loss of control, changing boundaries, or complete dissociation was anxiety provoking, others found these sensations pleasant.

> In the beginning, my body was shaking. Like, my spirit wants to separate from my body and then my body was resisting because I was scared, I guess. But at some point, I was totally separated from my body. -P3, 6 mg.

> The best way to describe it without sounding terrifying is your soul basically leaving, or you think it's your soul or spirit leaving. You kind of feel that… You will totally start feeling lighter and moving away from your body. -P2, 12 mg.

At the start of the experience, lower doses produced positive emotions like contentment and relaxation. At higher doses, it was more common to initially experience anxiety and fear related to loss of control, changes in breathing perception, uncertainty, confusion, and overwhelming sensations and emotions. Many participants commented on the importance of the preparation and the reassuring presence of the psychedelic monitors. Strategies offered to reduce anxiety included breathing techniques, positive thoughts, reassurance from the psychedelic monitor, and trying to relax into the experience.

> I was absolutely shocked by the level [of the drug intensity I experienced]. H [psychedelic monitor] did a great job. And I think knowing that she's there really did make a massive difference. -P1, 12 mg (s).

> I think because of the pre-frame that we had before and we had a conversation yesterday, and it was explained that this is how the process would look like or how it would feel. Just be with it because you

are in a safe environment. And that was something that's quite important to me to know that I was in a safe environment and there were people there with me. So, letting go didn't feel too difficult. -P5, 10 mg.

Then I remember what she said toward the end of this: 'If you feel anything that you feel that's too much or is hard or anything, just let it go because it will pass'. Then I just decided: 'you are doing it right'. From that moment, I think I touched my belly or something. I was breathing and then I just relaxed because my head was like: 'you are not going to stop this because your body is going to start to do it by itself. Just don't pay attention so much on that. -P3, 8 mg.

Peak and plateau (Typically within 8–15 min post-administration)

The peak was defined by the highest intensity, often occurring in waves across emotional, physical, and perceptual domains. Lower doses predominantly affected emotions, while higher doses elicited mystical experiences, ego-dissolution, non-duality, void states, rebirth, connection to higher power, visions, re-living memories, and extreme emotions. Intense emotions and loss of external and bodily awareness were common. Time perception was universally altered, and experiences were often difficult to describe.

Emotions

Low doses produced relaxation and happiness. A few participants experienced increased anxiety or vulnerability. At higher doses, emotional intensity was remarkable, described as "immense", "really strong", and "on another level". As intensity plateaued or participants relaxed, positive emotions emerged.

I just started to feel different emotions. It's really hard to explain. I don't know if I can call it sadness or anger or fear or happiness. I don't know. I just felt some… all kinds of mixed emotions … and it was in waves. I don't know. I still don't understand it. I don't know what I felt. What I can say is that I felt intense feelings, so the highest I've been happy and the highest been maybe upset or the highest I've been whatever in the past, it was just intense. The intensity is all I can say. -P6, 12 mg.

The emotional phenomenology was dynamic and variable between individuals, with some experiencing a clear valence shift, others oscillating between emotions, and a few feeling multiple emotions simultaneously. Experiences ranged from raw emotions to those tied to visions or memories. One participant relived a sexual assault. Some felt previously repressed emotions and appreciated the experience despite its challenge.

Mainly sadness, actually. A lot of sadness came out, like pain… I was crying a lot. I think it might have been… I remembered really positive times when I felt loved which kind of made me sad because I don't always feel like that. And it was nice to know that and just start reflecting on that made me sad. -P6, 10 mg.

Self/other/environment

At the peak, most were only partially aware of their external environment. Those with strong experiences often completely lost awareness of their surroundings. With increasing dose, spatial self-consciousness was frequently altered, with the sense of self variably experienced as inside the mind, floating in a void, ocean or universe, or an all-white or all-black space.

One participant described possession by a strange energy. All others reported either aloneness or connection to a larger whole, in one case described as God. The feeling of connectedness manifested as unity, oneness, enhanced sensory and somatic connection, or stronger connection to self, others (present or not), archetypes. This was often accompanied by a sense of transcending time and space through vast expansion or extreme contraction.

That's probably the feeling of the expansion that I talked about with my mind expanding. I felt as though it wasn't just me in this room, I felt like I was thinking and feeling everything beyond that. Whether it was even beyond the world, and anything that I wouldn't have been, oh, I feel like I'm on earth. Felt like I was beyond even that towards, I don't know, beyond everything. -P4, 12 mg.

Even at high doses, a sense of self was generally retained, with only a few reporting complete dissolution of the sense of self. Others reported loss of bodily self-awareness, altered spatial self-consciousness, loss of agency, and absence of thought, but not complete ego-loss. Some at medium doses felt they could have gone further and were disappointed, while others were content retaining some self-control to navigate the experience.

Bodily sensations

With the intense experiences, bodily sensations disappeared almost entirely. With lower intensity of experiences, participants reported altered visual perception, various bodily sensations, including pleasurable, ecstatic feelings and synaesthesia-like experiences.

But at the same time being out of the body, it also felt, as I said, very bodily. Part of it was the breath. Very big deep breathing. I really let it just happen, just let it come through. Taking these big deep breaths, I felt very deep and I could feel my legs writhing, actually. And again, it never felt sexual, but it was like it was a sexual experience, kind of very physical… This was a feeling of incredible joy, a sensation that I was almost enveloped in beauty. -P1, 6 mg.

This feeling of just letting my body go and just being pulled from the chest, but the sensations are creating this whiteness, it's almost like I didn't have a body… everything was bright white, completely white just everywhere, and I think at that point, there was no bodily sensations- P1, 6 mg.

Cognition

At the peak, an absence of thoughts was frequently reported. At medium and low doses, thoughts were present but less clear, slower, and effortless. Several participants reflected on how rare and blissful this thoughtless state was. At high doses, some were unable to remember or describe the experience in words. Content ranged from pure emotion and sensation to memories of varying complexity.

The key cognitive theme was losing or relinquishing control through acceptance and surrendering. Some participants continued resisting throughout the peak while others were able to surrender, although many found this process challenging. It is important to note that it wasn't a conscious/cognitive resistance but often an automatic response to fear of loss of control. Those who struggled to surrender had more difficult experiences overall. At the peak intensity, most were able to relinquish control, especially upon realising the experience wasn't escalating further. After letting go, participants often felt relief and were better able to appreciate the experience or gain insights.

> I think it was scary, but after it was nice… It was about the intensity of the experience, when you don't have any control about what is happening to the body, this was the scary part of this… I remember that it was a bit in waves, [pause] because at some point I started to be scared again… when I enjoyed it was nice, it was going up and down with my feelings as well. [the feeling of happiness] was strong because I remember smiling. After all these strong feelings that were a bit scary and this fight, I think, I went to stop fighting, and enjoy the trip. It's when you started to feel this happiness, this peace… It was peaceful. It was- I feel happy and scary basically. It was really peaceful and really- I don't know. It was- because I remember my face is smiling at the same time that I have these strong feelings that I had. But, it's scary, peaceful, and happy, those were the three main things. -P3, 12 mg.

Metacognition

At higher doses, metacognition was minimal, mostly related to surrendering and avoiding resistance. Experiences were largely described as ineffable. At medium doses, metacognitive processes were frequently reported, with participants simultaneously experiencing effects while aware of perceptual and emotional changes and attempting to regulate thoughts. Common modulation strategies included positive thoughts, thoughts about family and friends, therapeutic touch, and breathing. This dual experiencer-observer role defined the medium dose sessions. The most common metacognitive feelings at high and medium doses were confusion and unfamiliarity compared to normal consciousness. At lower doses, some likened the experience to intense meditation or hypnosis.

> It's so hard to describe to someone well in words. It's one of those things where if someone said to you, who didn't know, describe love, you'd be like, I don't know how to describe love in words, you get the feeling, this was the feeling of this experience that you can't put into words. -P4, 12 mg.

Decrease of effects (15–40 min post-administration)

Effects diminished gradually, often in waves of decreasing intensity. As they subsided, participants regained self-awareness, bodily awareness, and awareness of their surroundings, feeling increasingly present. Some experienced lingering connectedness after the peak, towards the universe, loved ones, others, themselves, or their bodies.

Participants regained agency over mind and body as effects dissipated. Some continued allowing the experience to flow naturally, while others directed it by thinking of specific people or memories, returning to intentions, trying to manifest expectations or finding answers to existential questions. Others regained control to ground themselves through opening eyes, moving, or talking. Some attempted to extend the experience through breathing or thought suppression.

> I became aware again of the feelings. Before, I was in that period where I was beginning to feel like I wasn't aware of anything. That's when I noticed that I was thinking, I noticed I was starting to come back down, and I became aware again of my feeling. -P4, 12 mg.

The return of metacognition, like other cognitive processes, could be a distinct transition or gradual re-emergence with fluctuations. Participants shifted from being overwhelmed by intense emotions to regaining emotional and cognitive regulation capacity.

At lower doses or overall experience intensity, participants reported calmness and peace. At higher doses, most felt joy, happiness, calmness, and bliss. Some reported bittersweetness as the experience began to subside, wanting to remain longer in the altered state. Many reported gratitude for life, family, friends or the study team's support. Some continued experiencing strong or mixed emotions from the peak. Several cried, laughed, or smiled. Those with challenging experiences reported relief returning to normal consciousness. Some whose experience misaligned with expectations reported disappointment.

> I felt very at peace, like everything was right…I was just very content. -P4, 12 mg.

Participants continued experiencing altered body sensations and some visuals. They became aware of the music, which helped them relax or visualise.

End of consciousness altering effects (40–90 min post-administration)

As effects gradually subsided, participants reported increasing awareness of surroundings and returning to normal sensations. Nearly all felt relaxed, calm, and peaceful. They often continued reflecting on the experience or expressed disappointment about the lack of profundity (at lower doses or unmet expectations). Thoughts

turned to everyday matters like work, to-do lists, and post-session plans. Many thoughts about family, loved ones, or sharing their experience. Some simply relaxed in a meditative state with minimal mental activity.

> I expected to have a lot of questions in my head arise as I'm feeling things so I can try and look for answers and stuff, but weirdly enough, no questions, nothing in my head. -P2, 12 mg.

Reflections

Several participants spontaneously reported reflections on the experience. Many emphasized the importance of preparation and the psychedelic monitor's presence, appreciating the verbal and touch support. Several expressed a desire to repeat the experience, believing knowing what to expect would facilitate letting go and gaining more. Some reported feeling changed and gained future resolutions like spending more time with loved ones or learning meditation.

> I feel like I have a different perspective… It's nothing like you've ever experienced, so kind of feels there's more to things than [everyday concerns]. And I think for me that was reassuring… from the angle of worrying about things. So, I think if you were to use that experience to be like there were more… things bigger than your problems, your worries, your death, I think that might help you think more positively. Help you be more connected. So, it gives you perspective. -P1, 12 mg (s).

Several indicated prior experience with altered states, like meditation, was beneficial. Some reflected on the discrepancy between expectations and the actual experience. Lastly, a few commented on perceived therapeutic benefits and belief that 5-MeO-DMT therapy could help others, which is encouraging for further clinical development.

> It's just like, well the amount I did cry then, it did make you realise I found something down in there. You probably have an idea, but you don't realise it is going to come out like that. So, I could definitely see how it would benefit people with any sort of trauma or emotional problems. I felt it benefited me, even with that. So, obviously I got something positive from it, and once I got over that scary part, it became more in control, so like I said, emotional benefit. Yes, emotional benefit … Quite a profoundness really. -P6, 10 mg.

Quantitative analysis

In addition to qualitative analysis, we performed quantitative analysis using both unsupervised and supervised topic modelling techniques.

Unsupervised topic modelling

Static topic modelling of the interview transcript corpus using sentence embeddings, dimensionality reduction, clustering, and natural language labelling revealed 42 distinct topics in participant reports (Figs. 4 and S1). These topics, automatically labelled by a large language model, included themes such as visual patterns and colours, intensity of effects, physical sensations, emotions, and metacognitive reflections on the experience. Many of the topics identified through this unsupervised approach aligned with the themes extracted from the qualitative analysis (Fig. 2), providing quantitative support for the main experiential domains impacted by 5-MeO-DMT.

Importantly, the prevalence of certain topics exhibited a dose-dependent relationship. The frequency of sentences related to visual effects (e.g. "Visual hallucinations and geometric patterns"), positive emotions ("Feelings of happiness and joy"), and overall intensity and ineffability of the experience ("Intensity", "Difficulty explaining") showed a trend of increasing with higher doses (Fig. 5A). Conversely, sentences related to bodily relaxation, fear, and thinking anxiety, physical discomfort, and unawareness of drug effects were more prevalent in the low dose condition and seemed to decrease with increasing doses (Fig. 5B). These results corroborate the dose-dependent modulation of 5-MeO-DMT's subjective effects uncovered by the qualitative analysis. It is important to note that while the "Visual hallucinations and geometric patterns" topic was prevalent based on the frequency of visual terms used, the qualitative data indicate that these references largely pertain to elementary visual phenomena, such as changes in light or colour perception and simple patterns, rather than complex hallucinatory scenes characteristic of some other psychedelics.

Dynamic topic modelling, enabled by temporally aligning sentences with intensity rating timestamps, revealed how the prevalence of topics evolved throughout the course of the 5-MeO-DMT experience (Fig. S2).

Supervised topic modelling

Complementing the unsupervised approach, supervised topic modelling was performed by computing the semantic similarity of participant sentences to researcher-specified reference sentences describing key experiential themes (Figs. S3 and S4).

Discussion

This study provides the first systematic microphenomenological analysis of the acute subjective effects of 5-MeO-DMT in a clinical trial setting. Using microphenomenology interviews, we obtained detailed reports of participants' subjective experiences, revealing the rapid onset, short duration, emotional intensity, and personally meaningful and/or transcendental nature of 5-MeO-DMT experiences.

Key features included alterations in bodily sensations, sense of self, and the importance of "letting go" and surrendering to the experience. Challenging experiences, while difficult, also provided opportunities for emotional breakthroughs and insights. The dynamic nature of the experience, with varied and at times apparently conflicting emotions, was notable. Rapid change in the state of consciousness often produced initially fear and anxiety responses, sometimes resulting in resisting the experience. The intensity of the experience, particularly

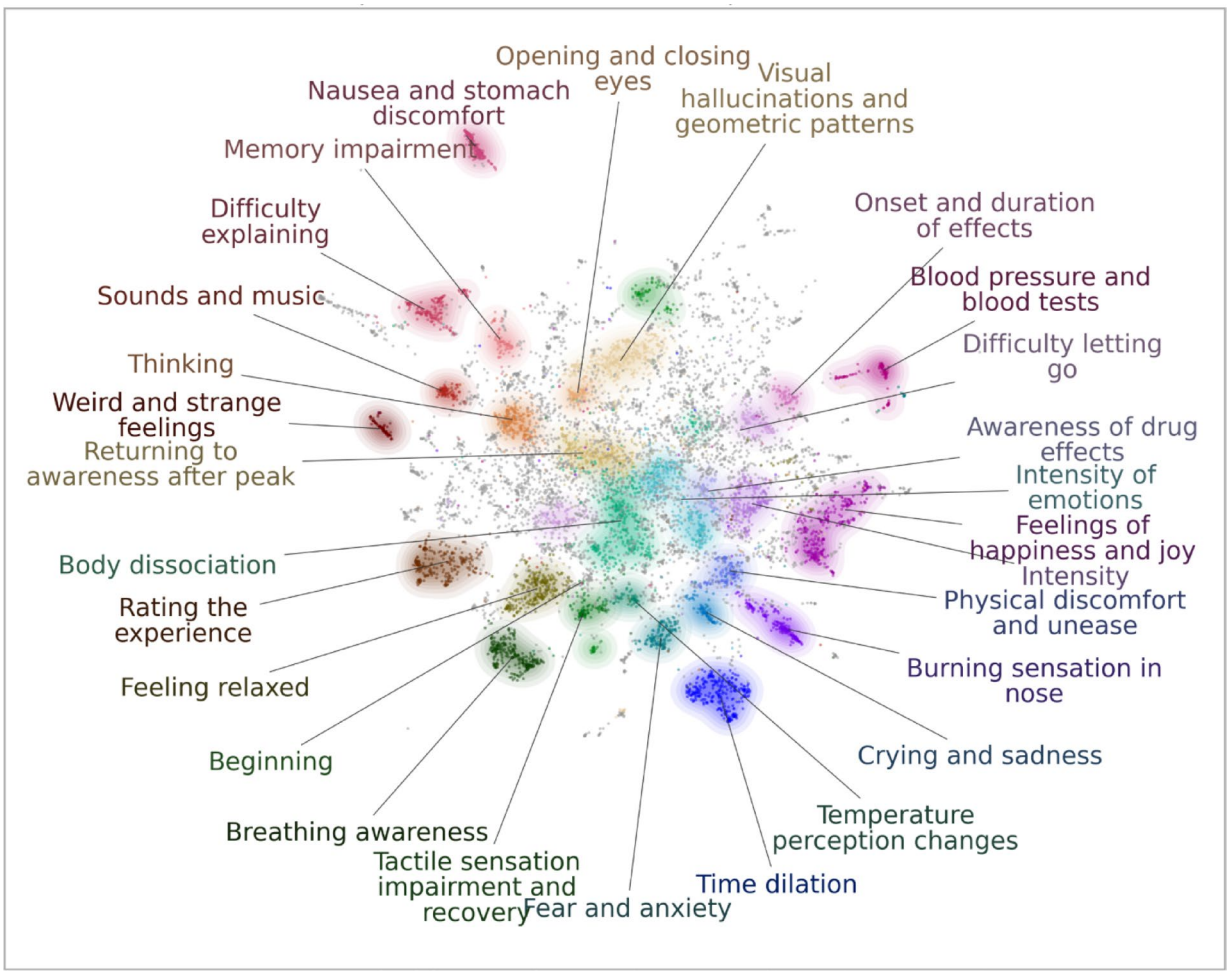

Fig. 4. Two-dimensional projection of unsupervised topic clusters in participant reports. This figure shows a 2D UMAP (Uniform Manifold Approximation and Projection) projection of sentence embeddings from participant reports, with each point representing a single sentence. Colours denote distinct topic clusters identified by HDBSCAN (Hierarchical Density-Based Spatial Clustering of Applications with Noise). Labels for each cluster were generated using the Llama 3 70B large language model, based on the most distinctive terms (identified via c-TF-IDF) and representative sentences within each cluster. This visualisation reveals the semantic landscape of 5-MeO-DMT experiences, illustrating both the diversity of reported phenomena and the relationships between different experiential themes. The spatial proximity of points and clusters reflects semantic similarity.

emotionally, was another prominent theme, highlighting the importance of letting go of control and surrender to the experience for maximizing benefits and minimizing challenges. The theme of letting go and surrendering or accepting the experience was previously identified in the patients undergoing esketamine treatment[44] and recently highlighted in a qualitative study of patients undergoing psilocybin treatment[45]. Surrendering to the experience could be particularly challenging for patients with mental health problems, or in our case for psychedelically-naïve participants who had no prior experience of the altered states of consciousness, emphasising again the importance of adequate preparation and trust-building with the psychedelic monitors. Remembering the preparation sessions, as well as presence and/or therapeutic touch from the psychedelic monitor helped participants relax into the experience. This is similar to previous clinical trials with psychedelics, where trust and relationship with psychedelic therapists/monitors are named as highly important[15,46]. Other strategies employed were positive thoughts, recalling friends' experiences, visualising nature, body relaxation, prayer or mantra, and breathing techniques. Even in healthy volunteers, we observed themes previously identified as mechanisms of change in therapeutic use of psychedelics, such as emotional breakthroughs, insights into personal issues, and connectedness[12,17,47].

Qualitative data can also elucidate challenging experiences. Our results replicate previous reports[48] that challenging experiences can provide learning or healing opportunities. For example, one participant found reliving a sexual assault trauma emotionally painful but ultimately therapeutic due to the psychedelic monitor's support and the ability to discuss the experience and feeling safe. Another participant's challenging experience of feeling possessed by a strange energy was attributed to watching a horror TV show the night before, and while not found particularly meaningful, provided an insight into participant's coping mechanisms with adversity.

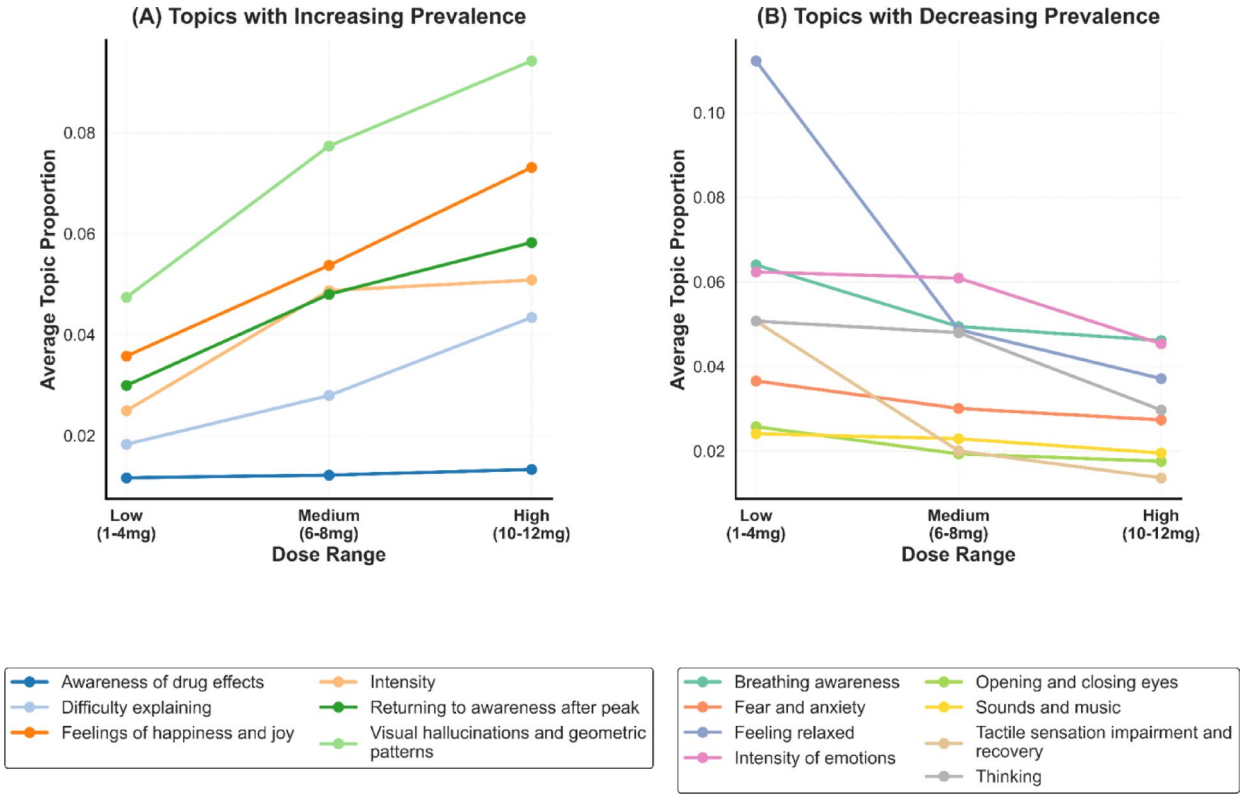

Fig. 5. Exploratory dose-dependent trends in unsupervised topic prevalence. Line charts display the average proportion of participant sentences assigned to different topics across low (1–4 mg), medium (6–8 mg), and high (10–12 mg) dose ranges. Topics were identified using a two-step unsupervised approach: (1) dimensionality reduction of participant sentence embeddings via Uniform Manifold Approximation and Projection (UMAP), followed by (2) Hierarchical Density-Based Spatial Clustering (HDBSCAN) to identify topics from sentences. Topics were labelled using c-TF-IDF for distinctive terms then a language model for concise natural language descriptors. Each line represents a unique topic. (**A**) Topics showing increased prevalence with higher doses. (**B**) Topics showing decreased prevalence with higher doses.

It is important to note that psychedelic experiences can be neither transcendental nor particularly challenging or insightful. They may involve perceptual changes, meditative states, or limited recall, with disappointment arising from mismatched expectations. Managing expectations during preparation (e.g. by highlighting a spectrum of possible experiences) is crucial to avoid disappointment[49].

Currently it is not known whether mystical, challenging or insightful experiences are necessary to achieve therapeutic outcomes, and opinions about it range from pure neuroplasticity effect to the need for the full mystical experience. Future work in patient populations could help elucidate this question.

Compared to other psychedelics, 5-MeO-DMT appears to have some distinctive characteristics, but also similarities. Like psilocybin, LSD, and N,N-DMT, it can induce profound alterations in consciousness, mystical experiences, ego dissolution, emotional breakthroughs and cathartic experiences, and feelings of insight and connection. 5-MeO-DMT is characterised by rapid onset, short duration (like N,N-DMT), prominence of bodily and emotional effects over visual effects (unlike N,N-DMT), and intensely elicited effects. This is congruent with the previous study where 5-MeO-DMT-induced mystical experiences comparable to those after 30 mg psilocybin[6]. In 5-MeO-DMT experiences, somatic and interoceptive effects seem to predominate, with visual effects less prominent, especially at high doses where sensory awareness may disappear entirely. The emotional effects, both positive and challenging, can be intense. Additionally, 5-MeO-DMT rarely induces entity encounters, unlike N,N-DMT[50,51]. It is interesting how self-consciousness is altered by high doses of 5-MeO-DMT—both in a sense of body awareness, which disappears at higher doses, and spatial self-location, where people describe being "elsewhere", in the "void", "universe" or "ocean". Congruent with previous reports from non-clinical use of 5-MeO-DMT[9], some of our study participants reached a state of "non-dual awareness" or "pure consciousness", i.e. a state of consciousness empty of any content, containing "everything and nothing". In *The Philosophy of Psychedelics*, Chris Letheby[52] examines mystical experiences in which psychedelics temporarily dissolve the "narrative self" (our autobiographical story) and the "bodily self" (our sense of embodiment). Mystical here is interpreted naturalistically, not as contact with a supernatural realm but as revealing the constructed and flexible nature of selfhood. Therapeutically, this transient self-dissolution can loosen rigid thought patterns—such as depressive narratives or anxious self-models—providing a "reset" that allows the ordinary sense of self to return reorganized in a healthier, more adaptive form. However, some participants also reported a few minutes where

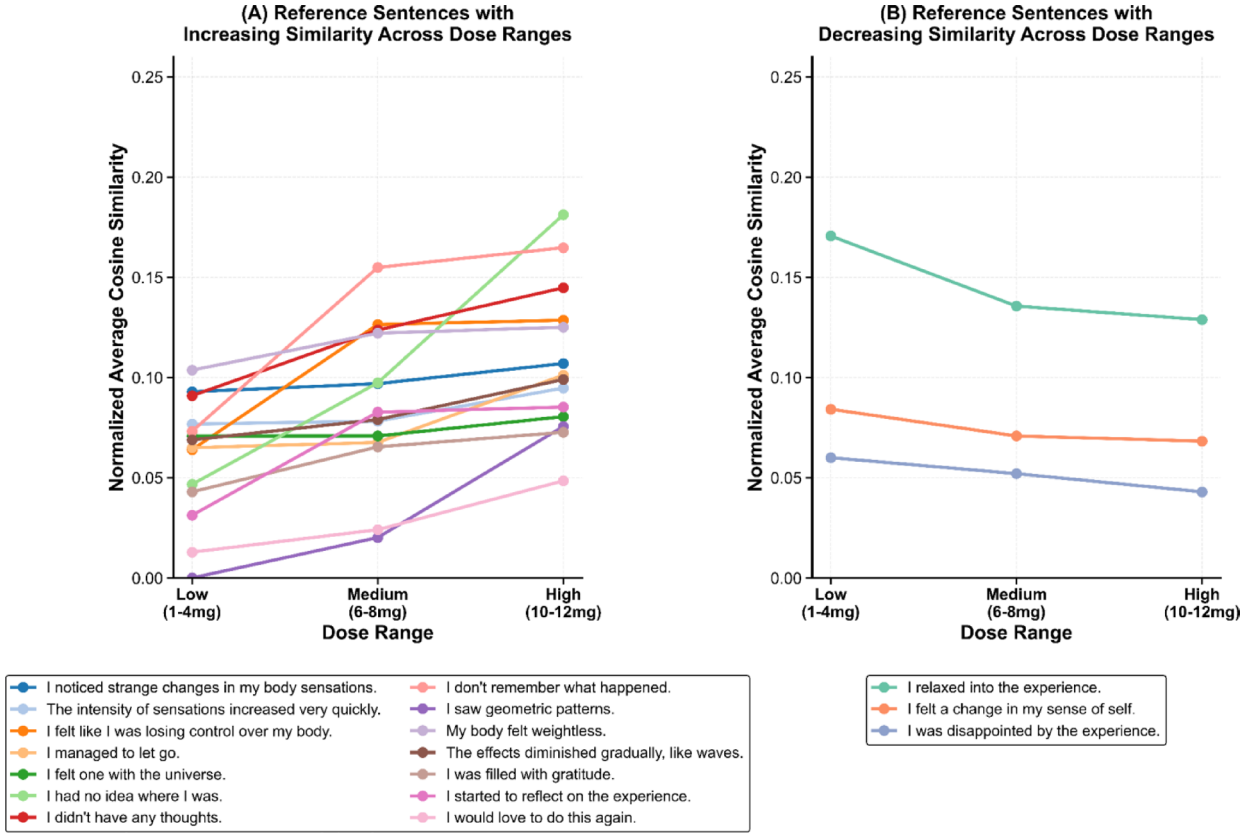

Fig. 6. Exploratory dose-dependent trends in semantic similarity to canonical effect reports. Line charts display normalised average cosine similarity between actual participant sentences from interview transcripts and hand-crafted reference sentences across low (1–4 mg), medium (6–8 mg), and high (10–12 mg) dose ranges. Reference sentences were designed to describe canonical 5-MeO-DMT effects derived from qualitative analysis of interview transcripts, enabling supervised topic modelling. Normalised average cosine similarity is calculated by (1) computing cosine similarities between embeddings for participant sentences and each reference sentence, (2) applying a 0.50 cosine similarity threshold to exclude irrelevant sentences, (3) normalising remaining cosine similarities values to 0–1, and (4) averaging normalised cosine similarity values to each reference sentence across participants per dose range. Each line represents a distinct reference sentence. (**A**) Reference sentences showing increased semantic similarity with higher doses. (**B**) Reference sentences showing decreased similarity with higher doses.

they have no memory of the experience. These preliminary findings suggest a distinctive phenomenological signature for 5-MeO-DMT, but further comparative research is needed.

The quantitative analysis of the interview transcripts using natural language processing techniques provided a complementary perspective, converging with and extending the findings from the qualitative analysis. Unsupervised topic modelling allowed objective validation of the qualitative analysis and revealed distinct experiential domains modulated by 5-MeO-DMT, such as visual effects, physical sensations, emotions, and meta-cognitive reflections, which aligned closely with the themes identified in the qualitative analysis. Furthermore, the quantitative approach suggested potential dose-dependent effects on the prevalence of certain topics, with increasing doses appearing to be associated with higher frequency of reports related to visual phenomena, positive emotions, and the overall intensity and uniqueness of the experience. These results corroborate the qualitative finding that 5-MeO-DMT's subjective effects are dose-dependent. Another interesting exploratory finding was that participants at medium doses appeared to report more body perception changes, confusion and fear and mention more often tolerability of the experience. This aligns with qualitative findings where some people who had medium doses found experiences more challenging. Our description of 5-MeO-DMT effects as featuring a relative lack of complex visuals, especially compared to substances like N,N-DMT, is based on the qualitative nature of participant reports. Although the quantitative NLP analysis identified a 'visual' topic as frequent due to the common use of perceptual terms, the experiences described within this topic were typically elementary (e.g., light changes, simple colours/patterns), contrasting with the complex visual narratives often reported with other agents, and were often less prominent than the powerful somatic and emotional effects.

Dynamic topic modelling enabled a quantitative characterisation of the temporal trajectory of different experiential components, mirroring the chronology described in the qualitative analysis. For example, the rapid onset and subsidence of physical sensations, the gradual tapering of visual effects, and the peak of intensity around 8 min post-administration were all captured by the time-resolved linguistic analysis. This reveals

temporal phenomenological signatures that extend beyond the qualitative analysis, with three distinct phases that have potential clinical implications. First, the somatic-dominant onset phase (0–5 min) is characterized by peak physical discomfort, with an initially high prevalence of the themes "burning sensation" and "breathing awareness". These physical symptoms also coincide with the maximum prevalence of "fear and anxiety", identifying a critical window that might require therapeutic support. Second, during the cognitive-emotional transition (8–20 min), the quantitative approach revealed a previously unrecognised bimodal pattern in "difficulty letting go", with two peaks around 9–10 and 19–21 min. This pattern suggests two distinct surrender challenges—initial resistance and mid-experience re-emergence—that could guide real-time therapeutic interventions. Third, the late-phase emotional processing period (28–35 min) shows unexpected resurgence in "crying and sadness", coinciding with participants becoming lucid and grappling with emotions provoked by the experience.

These temporal phenotypes could inform support protocols in a clinical setting: enhanced breathing guidance during minutes 2–10 when respiratory distress peaks; facilitation of surrender at the two identified resistance points; and extended integration support through minute 35 to capture late emotional processing. Dynamic topic modelling also provides a quantitative framework for cross-substance comparison in future research. 5-MeO-DMT's rapid somatic onset and minimal visual persistence contrasts sharply with psilocybin's gradual onset and sustained perceptual effects, suggesting distinct therapeutic applications. The methodology establishes a reproducible phenotyping standard applicable to novel psychedelics. It enables prediction of experiential trajectories from early markers (e.g., somatic intensity at 2 min correlating with peak effects) and optimization of dose-timing strategies. Future studies should integrate these temporal signatures with physiological markers (EEG, HRV) to develop real-time experience prediction models.

Supervised topic modelling confirmed the significant individual variability in responses uncovered by the qualitative interviews while also suggesting a dose–response relationship in the semantic similarity of participant reports to reference descriptions of key 5-MeO-DMT effects.

This study has several strengths. The microphenomenological interviews provided reliable, fine-grained descriptions of 5-MeO-DMT experiences. Interviewing subjects shortly after sessions helped accurate recall, facilitating integration. The diverse sample, with 40% non-white, psychedelic-naïve participants, is more representative of future clinical populations and less biased by prior experiences or knowledge. The detailed descriptions are valuable for studying the neural correlates of psychedelic experiences and their temporal unfolding. The synchronic structures can refine hypotheses, develop questionnaires, and highlight key aspects for future studies. The ability to zoom in on specific parts of the experience can inform research and therapeutic applications. The rich qualitative data, including participants' meanings and treatment context, provides a detailed understanding of the psychological mechanisms in psychedelic therapy. The interviews also offered direct trial feedback, allowing for agile improvements. The information gleaned is useful for preparing future participants and training therapists.

Another major strength of this study is the novel combination of microphenomenology interviews with advanced natural language processing methods. To our knowledge, this is the first time that these two approaches have been integrated. Unsupervised qualitative analysis provides objective validation of the qualitative work as it is free of bias. However, the topic modelling analysis not only validated the findings from the qualitative interviews but also provided additional insights into dose-dependent effects and the temporal dynamics of different experiential components. This highlights the value of combining qualitative and quantitative methods to obtain a more comprehensive understanding of altered states of consciousness.

The study also has some limitations. A dose–response study is underpowered for drawing definitive conclusions on the dose differences, but does show a dose-related effect on consciousness. The healthy volunteer participants limit generalizability to therapeutic contexts. Another potential limitation is that the interviews were conducted both online and in-person—any potential differences that may have arisen from this are unknown. Variability in participants' introspective abilities, with meditators being more adept, highlights the importance of considering individual differences in introspective skill. The longer time scale of 5-MeO-DMT experiences compared to traditional microphenomenology applications may impact the granularity of descriptions. Future work could explore adapting the methodology for different experience durations.

Despite these limitations, this study provides a uniquely detailed view into the phenomenology of 5-MeO-DMT, informing further research into its therapeutic mechanisms and effects on consciousness. Future studies could combine microphenomenology with neurophysiological measures to illuminate the neural correlates of specific experiential components.

Conclusion

This qualitative study provides the first systematic phenomenological analysis of the acute subjective effects of 5-MeO-DMT in a clinical trial setting. Using microphenomenology interviews, we obtained detailed diachronic and synchronic maps of participants' inner experiences after administration of 5-MeO-DMT.

Key features that emerged include the rapid onset and short duration of effects, emotionally intense and personally meaningful experiences, alterations in bodily sensations and the sense of self/ego, and the importance of "letting go" and surrendering to the experience. Challenging experiences, while difficult, also appeared to provide opportunities for emotional breakthroughs and insights. Overall, the rich phenomenology elicited by 5-MeO-DMT touches on fundamental aspects of human consciousness related to the sense of self, embodiment, emotion, and meaning.

These results provide a solid foundation for future research on the experiential and therapeutic effects of 5-MeO-DMT. By combining microphenomenology with neurophysiological measures, future work on the acute effects of 5-MeO-DMT could illuminate aspects of consciousness related to emotion, somatic sensations, and the sense of self.

Data availability

Some data that support the findings of this trial are available on www.ClinicalTrials.gov: NCT05347849. The interview transcripts and extended quotes are not publicly available due to reasons of privacy of the respondents, and data protection regulations. Data may be made accessible upon request and after consultation with the data managing officers from Beckley Psytech by contacting the corresponding author.

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References

1. Ermakova, A. O., Dunbar, F., Rucker, J. & Johnson, M. W. A narrative synthesis of research with 5-MeO-DMT. *J Psychopharmacol* https://doi.org/10.1177/02698811211050543 (2021).
2. Halberstadt, A. L., Nichols, D. E. & Geyer, M. A. Behavioral effects of α,α, β,β-tetradeutero-5-MeO-DMT in rats: comparison with 5-MeO-DMT administered in combination with a monoamine oxidase inhibitor. *Psychopharmacology* **221**, 709–718 (2012).
3. Ray, T. S. Psychedelics and the Human Receptorome. *PLoS ONE* **5**, e9019 (2010).
4. Reckweg, J. T. et al. A phase 1/2 trial to assess safety and efficacy of a vaporized 5-methoxy-N,N-dimethyltryptamine formulation (GH001) in patients with treatment-resistant depression. *Front. Psychiatry.* **14**, 1133414 (2023).
5. ClinicalTrials.gov. 5-MeO-DMT | List Results | ClinicalTrials.gov. https://clinicaltrials.gov/search?intr=5-MeO-DMT (2024).
6. Barsuglia, J. et al. Intensity of mystical experiences occasioned by 5-MeO-DMT and comparison with a prior psilocybin study. *Front. Psychol.* **9**, 2459 (2018).
7. Davis, A. K., Barsuglia, J. P., Lancelotta, R., Grant, R. M. & Renn, E. The epidemiology of 5-methoxy-N, N-dimethyltryptamine (5-MeO-DMT) use: Benefits, consequences, patterns of use, subjective effects, and reasons for consumption. *J. Psychopharmacol.* **32**, 779–792 (2018).
8. Erowid. 5-MeO-DMT : Erowid Experiences: Main Index. https://erowid.org/experiences/subs/exp_5MeODMT.shtml (2024).
9. Millière, R., Carhart-Harris, R. L., Roseman, L., Trautwein, F.-M. & Berkovich-Ohana, A. Psychedelics, meditation, and self-consciousness. *Front. Psychol.* **9**, 1475 (2018).
10. Metzner, R. *Toad and the Jaguar a Field Report of Underground Research on a Visionary Medicine: Bufo Alvarius And 5-Methoxy-Dimethyltryptamine*. (Regent Press, 2013).
11. Roseman, L., Nutt, D. J. & Carhart-Harris, R. L. Quality of acute psychedelic experience predicts therapeutic efficacy of psilocybin for treatment-resistant depression. *Front. Pharmacol.* **8**, 974 (2018).
12. Yaden, D. B., Goldy, S. P., Weiss, B. & Griffiths, R. R. Clinically relevant acute subjective effects of psychedelics beyond mystical experience. *Nat. Rev. Psychol.* **3**, 606–621 (2024).
13. Yaden, D. B. & Griffiths, R. R. The subjective effects of psychedelics are necessary for their enduring therapeutic effects. *Acs Pharmacol. Transl. Sci.* **4**, 568–572 (2021).
14. McMillan, R. M. & Fernandez, A. V. Understanding subjective experience in psychedelic-assisted psychotherapy: the need for phenomenology. *Australia. New Zealand J. Psychiatry.* https://doi.org/10.1177/00048674221139962 (2022).
15. Breeksema, J. J., Niemeijer, A. R., Krediet, E., Vermetten, E. & Schoevers, R. A. Psychedelic treatments for psychiatric disorders: a systematic review and thematic synthesis of patient experiences in qualitative studies. *CNS Drugs* **34**, 925–946 (2020).
16. Crowe, M., Manuel, J., Carlyle, D. & Lacey, C. Experiences of psilocybin treatment for clinical conditions: a qualitative meta-synthesis. *Int. J. Ment. Heal. Nurs.* **32**, 1025–1037 (2023).
17. Walther, R. F. E. & van Schie, H. T. 'Mind-revealing' psychedelic states: psychological processes in subjective experiences that drive positive change. *Psychoactives* **3**, 411–436 (2024).
18. Agin-Liebes, G. et al. Reports of self-compassion and affect regulation in psilocybin-assisted therapy for alcohol use disorder: an interpretive phenomenological analysis. *Psychol. Addict. Behav.* https://doi.org/10.1037/adb0000935 (2023).
19. Belser, A. B. et al. Patient experiences of psilocybin-assisted psychotherapy: an interpretative phenomenological analysis. *J. Humanist. Psychol.* **57**, 354–388 (2017).
20. McCulloch, D.E.-W. et al. Psilocybin-induced mystical-type experiences are related to persisting positive effects: a quantitative and qualitative report. *Front Pharmacol* **13**, 841648 (2022).
21. Nielson, E. M., May, D. G., Forcehimes, A. A. & Bogenschutz, M. P. The psychedelic debriefing in alcohol dependence treatment: illustrating key change phenomena through qualitative content analysis of clinical sessions. *Front. Pharmacol.* **9**, 132 (2018).
22. Noorani, T., Garcia-Romeu, A., Swift, T. C., Griffiths, R. R. & Johnson, M. W. Psychedelic therapy for smoking cessation: qualitative analysis of participant accounts. *J. Psychopharmacol.* **32**, 756–769 (2018).
23. Swift, T. C. et al. Cancer at the dinner table: experiences of psilocybin-assisted psychotherapy for the treatment of cancer-related distress. *J. Humanist. Psychol.* **57**, 488–519 (2017).
24. Watts, R., Day, C., Krzanowski, J., Nutt, D. & Carhart-Harris, R. Patients' accounts of increased "connectedness" and "acceptance" after psilocybin for treatment-resistant depression. *J. Humanist. Psychol.* **57**, 520–564 (2017).
25. Loizaga-Velder, A. & Verres, R. Therapeutic effects of ritual ayahuasca use in the treatment of substance dependence—qualitative results. *J. Psychoactive. Drugs.* **46**, 63–72 (2014).
26. Lafrance, A. et al. Nourishing the spirit: exploratory research on Ayahuasca experiences along the continuum of recovery from eating disorders. *J. Psychoact. Drugs* **49**, 427–435 (2017).
27. Gasser, P., Kirchner, K. & Passie, T. LSD-assisted psychotherapy for anxiety associated with a life-threatening disease: a qualitative study of acute and sustained subjective effects. *J. Psychopharmacol.* **29**, 57–68 (2015).
28. Brown, T. K., Noller, G. E. & Denenberg, J. O. Ibogaine and subjective experience: transformative states and psychopharmacotherapy in the treatment of opioid use disorder. *J. Psychoact. Drugs* **51**, 155–165 (2019).
29. Barone, W. et al. Facing death, returning to life: A qualitative analysis of MDMA-assisted therapy for anxiety associated with life-threatening illness. *Front. Psychiatry* **13**, 944849 (2022).
30. Danforth, A. L. Embracing neurodiversity in psychedelic science: a mixed-methods inquiry into the MDMA experiences of autistic adults. *J Psychoactive Drugs* **51**, 1–9 (2019).
31. Hurlburt, R. T. & Schwitzgebel, E. *Describing Inner Experience? Proponent Meets Skeptic*. (MIT Press, 2007).
32. Richards, W. A. *Sacred Knowledge: Psychedelics and Religious Experiences*. (Columbia University Press, 2015).
33. Petitmengin, C. Describing one's subjective experience in the second person: an interview method for the science of consciousness. *Phenomenol Cogn Sci* **5**, 229–269 (2006).
34. Petitmengin, C., Remillieux, A. & Valenzuela-Moguillansky, C. Discovering the structures of lived experience. *Phenomenol. Cogn. Sci.* **18**, 691–730 (2019).
35. Timmermann, C. et al. Neural correlates of the DMT experience assessed with multivariate EEG. *Sci Rep-uk* **9**, 16324 (2019).
36. ClinicalTrials.gov. NCT05347849. *Single Ascending Dose Study With BPL-003 in Healthy Subjects* https://clinicaltrials.gov/study/NCT05347849?term=NCT05347849&rank=1 (2024).

37. Rucker, J. J. et al. Phase 1, placebo-controlled, single ascending dose trial to evaluate the safety, pharmacokinetics and effect on altered states of consciousness of intranasal BPL-003 (5-methoxy- N, N -dimethyltryptamine benzoate) in healthy participants. *J. Psychopharmacol.* https://doi.org/10.1177/02698811241246857 (2024).
38. Vásquez-Rosati, C.V.-M.A. & Vásquez-Rosati, A. An analysis procedure for the micro-Phenomenological interview. *Constr. Found.* **14**, 123–145 (2019).
39. Miles, M. B. & Huberman, A. M. *Qualitative Data Analysis: An Expanded Sourcebook*. (SAGE Publications, 1994).
40. Lee, C. *et al.* NV-Embed: Improved Techniques for Training LLMs as Generalist Embedding Models. *ArXiv* (2024).
41. NV-Embed-v2. https://huggingface.co/nvidia/NV-Embed-v2.
42. Muennighoff, N., Tazi, N., Magne, L. & Reimers, N. M. T. E. B. Massive Text Embedding Benchmark. *arXiv* https://doi.org/10.48550/arxiv.2210.07316 (2022).
43. McInnes, L., Healy, J. & Melville, J. UMAP: Uniform Manifold Approximation and Projection for Dimension Reduction. *arXiv* (2018) https://doi.org/10.48550/arxiv.1802.03426.
44. Breeksema, J. J. et al. Holding on or letting go? Patient experiences of control, context, and care in oral esketamine treatment for treatment-resistant depression: a qualitative study. *Front. Psychiatry* **13**, 948115 (2022).
45. Breeksema, J. J. et al. Patient perspectives and experiences with psilocybin treatment for treatment-resistant depression: a qualitative study. *Sci. Rep.* **14**, 2929 (2024).
46. Thal, S., Engel, L. B. & Bright, S. J. Presence, trust, and empathy: preferred characteristics of psychedelic carers. *J. Humanist. Psychol.* https://doi.org/10.1177/00221678221081380 (2022).
47. van Elk, M. & Yaden, D. B. Pharmacological, neural, and psychological mechanisms underlying psychedelics: a critical review. *Neurosci Biobehav Rev* **140**, 104793 (2022).
48. Gashi, L., Sandberg, S. & Pedersen, W. Making, "bad trips" good: How users of psychedelics narratively transform challenging trips into valuable experiences. *Int. J. Drug. Policy* **87**, 102997 (2021).
49. Szigeti, B. & Heifets, B. Expectancy effects in psychedelic trials. *Biol. Psychiatry: Cogn. Neurosci. Neuroimag.* https://doi.org/10.1016/j.bpsc.2024.02.004 (2024).
50. Michael, P., Luke, D. & Robinson, O. An encounter with the other: a thematic and content analysis of DMT experiences from a naturalistic Field study. *Front Psychol* **12**, 720717 (2021).
51. Davis, A. K. et al. Survey of entity encounter experiences occasioned by inhaled N,N-dimethyltryptamine: Phenomenology, interpretation, and enduring effects. *J Psychopharmacol* **34**, 1008–1020 (2020).
52. Letheby, C. Philosophy of psychedelics. *Oxford University Press*. (2021).

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Author contributions

This qualitative study was conceived of and designed by A.O.E.. and R.M. Data collection was done by A.O.E. and R.M., qualitative analysis was conducted by A.O.E and F.D., and in part by the other authors; quantitative analysis was conducted by R.M. All authors contributed to the writing of the manuscript and approved the final manuscript.

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Declarations

Competing interests

A.O.E. is a consultant to Beckley Psytech Ltd. F.D. is a medical advisor to Beckley Psytech Ltd. M.S. is currently an employee of Beckley Psytech Ltd but was employed by King's College London (until July 2022) and is currently completing a PhD with King's College London. R.M. is a consultant to Beckley Psytech Ltd.

Informed consent

Written informed consent was obtained from each participant before any trial-related procedures were performed. The dosing experience interview part of the BPL-003–103 study was optional. Subjects may decide not to do the interview without it affecting their participation in the rest of the main study. The information sheet and consent form for the main study contained an optional consent for the qualitative interview study part. If individuals declined to participate, or withdrew their participation, this decision was respected, and subjects are not required to give a reason for declining or withdrawing their participation. This was made clear to patients on the information sheet and by researchers during the consent process.

Human and animal participants

This trial was conducted in accordance with International Council for Harmonisation Good Clinical Practice guidelines and ethical principles that have their origin in the Declaration of Helsinki. Protocols were approved by the Medicines and Healthcare Products Regulatory Agency and an independent recognised research ethics committee before eligibility screening. Audio recordings and demographic information of participants were stored on separate secure servers.

Additional information

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