Measuring and Enhancing Psychedelic Preparedness

Rosalind G. McAlpine

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Supervised by Sunjeev K. Kamboj

Declaration

I, Rosalind Gabriella McAlpine confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signature

[redacted]

Date

31st March 2025

Abstract

Although preparation is widely recognised as essential for safe and meaningful psychedelic experiences, it remains surprisingly under-researched. This thesis seeks to bridge this gap by developing and validating novel tools to measure and enhance *psychedelic preparedness*. **Chapter 1** introduces the concept of preparedness, reviews theoretical perspectives and clinical approaches, summarises existing protocols, and presents feedback from an early pilot study of a brief digital intervention for psychedelic preparation. **Chapter 2** details the development of the 20-item Psychedelic Preparedness Scale (PPS), constructed using a novel Delphi-Focus ('DelFo') methodology that integrates input from both experts and key stakeholders. The PPS was validated across two large online samples (N = 1232) and a psilocybin retreat sample (N = 46), revealing a robust four-factor structure and demonstrating strong reliability, construct validity, and predictive utility for change in well-being. **Chapter 3** describes the development and co-design of the Digital Intervention for Psychedelic Preparation (DIPP), a 21-day self-led programme structured around the PPS framework and developed in accordance with UK Medical Research Council (MRC) guidelines for complex interventions. Informed by interviews (N = 19) and co-design workshops (N = 28), DIPP includes daily meditation practices, reflective exercises, and mood tracking. To refine the meditation component, **Chapter 4** presents findings from a survey of experienced practitioners (N = 123), revealing a clear preference for compassion-based practices over concentration-focused techniques. Respondents recommended a three-week course of 30-minute daily sessions, delivered asynchronously and online - an approach consistent with the implementation design outlined in Chapter 3. **Chapter 5** outlines the protocol for an upcoming randomised controlled trial (N = 40) assessing the feasibility, acceptability, and preliminary efficacy of DIPP. **Chapter 6** explores psychedelic preparedness in the context of 5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT), using self-report data, pre-session linguistic markers, and EEG recordings during dosing (N = 29). **Chapter 7** provides a general discussion, outlining theoretical contributions and implications, methodological limitations, and directions for future research. Collectively, these studies establish a novel, empirically grounded framework for understanding and enhancing psychedelic preparedness, with practical relevance across clinical and non-clinical settings.

Impact Statement

Research Impact

This thesis conceptualises *psychedelic preparedness* as a measurable, multidimensional construct and presents the first validated, open-access tool for its assessment: the **Psychedelic Preparedness Scale (PPS)**. The PPS provides researchers with a standardised framework to systematically investigate how preparatory processes influence psychedelic outcomes, thereby facilitating consistent measurement practices and enabling cross-study comparisons. This thesis also introduces the **Digital Intervention for Psychedelic Preparation (DIPP)** - the first self-led, meditation-based program designed to enhance psychedelic preparedness. Developed in line with Medical Research Council (MRC) guidelines for complex interventions, DIPP represents a novel approach to systematically preparing individuals for psychedelic experiences. Beyond these contributions, the work exemplifies the integration of co-production principles throughout the development of both tools. It challenges prevailing assumptions about the most effective contemplative practices for psychedelic preparation, highlighting the potential effectiveness of compassion-based approaches over concentration-based ones. Additionally, it identifies novel predictive markers of psychedelic response, including pre-session linguistic features, and introduces the first phenomenology scale specifically designed to capture the subjective effects of 5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT) (pending psychometric validation).

Clinical Impact

This thesis has already begun to influence clinical practice by providing tools and frameworks directly applicable to psychedelic care. The PPS has already been adopted by more than ten retreat centres, clinical trials, and psychedelic facilitator training programs, enabling clinicians to systematically assess readiness, tailor preparation, and track progress over time. DIPP offers a low-cost, accessible alternative to clinician-led preparation. Following a successful pilot, we intend to make the platform openly available. Together, these contributions support a shift toward more scalable, inclusive, and person-centred models of psychedelic care, grounded in empirical evidence and co-designed with both practitioners and stakeholders.

Dissemination

The findings from this thesis have been disseminated through a range of academic and public forums. Peer-reviewed publications and pre-prints are listed in the **Research Paper Declaration** section; selected presentations are outlined below.

Academic:

- Philosophy of Psychedelics Conference, University of Exeter, Exeter, UK (2022) - Academic talk and panel: '*Psychedelics, Spirituality & Scientific Snags*' - Presented early conceptual work on psychedelic preparedness (pre-Chapter 2).
- International Society for Contemplative Research (ISCR) International Conference, University of California, San Diego, USA (2023) - Poster presentation: '*Development, Psychometric Validation and Implementation of a Novel Scale for Measuring Psychedelic Preparedness*' - Presented psychometric validation data of the PPS (Chapter 2).
- Breaking Convention, University of Exeter, Exeter, UK (2023) - Academic talk: '*Investigating Psychedelic Preparedness*' - Presented findings on the PPS and DIPP (Chapters 2 and 3).
- Institute of Mental Health (IoMH) International Conference, University College London, London, UK (2023) – Poster: '*Development and psychometric validation of a novel scale for measuring psychedelic preparedness*' - Presented findings on the PPS (Chapter 2).
- Exeter Psychedelic Research Colloquium, Exeter University, Exeter, UK (2024) - Academic talk: '*Quantifying and Cultivating Psychedelic Preparedness: A Systematic Approach to Meditation-Based Interventions*' - Presented findings from the development and implementation of the PPS and DIPP (Chapters 2 and 3).
- Breaking Convention, Conway Hall, London, UK (2024) - Panel discussion: '*Contemporary Clinical Practice in Psychedelic Research*' - Discussed findings from the 5-MeO-DMT study (Chapter 6).

Public:

- The New Scientist (Online Event) (2022) - Public panel discussion: '*Psychedelics and Mental Health: Your Questions Answered*' - Discussed early ideas behind psychedelic preparation and the development of the PPS (pre-Chapter 2).
- Medicine Festival, Reading, UK (2022) - Panel discussion: '*Psychedelic Medicalisation: Challenges, Pitfalls, Pleasures and Hopes*' - Shared emerging findings on the PPS and DIPP (Chapters 2 and 3).
- Phaneros Institute, Brazil (2024) - Public presentation: '*Exploring 5-MeO-DMT: Overview and Recent Study Findings*' - Discussed findings from the 5-MeO-DMT study (Chapter 6) to practitioner audience.
- Pint of Science Festival, London, UK (2024) - Public talk: '*5-MeO-DMT: Journey into the Mysteries of the "God Molecule"*' - Presented findings from the 5-MeO-DMT study (Chapter 6).

Research Paper Declaration

Publications/preprints directly associated with the work in this thesis:

1. **McAlpine, R. G**., Blackburne, G., & Kamboj, S. K. (2024). Development and psychometric validation of a novel scale for measuring 'psychedelic preparedness'. *Scientific Reports*, 14(1), 3280. (Chapter 2)
2. **McAlpine, R. G**., Sacchet, M. D., Simonsson, O., Khan, M., Krajnovic, K., Morometescu, L., & Kamboj, S. K. (2024). Development of a digital intervention for psychedelic preparation (DIPP). *Scientific Reports,* 14(1), 4072. (Chapter 3)
3. **McAlpine, R. G**., Utanğaç, M., Timmermann, C., Kamboj, S. K., … Sacchet, M. (2025). Practitioner perspectives on meditation-based preparation for psychedelic experiences, *PsyArXiv*. (Chapter 4)
4. Blackburne, G., **McAlpine, R. G**., Fabus, M., Liardi, A., Kamboj, S. K., Mediano, P. A., & Skipper, J. I. (2024). Complex slow waves radically reorganise human brain dynamics under 5-MeO-DMT. *bioRxiv*. (Chapter 6)

Publications/preprints tangential to the work in this thesis and completed during the last four years:

5. Wood, M. J., **McAlpine, R. G.,** & Kamboj, S. K. (2024). Strategies for resolving challenging psychedelic experiences: insights from a mixed-methods study. *Scientific Reports*, 14(1), 28817. (Chapter 1)
6. Evans, J., Robinson, O. C., Argyri, E. K., Suseelan, S., Murphy-Beiner, A., **McAlpine, R. G,** ... & Prideaux, E. (2023). Extended difficulties following the use of psychedelic drugs: A mixed methods study. *PLoS One*, 18(10), e0293349. (Chapter 1)
7. Robinson, O. C., Evans, J., Luke, D., **McAlpine, R. G.,** ... & Prideaux, E. (2024). Coming back together: A qualitative survey study of coping and support strategies used by people to cope with extended difficulties after the use of psychedelic drugs. *Frontiers in Psychology*, 15, 1369715. (Chapter 1)
8. Robinson, O. C., Evans, J., **McAlpine, R. G.,** Argyri, E. K., & Luke, D. (2024). An investigation into the varieties of extended difficulties following psychedelic drug use: Duration, severity and helpful coping strategies. *Journal of Psychedelic Studies*. (Chapter 1)
9. **McAlpine, G. R**., & Blackburne, G. (2024). (Dis) connectedness, suicidality and group psychedelic therapies. *PsyArXiv.* (Chapter 1)

10. Argyri, E. K., Evans, J., Luke, D., Michael, P., **McAlpine, R. G.,** ... & Robinson, O. (2024). Navigating Groundlessness: An interview study on dealing with ontological shock and existential distress following psychedelic experiences. *SSRN* 4817368. (Chapter 1)

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To my dad, Andrew - I often wonder what you'd make of all of this. I hope you'd be proud.

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11D-ASC	11-Dimensional Altered States of Consciousness
2C-B	4-Bromo-2,5-Dimethoxyphenethylamine
5-MeO-DMT	5-Methoxy-N,N-Dimethyltryptamine
5D-ASC	5-Dimensional Altered States of Consciousness Scale
5PS	5-MeO-DMT Phenomenology Scale
AA	Acoustic Alterations
AB	Abstract
ACT	Acceptance And Commitment Therapy
AED	Anxious Ego-Dissolution
AEs	Adverse Events
AF	Affective
ANOVA	Analysis Of Variance
ASCQ	Altered Self-Consciousness Questionnaire
AWS	Amazon Web Services
BBRO	Benefits, Barriers, Risks, And Outcomes
BDNF	Brain-Derived Neurotrophic Factor
BFI-Ex	Big Five Inventory–Extraversion
BML	Baseline Mindfulness Language
BPD	Borderline Personality Disorder
CADSS-6	Clinician Administered Dissociative Symptom Scale
CAMS-R	Cognitive And Affective Mindfulness Scale Revised
CBPR	Community-Based Participatory Research
CBT	Cognitive Behavioural Therapy
CEQ	Challenging Experience Questionnaire
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
CI	Confidence Intervals
CLKM	Compassion And Loving-Kindness
COES	Centrality Of Event Scale
CPU	Clinical Psychopharmacology Unit
CT	Concentration Techniques
DASS-21	Depression, Anxiety, And Stress Scale
DBT	Dialectical Behaviour Therapy

DelFo	Delphi-Focus
DEQ	Drug Effects Questionnaire
DIPP	Digital Intervention for Psychedelic Preparedness
DMC	Data Monitoring Committee
DMHIs	Digital Mental Health Interventions
DMN	Default Mode Network
DMT	N,N-Dimethyltryptamine
EBI	Emotional Breakthrough Inventory
EBT	Evidence-Based Therapy
ECG	Electrocardiogram
ECR-SAn	Experiences In Close Relationships Scale–Anxiety
EEG	Electroencephalography
EFA	Exploratory Factor Analysis
EMA	Ecological Momentary Assessment
EMD	Empirical Mode Decomposition
EMMs	Estimated Marginal Means
EN	Everything/Nothing
F.I.V.E	5-MeO-DMT Information & Vital Education
F2	Feasibility Score
FA	Focused-Attention
FDR	False Discovery Rate
FIR	Finite Impulse Response
GAD	Generalised Anxiety Disorder
GDPR	General Data Protection Regulation
GMP	Good Manufacturing Practice
GUIDED	Guidance For the Reporting of Intervention Development
HC3	Heteroscedasticity-Consistent
ICA	Independent Component Analysis
ICC	Intra-Class Correlation
IM	Immersion & Merging
IMP	Investigational Medicinal Product
IP	Intention-Preparation
ISS	Inner Speech Sampling
KAT	Ketamine-Assisted Therapy
KE	Knowledge-Expectation

KMO	Kaiser-Meyer-Olkin
LIWC	Linguistic Inquiry and Word Count
LKM	Loving-Kindness Meditation
LSD	Lysergic Acid Diethylamide
MAI	Mindful Awareness and Insight
MAPS	Multidisciplinary Association for Psychedelic Studies
MBCT	Mindfulness-Based Cognitive Therapy
MBIs	Mindfulness-Based Interventions
MBRP	Mindfulness-Based Relapse Prevention
MBSR	Mindfulness-Based Stress Reduction
MDD	Major Depressive Disorder
MDES	Multidimensional Experience Sampling
MEQ	Mystical Experience Questionnaire
MINI	Mini-International Neuropsychiatric Interview
ML	Maximum Likelihood
MRC	Medical Research Council
MSY	Meditative-Stretch Yoga
NHP	Non-Hallucinogenic Psychoplastogen
NLP	Natural Language Processing
NREM	Non-Rapid Eye Movement
OBN	Oceanic Boundlessness
OCD	Obsessive-Compulsive Disorder
OM	Open-Monitoring
P1	Priority Score
P2	Updated Priority Scores
PAT	Psychedelic-Assisted Therapy
PBMPP	Perceived Benefits of Meditation for Psychedelic Preparation
PES	Positive Emotional States
PGTI-SF	Post-Traumatic Growth Inventory Short Form
PPGI	Post-Psychedelic Growth Inventory
PPI	Patient And Public Involvement
PPS	Psychedelic Preparedness Scale
PR	Psychophysical-Readiness
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PY	Power Yoga

QPIs	Qualitative Pre-Test Interviews
RMSEA	Root Mean Square Error of Approximation
SAEs	Serious Adverse Events
SAPAS	Standardised Assessment of Personality
SARs	Serious Adverse Reactions
SD	Standard Deviation
SI	Stakeholder Involvement
SLESQ	Stressful Life Events Screening Questionnaire
SOP	Standard Operating Procedures
SP	Support-Planning
SPIRIT	Standard Protocol Items: Recommendations For Interventional Trials
SRMR	Standardised Root Mean Square Residual
ST	Self-Transcendence
ST-TA	Structured Tabular Thematic Analysis
SUD	Substance Use Disorder
SWEMWBS	Short Warwick-Edinburgh Mental Wellbeing Scale
TBG	Tabernanthalog
TIB	Therapy-Interfering Behaviour
TIDieR	Template For Intervention Description and Replication
TLI	Tucker-Lewis Index
TRC	Tandava Retreat Centre
TRD	Treatment Resistant Depression
TWIM	Tranquil Wisdom Insight Meditation
UCL	University College London
UNITy	Understanding Neuroplasticity Induced by Tryptamines
VAS	Visual Analogue Scale
VI	Visionary
VIR	Vigilance Reduction
VRS	Visionary Restructuralisation
WEIRD	White, Educated, Industrialised, Rich, Democratic
YPPS	Yale Program for Psychedelic Science

CHAPTER 1

"The dismantling of one's psychological boundaries is a frightening, gut-wrenching experience both physically and psychologically, but if you are prepared for this unravelling and meet it head-on, it can be both manageable and beneficial."

— Bache, C. M. (2019). LSD and the Mind of the Universe: Diamonds from Heaven.

1.1 Introduction

Psychedelics are powerful psychoactive substances capable of profoundly altering human consciousness [1–3].[1] At sufficiently high doses, they can radically transform perception, cognition, and emotion, inducing states "not experienced otherwise except in dreams or at times of religious exaltation" [7]. These states have been aptly described as "portentous" [8] - moments in which the mind perceives more than it can articulate, feels more than it can explain, and intuits meaning beyond the reach of rational thought**.** Once confined to the fringes of esoteric and countercultural thought, psychedelics have rapidly become a major focus of scientific research [9], with recent studies highlighting impressive potential of these experiences to enhance wellbeing [10], alleviate depression, anxiety, and substance use [11], shift existential and metaphysical beliefs [12, 13], and produce lasting changes in personality [14]. Yet the same intensity that lends these experiences their transformative potential can also make them psychologically destabilising [15]. As a result, thoughtful preparation is widely regarded as essential for navigating them safely and effectively [16]. Despite over two decades of renewed scientific interest [17, 18], surprisingly little empirical attention has been devoted to what it means to be 'prepared' for such encounters. This thesis addresses this gap by exploring how *psychedelic preparedness* can be conceptualised, measured and enhanced, with potential applications for both contemporary therapeutic and non-clinical contexts.

The sections that follow map the landscape from which this research emerges. **Section 1.2** situates psychedelics within their historical and contemporary contexts, tracing their use from Indigenous traditions to early psychiatric research, the era of prohibition, and the recent resurgence of psychedelic science. It also

[1]The term 'psychedelic' was coined by psychiatrist Humphry Osmond in 1956, from the Greek words *ψυχή* (*psyche*), meaning 'mind' or 'soul', and *δήλος* (*delos*), meaning 'manifest' or 'reveal' [4]. It became the dominant term over alternatives like psychephoric, psycheplastic, psychezymic, psycherhexic, fantasticants, entheogens, and psychelytic psychelytic [5]. While some scholars continue to propose new terms, such as 'psychosomadelics' to capture both mental and physical effects [6], this thesis uses 'psychedelic' for consistency with the scientific literature.

introduces key debates surrounding therapeutic mechanisms, including whether the subjective effects of psychedelics are necessary for clinical benefit. **Section 1.3** examines theoretical perspectives on psychedelic preparedness, outlining how psychological, environmental, and cultural factors shape psychedelic experiences. **Section 1.4** reviews a range of psychotherapeutic approaches applied to psychedelic preparation. **Section 1.5** summarises a systematic review of preparation protocols used in **psychedelic-assisted therapy (PAT)** trials, identifying methodological inconsistencies, conceptual gaps, and the need for more rigorous reporting of protocols. **Section 1.6** presents preliminary feasibility testing of an early digital preparation protocol, summarising participant feedback and highlighting limitations in both measurement and intervention design. Finally, **Section 1.7** outlines the thesis objectives and structure, providing a roadmap for the chapters that follow.

1.2 Psychedelic therapeutics: historical context, psychological mechanisms, and clinical considerations

For millennia, humans have turned to the psychoactive properties of plants and fungi as pathways to altered consciousness, healing, and spiritual exploration [19, 20]. Notable examples include the use of psilocybin-containing mushrooms in prehistoric Saharan cultures, dating back at least 6,000 years [21, 22]; the ceremonial drinking of ayahuasca in Amazonian shamanic traditions [23, 24]; and the sacramental use of peyote by Indigenous communities in North America - a practice with roots extending over 5,700 years and continuing today within the Native American Church [25, 26]. These substances were never just a means to 'get high'. They were woven into rituals that guided people in making sense of themselves, their place in the world, and their relationships with both other humans and the *more-than-human world* [27–29]. In the mid-20th century, psychedelics began attracting significant attention in Western science, as early clinical research highlighted their potential for treating conditions such as alcoholism, anxiety, and depression [4, 30, 31], while also offering novel insights into the workings of human consciousness [32, 33]. However, their growing association with countercultural movements during the 1960s sparked widespread societal backlash, leading to their criminalisation and a near-total halt in scientific investigation [2, 34, 35]. This abrupt prohibition not only stifled a promising line of clinical research but also disrupted the cultural and historical connections that had, for centuries, informed the responsible use of these substances [17, 36].

Psychedelics have now re-emerged as promising therapeutic tools, gaining widespread recognition across scientific, clinical, and cultural domains [18, 37–39]. What began as a cautious 'renaissance' of research in the early 2000s has quickly grown into a wave of enthusiasm, fuelled by early clinical findings suggesting that just one or two psychedelic sessions can produce rapid and enduring therapeutic effects [40–44] - outcomes rarely observed with conventional psychotherapeutic treatments [45–47]. These results caught the attention of both researchers and the wider public, paving the way for media portrayals that frame psychedelics as near-miraculous solutions for mental health care [48, 49].[2] Such coverage has not only captured public imagination but also attracted substantial investment from philanthropists, biotech

[2]In 2021, a widely circulated BBC article titled "Psychedelic therapy could 'reset' depressed brain" portrayed N,N-Dimethyltryptamine (DMT) as a potential "*cure for depression*" [50]. This media framing exemplifies the "Pollan Effect" [51, 52], named after science writer Michael Pollan, whose book *How to Change Your Mind* [53] popularised the therapeutic potential of psychedelics. The Pollan Effect captures how media portrayals shape public perception by presenting psychedelics as transformative health interventions, reflecting a convergence between emerging medical research and a "*surging social movement*" around psychedelic therapy [54].

companies, and venture capital firms, accelerating the development of psychedelic-based treatments for a huge range of clinical conditions, including **treatment-resistant depression (TRD)**, **generalised anxiety disorder (GAD)**, **Post Traumatic Stress Disorder (PTSD)**, **obsessive-compulsive disorder (OCD)**, **body dysmorphic disorder (BDD)**, anorexia nervosa, headache, **substance use disorder (SUD)**, and a variety of other conditions [55]. As a result, psychedelics have moved from the periphery of psychiatric research to the forefront of therapeutic innovation, with near-weekly announcements of new trials, patents, and commercial ventures [56–58].

Yet beneath this surge of enthusiasm, the clinical evidence for psychedelic therapy is thinner than it seems. A bibliometric review of clinical studies from 1965 to 2021 found that fewer than 20% examined therapeutic applications, with most focused instead on safety, pharmacology, or non-clinical outcomes (**Fig 1.1a**) [59]. Although publication rates have climbed steadily since the mid-1990s, this growth has centred on just a few compounds (i.e., MDMA, LSD, and psilocybin; see **Fig. 1.1b**) and has been driven by a handful of research hubs in North America and Europe [59, 60]. A recent analysis of psilocybin trials registered on ClinicalTrials.gov[3] found that although 134 studies had been launched by the end of 2023, only 28 had been completed, and just 9 had posted results, despite legal requirements to do so [61]. Trials were typically unblinded studies of 10-20 participants, recruited over years at a single site. Only four trials had reached Phase II/III or III by late 2023 (**Fig. 1.1c**), while the vast majority remain in early stages - unlikely to deliver the kind of robust evidence required for regulatory approval anytime soon (**Fig. 1.1d**). Hence, despite rapid expansion and growing investment, psychedelic therapy remains in its early stages, with enthusiasm currently exceeding evidence. Meaningful clinical and regulatory advancement depends on more rigorous and scalable research.

[3] ClinicalTrials.gov is a publicly accessible database maintained by the U.S. National Library of Medicine, providing information on registered clinical studies, including their design, status, and results.

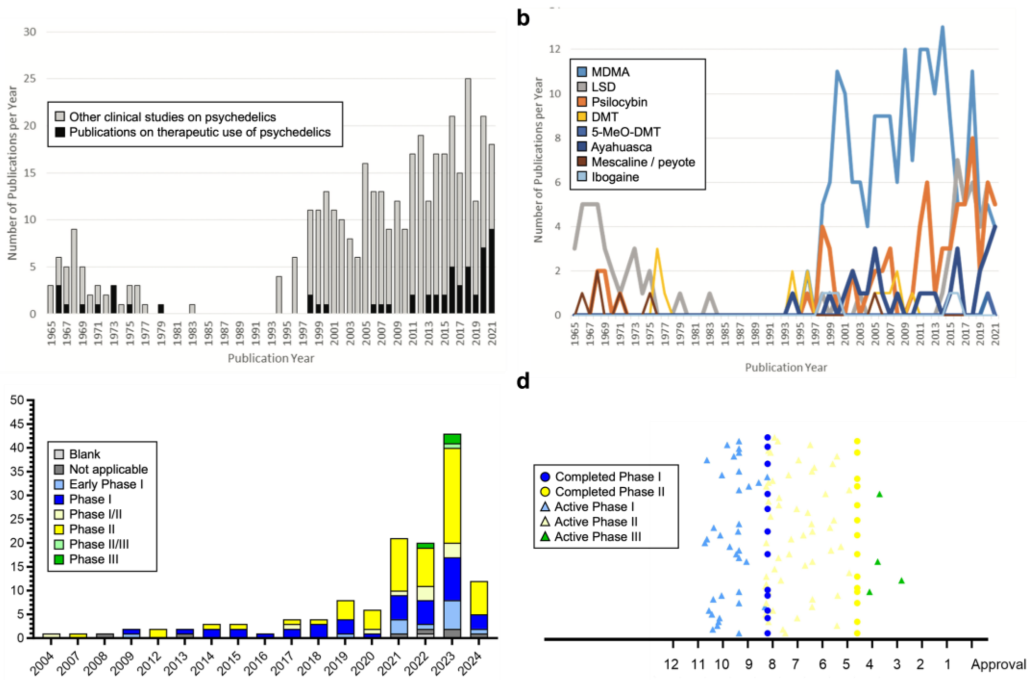

Figure 1.1 Trends in psychedelic clinical research and trial development

(a) Number of clinical publications per year by psychedelic compound; (b) Annual publication counts of psychedelic clinical studies, differentiated by therapeutic vs. non-therapeutic focus; (c) Growth of registered psilocybin trials on ClinicalTrials.gov by year and study; (d) Estimated proximity of psilocybin trials to regulatory approval; Note. panels a-b are adapted from Weleff et al. (2023), panels c-d are adapted from Norring & Spigarelli (2024).

As clinical research on psychedelics continues to expand, so too does a parallel effort to understand the mechanisms driving therapeutic change. Rather than treating the psychedelic state as a uniform or enigmatic force, researchers are increasingly focused on identifying the specific aspects of the experience that contribute to clinical outcomes. Early studies highlighted *mystical-type* experiences, characterised by feelings of unity, transcendence, and ineffability, which have been consistently linked to positive treatment effects [62–64]. However, it remains unclear whether these experiences are causally responsible for therapeutic benefits or simply co-occur with other active processes [65–67]. This has led to more targeted investigations into experiential features such as emotional breakthroughs [68], psychological insights [69], and profound experiences of connectedness [70], which may more directly mediate therapeutic outcomes. Evidence suggests that the therapeutic impact may depend less on the overall intensity of the psychedelic state [71], and more on how effectively it facilitates engagement with psychologically meaningful material [72–74]. Advances in qualitative methodology, including microphenomenology and detailed experiential interviews [75, 76], are also clarifying the affective, cognitive, and perceptual processes through which change occurs [77]. These efforts underscore the need for an integrative mechanistic framework that maps specific experiential features onto clinical outcomes, guiding both research and therapeutic practice.

There is, however, ongoing debate within modern psychedelic science over whether the subjective effects of psychedelics are even necessary for their therapeutic benefits [78, 79]. This debate reflects a broader epistemological tension between Indigenous understandings of healing, in which subjective experience is central to the therapeutic process, and reductionist neuroscientific frameworks, which tend to prioritise biological mechanisms [80]. Among Indigenous healing systems, the visionary states induced by psychedelics are not treated as incidental side-effects, but rather as the primary medium through which insight, 'diagnosis', and transformation occur [81]. Mazatec mushroom ceremonies (*veladas*), for instance, were specifically conducted at night to enhance visions, with healers and patients working directly with visionary content as the primary source of diagnostic and therapeutic information [82–84].[4] Similarly, in Amazonian ayahuasca shamanism, the visions are explicitly described as "teachings" (*enseñanzas*), with practitioners undergoing years of specialised training to interpret and work with these experiences [28, 86]. Far from being ancillary, these practices suggest that healing is not merely facilitated *during* altered states, but *through* them, implying that the therapeutic potential of psychedelics may be inextricable from the experiential and meaning-making dimensions they reliably evoke [87, 88].

This perspective stands in marked contrast to emerging scientific efforts to isolate the therapeutic potential of psychedelics from their phenomenological effects, most notably through the development of **non-hallucinogenic psychoplastogens (NHPs)** [89] (e.g., **tabernanthalog [TBG]**). These compounds are designed to promote neuroplasticity (e.g., dendritic growth, synaptic remodelling) while ostensibly avoiding the intense subjective experiences associated with classical psychedelics [89–91]. While preclinical studies suggest that NHPs can induce structural and functional neural changes, the extent to which these effects translate into meaningful therapeutic outcomes remains unknown. Without supporting data from human trials, it is unclear whether these compounds are truly non-hallucinogenic or whether they

[4] Illustrative quotes from select participants at one of our psilocybin research retreats in Mexico highlight how visionary experiences played a pivotal role in their healing processes [85]: P1: "*I was speaking to a massive mushroom. I asked the mushroom for healing for me and everyone in the circle, and it said there was nothing to fix because we are not broken. We are made as we are meant to be. The ceremony left me with the message that we are never truly alone. We are a part of something so much bigger than ourselves*" [suicidal ideation >4 years]. P2: "*I had a visual experience that we were all trees, and the closer I looked, the more connected I realised we all were, and I saw that we are all part of the same tree. I saw myself die, break down, flow through the ground, and into the network of the mycelium. I watched it all with a peaceful heart, knowing it was natural and a part of life. That death is an ending and a beginning, and by becoming nothing, we join everything*" [treatment-resistant depression, suicidal ideation >4 years].

elicit subtler experiential effects that remain poorly characterised.[5] Moreover, recent meta-analyses challenge the assumption that psychoplastogens reliably increase levels of **brain-derived neurotrophic factor (BDNF)** - a key marker of neuroplasticity - in humans, raising questions about the translational relevance of these preclinical findings [93]. These uncertainties suggest that reducing PAT to its neurobiological substrates may risk overlooking the central role that subjective experience may play. Rather than viewing these effects as incidental, a more integrative perspective recognises that therapeutic change may arise from the dynamic interaction between neurobiological mechanisms and lived phenomenological experience [94, 95].[6]

If subjective experience is indeed central to the therapeutic action of psychedelics, then their psychological intensity must be recognised as a core feature rather than a side effect. While psychedelics can induce deeply immersive and blissful states [1, 97, 98], they can also bring individuals into direct contact with unresolved trauma, existential distress, or other emotionally charged material that typically remains beyond reach through conventional therapeutic approaches [15, 99–101]. This duality underscores the importance of addressing both the potential benefits and risks inherent in psychedelic experiences. Indigenous communities have long recognised this complexity and developed sophisticated cultural frameworks to guide and contain such challenging experiences, embedding them within ritual, symbolism, and community support [102]. In contrast, modern clinical models are still developing approaches to navigate the psychological intensity that psychedelics can provoke. Within these emerging frameworks, differing philosophies have developed regarding how to handle difficult experiences. Some practitioners advocate fully embracing challenging content, encouraging participants to “trust, let go, be open” and move “in and through” discomfort rather than resist it [103]. This perspective, exemplified by Watts and Luoma [104], suggests that in a therapeutically supported setting, “there are no bad trips” - only material to be worked with.

[5] David Olson (2024), the leading pharmacologist pioneering research on NHPs compounds at UC Davis, states: “*Tabernanthalog (TBG) has not been tested in the clinic yet, and so we won't know [what they are going to be experiencing] for certain. Based on all of our preclinical data, we predict that they would not have a mystical-type experience like you would have if you took psilocybin. It’s unclear exactly what you would feel… Most drugs that act on the central nervous system make you feel something. When I take Benadryl for my allergies, I definitely feel something. And so, it's unreasonable to expect that CNS drugs will not make you feel anything. The trick is to keep the subjective effects manageable so that it doesn’t impair you and you can still operate a car and go about your daily business*”. [92]

[6] As cultural critic Erik Davis (2013) writes: “*Rarely has the new neuro-reductionism been so naked in its repackaging of human experience… By sweeping such sublimities under the rug of toxic ‘side effects’, the researchers and their partners in industry want to sidestep the remarkable paradox that psychedelic substances present to brain-based reductionists: psychedelics are material molecules that frequently occasion experiences that look and feel, for all the world, like the sort of mystical or religious raptures whose unfolding cognitive content calls into question strict materialism. In other words, reductionist researchers of powerful psychedelic effects must still squirm before God - or at least before the experiential states that recall the ecstatic reports of traditional religious mystics, or of shamans making pacts with non-human entities, or of meditators seeing into the knitted web of self and world*.” [96]

However, this blanket assertion overlooks individual differences in psychological resources. Even in carefully controlled therapeutic environments, some individuals may lack the emotional resilience and coping skills needed to productively engage with the intense psychological material that emerges, potentially resulting in destabilisation rather than therapeutic benefit. This highlights a central paradox within PAT: the same phenomenological intensity that can catalyse healing may also increase the risk of psychological destabilisation [105–108]. While challenging experiences can facilitate emotional catharsis [109, 110] or loosen rigid cognitive patterns [111, 112], they can also overwhelm an individual's capacity to integrate, leading to difficulties such as prolonged depersonalisation, existential distress, or exacerbation of pre-existing vulnerabilities [113, 114]. This dual potential becomes especially pronounced for individuals with precarious life circumstances or limited support systems, where the balance between benefit and harm may be particularly fragile. As PAT moves toward mainstream clinical adoption, it is crucial to move beyond universal narratives about challenging experiences and instead develop nuanced, person-centred approaches. These approaches must account for the complex interplay between subjective intensity, psychological risk, and individual preparedness, recognising that what constitutes a therapeutic challenge for one person may represent unbearable distress for another.

1.3 Theoretical perspectives on psychedelic preparedness

The importance of *set and setting* - referring to an individual's internal state and the surrounding environment - has long been acknowledged in shaping the quality and outcome of psychedelic experiences [115, 116]. In principle, both constructs are broad: *set* includes enduring traits (e.g., openness and absorption), transient emotional states (e.g., anxiety or anticipation) and wider contextual factors (e.g., social support or ongoing stressors) [117–122]; *Setting* encompasses the physical, social, and cultural environment in which the experience takes place [123–125]. Yet in practice, discussions of set and setting often centre on the immediate conditions surrounding the dosing session: what music will be playing, who will be present, how will the room be arranged? While these elements matter, they represent only a narrow slice of the broader psychological and environmental conditions that shape a psychedelic experience. The internal landscape a person brings into the session - along with the trust, safety, and coherence of the surrounding context - is not created in a matter of hours. These dimensions unfold over time. In this sense, preparation is not separate from set and setting, but integral to their development. What is needed is a more temporally extended view; one that recognises that the qualities of set and setting on the day of dosing are the result of processes, intentional or otherwise, that unfold in the days and weeks leading up to the session. Attending to these longer timeframes may be crucial for creating the conditions in which psychedelic experiences are not only safer, but more meaningful and psychologically integrable.

A useful lens for expanding this perspective is the concept of *preparedness* - a term well-established across disciplines such as disaster response [126, 127], education [128, 129], sports psychology [130, 131], and surgical practice [132, 133]. In these contexts, preparedness refers to a structured process through which individuals develop the cognitive, emotional, and behavioural capacities needed to navigate high-stakes or uncertain situations. Carroll et al. (2006), for example, define preparedness as an adaptive motivational state aimed at anticipating and managing future challenges [134]. Despite its relevance, this construct has not yet been systematically applied within psychedelic science, a field in which individuals face uniquely intense, unpredictable, and sometimes ontologically destabilising experiences [135]. In response, we propose the construct of *psychedelic preparedness*: a modifiable anticipatory state reflecting an individual's psychological, relational, and contextual readiness to engage both the content and consequences of the psychedelic experience. This framing expands preparation beyond harm reduction[7], defining it not simply

[7] "Harm reduction" developed in response to prevailing conceptualisations of illicit drug use, specifically the zero-tolerance approach to deter use. Harm reduction focuses on reducing the consequences of drug use rather than eliminating drug use. It seeks to adopt practical rather than idealised goals. Thus, focus is placed on safer use patterns rather than the immediate deterrence of use per se [136].

as a means of minimising risk, but as a process of cultivating the psychological and contextual conditions that support openness, engagement, and lasting integration. Psychedelic preparedness, then, is not simply about protection; it plays an active role in shaping both the depth of the experience and the integration that follows (see **Chapter 7**, **Section 7.3.3** for broader discussion on integration as a critical counterpart to preparation).

Although the concept of psychedelic preparedness has not been explicitly articulated within psychedelic research, Indigenous traditions have long recognised the importance of thorough preparation for psychedelic experiences [137–139]. Many of these traditions incorporate structured practices (e.g., intention-setting, dietary guidelines[8], and ceremonial rituals) within a broader cultural and spiritual context that not only ensures safety but also supports meaningful integration afterward [141–150]. In these traditions, preparation is more than a practical step; it is an ongoing relational process that connects the individual to their community, lineage, and guiding cosmologies [145, 151, 152]. While contemporary PAT has drawn both explicit and implicit influence from Indigenous practices [142, 153, 154], the specific role of preparation in these traditions has received relatively little systematic study, despite growing recognition of its therapeutic significance [16, 155, 156]. As a result, Western PAT risks overlooking key preparatory elements that may influence therapeutic outcomes and increase risk. Moreover, directly transplanting Indigenous frameworks into Western contexts is neither practical nor appropriate, as these practices are deeply embedded within cultural and spiritual systems that shape their meaning and effectiveness. Instead, further research is needed to clarify how certain preparatory practices foster psychedelic preparedness across different cultural settings. Developing approaches that integrate key insights from traditional practices, while respecting cultural integrity and aligning with contemporary clinical and ethical standards, is crucial [157–161]. This process requires careful navigation of cultural differences to ensure that preparation practices enhance both safety and therapeutic depth without reducing Indigenous wisdom to decontextualised techniques [22, 145, 162–170].

If psychedelic preparedness is to serve as a meaningful construct, it must go beyond offering a label for pre-session activity and instead provide a framework for understanding how individuals might be supported in facing the uncertainty and intensity that psychedelic experiences often entail. Unlike conventional

[8] In Amazonian medicine, particularly within *vegetalismo* traditions of the Peruvian Amazon, *dietas* are holistic practices involving the intake of specific plants, social isolation, dietary restrictions (such as avoiding salt, sugar, and certain foods), and sexual abstinence. While some contemporary practices may frame *dietas* as preparatory for ayahuasca ceremonies, traditional *vegetalismo* perspectives view them as distinct, multifaceted practices aimed at physical healing, psychological transformation, and spiritual growth [137, 140]

treatments, psychedelics do not act on symptoms in a linear or predictable fashion; rather, they open an experiential space in which insight, distress, and transformation may arise in rapid succession, or even simultaneously [171, 172]. In this context, preparedness may involve more than simply acquiring knowledge or managing expectations; it likely depends on a combination of factors, including psychological orientation, emotional resources, and how well the surrounding context supports and aligns with the intended experience. While some aspects may reflect relatively stable traits, others may be shaped through intentional practices or supportive interventions [173]. It is plausible, then, to view preparedness as a dynamic configuration, formed over time through the interplay of dispositional, relational, and environmental influences. This conceptual framing raises important questions for both research and practice: What kinds of preparation best support this orientation? How can readiness be meaningfully assessed? And how might approaches be adapted to the varying needs and vulnerabilities of individuals? These questions are especially pressing in clinical contexts, where preparation is widely acknowledged as important, yet remains inconsistently defined, implemented, and evaluated [16].

1.4 Clinical approaches to psychedelic preparation

Despite growing recognition of the importance of preparation in PAT, there is still no clear consensus on how it should be structured, delivered, or evaluated in clinical practice [174, 175]. Existing models range from brief psychoeducational sessions to more intensive psychotherapeutic approaches, but there is little standardisation, and few studies have systematically compared their effectiveness. This inconsistency leaves fundamental questions unanswered: What specific preparatory elements are most beneficial? How much preparation is optimal? How can interventions be tailored to individual needs while respecting cultural contexts? As Thal et al. (2022) point out, without systematic study, it remains impossible to draw "definitive conclusions regarding the significance and impact of specific facets of preparatory sessions on therapeutic outcomes". Addressing these challenges requires both conceptual clarity and rigorous empirical investigation, integrating insights from clinical practice with lessons drawn from traditional approaches.

The ways in which psychedelic preparation is structured have evolved alongside broader cultural and clinical paradigms. Early approaches, particularly in the 1960s, were largely shaped by transpersonal and spiritual frameworks that framed psychedelics as tools for mystical insight and expanded consciousness [176–178]. Figures such as Timothy Leary and Richard Alpert (later Ram Dass) promoted these substances not just as psychological aids, but as catalysts for profound existential transformation, often drawing on Hindu, Buddhist, and esoteric traditions [179–181][9]. Their approach encouraged participants to expect transcendent experiences, with preparation involving specific ritual elements such as mantra chanting or symbolic enactments meant to shape the trajectory of the acute experience [183, 184]. While this undeniably provided participants with structure, it also raised important epistemic concerns [185]. Psychedelics increase suggestibility [186, 187], which means that imposing spiritual frameworks before or during a session can shape participants' experiences, guiding them toward culturally constructed narratives rather than encouraging open-ended exploration of their own psychological material [102, 188]. This led to debates around the potential for psychological and ethical risks, where spiritual narratives imposed during preparation could blur the line between therapeutic guidance and ideological influence [189, 190].

[9] Timothy Leary, Richard Alpert, and Ralph Metzner's *The Psychedelic Experience: A Manual Based on the Tibetan Book of the Dead* (1964) exemplifies the early transpersonal approach to psychedelic preparation. Drawing from the *Bardo Thodol*, the manual posited that the dissolution of ego during a psychedelic trip mirrored the soul's journey through death and rebirth. This analogy framed psychedelics as tools for spiritual awakening, rather than mere therapeutic agents, and reinforced the expectation that psychedelic experiences could reveal profound, transcendent insights. This framework, while influential in shaping early preparation practices, also risked embedding culturally specific spiritual narratives into participants' experiences, potentially limiting open-ended, personal exploration [182].

While some contemporary PAT settings remain influenced by early transpersonal models [103, 177, 191], the field has increasingly moved toward structured, manualised, and secular approaches [192]. Nevertheless, preparation methods continue to vary widely [16], broadly categorised into **evidence-based therapy (EBT)**-inclusive and non-directive models [174, 193, 194]. EBT-inclusive models integrate established therapeutic frameworks that exist independently of psychedelic administration. Although these approaches differ in structure, therapeutic engagement, and interpretative framing, they share a commitment to intentional therapeutic input to enhance psychological preparedness. In contrast, non-directive models emphasise creating a safe and supportive environment while allowing the psychedelic experience to unfold naturally. These approaches rest on the idea that, given the right conditions, the mind will spontaneously process emotions, thoughts, and insights without structured guidance or interpretative input from facilitators. Facilitators in these settings aim to create a safe, open environment without imposing structured frameworks or interpretative lenses, allowing participants to explore their experiences with greater autonomy. The following sections outline two EBT-inclusive approaches - psychodynamic (**Section 1.4.1**) and cognitive-behavioural (**Section 1.4.2**) - before turning to non-directive methods (**Section 1.4.3**).

1.4.1 Psychodynamic

Psychoanalytic and psychodynamic therapies are rooted in the idea that unconscious processes shape thoughts, emotions, and behaviour, with early life experiences playing a crucial role in psychological development [195, 196]. Classical psychoanalysis, first developed by Freud (1856-1939), is an intensive, long-term treatment that seeks to uncover and resolve unconscious conflicts through free association, dream analysis, and transference interpretation [197, 198]. Over time, psychodynamic therapy emerged as a broader, more flexible framework incorporating later developments [199] such as object relations theory [200, 201], self-psychology [202, 203], and attachment theory [204, 205]. While maintaining a focus on unconscious processes and relational patterns, psychodynamic therapy is typically practiced in a less intensive format (e.g., weekly face-to-face sessions) and has been adapted for a range of clinical settings, including structured short-term models with empirical support [206]. Importantly, both approaches emphasise that making unconscious material conscious is key to lasting psychological change, a principle that has informed diverse areas of psychotherapy [207, 208].

Many contemporary researchers claim that psychoanalytic perspectives are highly relevant to PAT, given their focus on unconscious processes and non-ordinary states of consciousness [209–211]. However, psychoanalytic theory historically developed with little engagement with psychedelics [192]. Freud and his contemporaries did not incorporate these substances into their theoretical work, and while Jung (1875-1961) briefly addressed psychedelics in correspondence, particularly in relation to their psychological and moral implications [212], the foundational texts of psychoanalysis offer no direct framework for understanding psychedelic experiences.[10] Nevertheless, foundational psychoanalytic texts emphasise that bringing unconscious content into awareness is central to therapeutic change [219, 220] - a process that contemporary psychodynamic frameworks suggest can be facilitated by psychedelic experiences [221]. From this perspective, psychedelics are thought to temporarily weaken ego defences, allowing repressed emotions, unresolved conflicts, and entrenched relational patterns to surface with heightened intensity and accessibility [211]. This convergence led to much of PAT in the mid-20th century being explicitly grounded in the psychoanalytic perspective, with clinicians viewing psychedelics as catalysts for emotional catharsis and existential insight [222–225]. Grof (1982) famously described LSD psychotherapy as "laboratory proof" of Freudian principles, positioning psychedelics as a direct gateway to the unconscious [226]. Reciprocally, Carhart-Harris et al. (2014) suggest that "scientific research with psychedelics has considerable potential for developing aspects of psychoanalytic theory" [227].[11] As a result, several influential psychodynamic frameworks have emerged, shaping how therapists conceptualise and engage with the psychological material that arises during psychedelic sessions [209, 221, 229].

Grof's (somewhat controversial) *perinatal theory* is one of the most well-known psychodynamic frameworks in PAT [226, 230, 231], which suggests that psychedelics can reactivate unconscious material related to birth and early development. According to Grof's model, psychedelic experiences unfold through

[10] While Freud and his contemporaries did not engage with psychedelics in their theoretical or clinical work, there is evidence that Freud himself was briefly captivated by the idea of *chemical transcendence*, particularly through his experimentation with cocaine. In the early 1880s, Freud advocated for the therapeutic potential of cocaine, influenced by his own subjective experiences of enhanced mood, energy, and intellectual vigour [213, 214]. His most controversial application involved recommending cocaine to his friend Ernst von Fleischl-Marxow to treat morphine addiction, which tragically led to a debilitating cocaine addiction and severe psychosis [215, 216]. Freud initially framed cocaine as a powerful tool for overcoming exhaustion and debility, seeing it as a "magic bullet" for the mind. However, as reports of addiction and toxic effects became undeniable, he distanced himself from his earlier enthusiasm, never formally incorporating cocaine into his psychoanalytic practice [217]. Although he later focused solely on talk-based therapeutic methods, his early fascination with the idea of chemically unlocking deeper mental states reflects a fleeting intersection between psychoanalytic ambitions and the pursuit of chemical transcendence [218].

[11] Carhart-Harris has drawn several connections between psychedelics and psychoanalytic concepts throughout his work. In *The Entropic Brain* (2014), he discusses how psychedelics facilitate ego dissolution, stating that the psychedelic state is a "*high-entropy state of consciousness*" where ego integrity is weakened, allowing unconscious material to become accessible: "*The psychedelic state is described as a prototypical high-entropy state of consciousness... The psychological counterpart of this process is the development of a mature ego, and its dissolution during psychedelic experiences may facilitate psychodynamic insights*". He further notes that psychedelic experiences often involve "*ego-dissolution*" or "*disintegratio*n", which are seen as opportunities for repressed material to surface [227]. In *Waves of the Unconscious* (2007), Carhart-Harris explicitly links psychedelic states to the emergence of unconscious content, describing them as conducive to revealing repressed memories and conflicts: "*The psychedelic state has been viewed as conducive to the emergence of unconscious material into consciousness... psychedelic drugs may allow the release of repressed memories and unconscious conflict*" [228]. He also highlights that "*bursts of electrical activity spreading from the medial temporal lobes to the association cortices are the primary functional correlate of discharging psychical energies, experienced on a subjective level as the emergence of unconscious material into consciousness*". This neurophysiological process, he suggests, resembles the dynamics seen in REM sleep and psychosis, where unconscious content similarly becomes accessible.

four “perinatal matrices”,[12] each representing a stage of labour and influencing deep existential struggles and psychological conflicts [32, 232, 233]. To prepare for these experiences, techniques like breathwork, guided introspection, and ‘archetypal’ framing[13] were used to help individuals embrace intense perinatal imagery, with resistance viewed as a barrier to catharsis and transformation [226, 230, 231]. However, Grof’s model has faced significant criticism. He himself acknowledged that there is no proven direct link between actual birth experiences and his perinatal matrices, describing the model as a helpful but unproven framework [235]. He also admitted that his “own experiences were absolutely critical in shaping [his] views” [236]. Critics argue that the claim of universally appearing perinatal imagery in psychedelic experiences is likely exaggerated, suggesting that such imagery may reflect symbolic representations shaped by cultural background and expectations, rather than actual birth memories [229, 237, 238]. In this view, the imagery may represent a regressive, dream-like mode of cognition where emotional salience takes precedence over literal memory [239, 240]. Some have even argued that Grof’s models contain a patriarchal bias through their emphasis on the “toxic maternal womb”, creating a framework reminiscent of Melanie Klein’s “good breast/bad breast”[14] dualism from the 1940s [245]. Despite these shortcomings, Grof’s concepts still influence some contemporary PAT, particularly in underground settings. Many practitioners now interpret his birth-related framework metaphorically rather than literally when explaining transformative experiences.

Following Grof’s influential work, most contemporary psychodynamic perspectives on PAT moved beyond birth trauma narratives [221]. At the core of the psychodynamic approach is the recognition that psychological and emotional pain is an inherent part of life, and that individuals develop defenses to

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[12] Grof’s perinatal theory delineates four “perinatal matrices” (BPM I-IV), each corresponding to a distinct stage of labour and reflecting fundamental existential and psychological patterns. BPM I (Primal Union with the Mother) represents the undisturbed intrauterine existence, marked by feelings of unity and security. BPM II (Antagonism with the Mother) corresponds to the onset of contractions in a closed uterine system, characterised by feelings of entrapment, existential despair, and suffering. BPM III (Synergism with the Mother) reflects the propulsion through the birth canal, involving intense struggle, explosive tension, and glimpses of liberation. Finally, BPM IV (Separation from the Mother) signifies birth and the beginning of independent existence, marked by relief, rebirth, and transformation. Grof posits that these matrices shape profound emotional and existential conflicts, and that psychedelics can facilitate the reactivation and integration of this unconscious material [32, 232, 233].

[13] Archetypal framing is the process of interpreting intense or symbolic experiences as manifestations of universal psychological patterns or motifs, such as birth, death, struggle, and transformation. In Grof’s framework, this approach helps individuals make sense of profound states by contextualising them within collective human themes rather than as isolated personal experiences [232, 234]

[14] Melanie Klein’s concept of the “good breast” and “bad breast” [241] is a fundamental idea in her object relations theory, positing that infants initially perceive the mother’s breast as either entirely good (nourishing, comforting) or entirely bad (frustrating, persecutory), depending on whether their needs are met. This splitting into idealised and persecutory objects is a defence mechanism that helps infants manage the ambivalence of dependency, forming the basis of the “paranoid-schizoid position”, where the good and bad aspects of the mother are kept separate. As the child develops, the integration of these conflicting experiences marks the transition to the “depressive position”, where the mother is seen as a whole person capable of both positive and negative actions. Klein’s focus on innate aggression as a driving force behind this splitting has been critiqued for its lack of attention to environmental and relational factors [242, 243], leading some to favour attachment theory perspectives that emphasise the child’s real-world interactions and caregiver relationships [244].

unconsciously mitigate this distress [246]. These defenses[15] are particularly relevant in PAT, where they are (ostensibly) temporarily lowered, permitting the emergence of repressed material and thereby facilitating therapeutic change [209, 229]. Jung, however, cautioned that the sudden dissolution of these defenses could be destabilising, as unconscious material may emerge too rapidly for the ego to integrate, leading to confusion, overwhelm, or even psychological disintegration [249]. He emphasised that engagement with the unconscious should be a gradual process, ideally unfolding through introspection, dream analysis, and long-term therapeutic work rather than through abrupt and unmediated exposure [250]. In a letter to Father Victor White, he warned, "The more you know of [the collective unconscious], the greater and heavier becomes your moral burden, because the unconscious contents transform themselves into your individual tasks and duties as soon as they begin to become conscious" (Jung, *Letters, Vol. 2*, 1976). While this approach assumes that surfacing unconscious content facilitates healing, some contemporary theorists align with Jung in cautioning that the rapid removal of defenses may leave individuals vulnerable to overwhelming internal conflict and psychic destabilisation [246]. Applying psychodynamic principles to PAT therefore requires careful ethical consideration, particularly regarding the assessment of an individual's readiness for deep psychedelic work and the potential risks of potentially exposing unconscious material too quickly. Nevertheless, PAT continues to attract many psychodynamic practitioners, with some advocating for the ongoing integration of psychoanalytic models into psychedelic therapy [209, 229, 251].

Additional concerns in relation to the use of psychodynamic frameworks in PAT are around suggestibility, empirical validity and therapeutic efficacy [252]. Early research documented that patients undergoing PAT often reported experiences that closely mirrored their therapist's theoretical orientation, indicating that therapeutic frameworks and expectations can significantly influence the content and nature of the patient's psychedelic experiences [187, 253]. For example, patients treated by Jungian therapists frequently described archetypal, self-transcendent encounters, while those working with Freudian analysts were more likely to recall childhood memories and psychosexual conflicts [187]. These findings highlight how the psychological framework introduced during PAT - particularly in the preparation phase - can shape the way individuals interpret their psychedelic experiences. This raises questions about whether psychodynamic models in PAT assist the uncovering of unconscious material or simply impose a lens through which such content is viewed. Moreover, while psychodynamic approaches arguably provide valuable insights into

[15] Unconscious defenses are psychological strategies that operate below conscious awareness to protect the individual from anxiety, conflict, or perceived threats. According to Anna Freud, they are "unconscious processes which are employed by the ego to protect itself from unpleasant feelings, anxiety, or internal conflict" [247, 248].

unconscious processes, transference, and emotional processing, they often prioritise interpretive narratives (e.g., linking present difficulties to childhood experiences or unconscious conflicts) over measurable therapeutic outcomes, making them difficult to validate within contemporary clinical science [254, 255]. Unlike structured, evidence-based approaches (e.g., **Cognitive Behavioural Therapy (CBT)**), psychodynamic interpretations risk imposing meaning rather than allowing participants to arrive at their own insights more naturally, which could be counterproductive in psychedelic preparation [256–258]. Additionally, the historical dominance of psychodynamic models in underground PAT may reflect tradition rather than demonstrated efficacy, necessitating a more critical evaluation of their continued relevance.

As PAT gains traction within mainstream clinical research, there is growing emphasis on aligning therapeutic frameworks with empirically validated models of psychological change [259]. While psychodynamic approaches have played a formative role in the historical development of PAT - particularly in underground and early therapeutic contexts - their influence within contemporary clinical trials has been more limited [260]. This reflects broader shifts in mental health care toward structured, time-limited, and outcome-oriented interventions, which more readily meet the demands of regulatory approval and scientific evaluation [261, 262]. Nevertheless, psychodynamic principles, such as the importance of ‘unconscious’ processes and relational dynamics, continue to inform the practice of many therapists working with psychedelics, offering a rich conceptual lens for understanding the therapeutic encounter [209, 263]. As the field evolves, a key challenge lies in integrating these insights with evidence-based standards that prioritise clinical effectiveness, psychological safety, and patient autonomy [251, 252, 264, 265].

1.4.2 Cognitive behavioural

In response to concerns about the speculative or metaphysical underpinnings of psychodynamic approaches to PAT, cognitive-behavioural models have been proposed as a more empirically grounded alternative [192]. These therapies have evolved across three distinct “waves”, each incorporating new theoretical and methodological advances to address the limitations of earlier models and broaden their clinical applicability [266]. The first wave, rooted in behaviourism (1950s - 1970s), focused on modifying observable behaviour through conditioning principles, prioritising measurable outcomes [267, 268]. While effective in shaping behaviour, it failed to account for internal cognitive processes [269]. The second wave (1970s - 1990s) addressed this gap by recognising the role of maladaptive thought patterns in psychological distress. CBT, for example, was developed to target and restructure unhelpful cognitions as a route to symptom reduction

[270]. However, this approach raised concerns of its own, with critics noting that changes in cognitive content alone did not always produce meaningful emotional or behavioural transformation [271].

These limitations led to the development of third-wave cognitive-behavioural therapies, emerging in the 1990s and early 2000s as extensions or evolutions of earlier CBT approaches [272]. Unlike their predecessors, which primarily focused on changing the content of maladaptive thoughts, third-wave therapies adopt a more principle-focused approach, emphasising the context and functions of psychological phenomena rather than their form [273]. These therapies aim to build broad, flexible coping strategies rather than narrowly targeting symptom elimination. They incorporate contextual and experiential change methods, emphasising acceptance, mindfulness, and values-driven living rather than solely focusing on symptom reduction [274]. Key examples include **Dialectical Behaviour Therapy (DBT)** [275], which combines acceptance and change strategies to enhance emotional regulation, distress tolerance, interpersonal effectiveness, and mindfulness skills, primarily for individuals experiencing emotional dysregulation; **Acceptance and Commitment Therapy (ACT)** [276], which integrates acceptance and mindfulness processes with commitment and behaviour change techniques to cultivate psychological flexibility and enable valued living despite the presence of challenging thoughts and feelings; and **Mindfulness-Based Interventions (MBIs)** [277], which focus on training attention and awareness of present experience with an attitude of acceptance. Rather than aiming to eliminate distress, these approaches promote a more open, accepting stance toward difficult thoughts and emotions. [278, 279].

There is growing support for the integration of second- and third-wave therapies with psychedelic treatments, given their empirical rigour, structured methodologies, and demonstrated efficacy [192] (see **Table 1.1** for an overview of their relevance to preparation). This position rests on several key justifications. First, cognitive-behavioural approaches are among the most extensively studied and empirically supported psychotherapies, with robust evidence across depression, anxiety, and substance use disorders [280] - the very conditions targeted by most psychedelic research. Second, these models offer structured and measurable interventions, aligning well with clinical trial requirements for standardisation and replicability [255, 281]. Third, they minimise speculative or metaphysical claims about consciousness, making them especially compatible with secular, evidence-based medical contexts [192]. While third-wave therapies incorporate experiential and contextual strategies, their empirical validation in clinical settings supports their compatibility with standardised medical contexts, even if some of their underlying concepts may be seen as less strictly scientific compared to traditional CBT.

ACT has emerged as a particularly well-suited framework for PAT preparation due to its emphasis on psychological flexibility: the capacity to remain open, aware, and engaged in the presence of difficult or unexpected experiences [282, 283]. This is especially relevant in PAT, where the psychedelic state often dynamic and unpredictable [284, 285]. By cultivating willingness and non-reactivity, ACT-based preparation may reduce experiential resistance and enhance therapeutic outcomes [86, 210]. ACT's six core processes (acceptance, cognitive defusion, present-moment awareness, self-as-context, values clarification, and committed action) offer structured yet adaptable tools that closely align with the challenges and opportunities presented by psychedelics [273, 286, 287]. For instance, cognitive defusion, which fosters distance from distressing thoughts, may help participants avoid becoming overwhelmed by transient, psychedelic-induced insights. Likewise, self-as-context supports a flexible and expansive sense of identity, resonating with the loosening of self-referential processing frequently observed in altered states [112, 288]..

Preliminary research supports the integration of ACT into PAT preparation. Sloshower et al. (2020) developed a manualised ACT-based protocol for psilocybin therapy for **Major Depressive Disorder (MDD)**, proposing that psychedelics offer direct experiential access to core ACT processes such as emotional acceptance and detachment from maladaptive self-narratives. Their model reinforced these processes throughout both preparation and integration, aiming to translate psychedelic insights into lasting behavioural change. Similarly, Watts and Luoma (2020) framed PAT through the lens of psychological flexibility, arguing that fostering openness and willingness during preparation can mitigate fear and avoidance responses during the session itself. Their **Accept, Connect, Embody (ACE)** model provides a structured yet flexible framework for guiding participants through the full therapeutic arc, emphasising non-reactivity, values-based engagement, and embodied awareness as key supports for psychedelic processing.

MBIs such as **Mindfulness-Based Cognitive Therapy (MBCT)** and **Mindfulness-Based Stress Reduction (MBSR)**, are increasingly recognised as evidence-based third wave approaches well-suited to psychedelic preparation [289]. Adapted from contemplative traditions into secular clinical frameworks, MBIs cultivate skills such as present-moment awareness, non-reactivity, psychological flexibility, and observational awareness without avoidance - capacities that may help individuals navigate the intensity and unpredictability of psychedelic states [290, 291]. While direct evidence for combining MBIs with classic psychedelics remains limited, preliminary findings from **ketamine-assisted therapy (KAT)** suggest that pairing mindfulness practices with altered states of consciousness may enhance therapeutic engagement and outcomes. For instance, combining ketamine with **Mindfulness-Based Relapse Prevention (MBRP)** has been associated with reduced craving and relapse in substance use populations [292–294]. More recently, a double-blind pilot study found that esketamine, when administered alongside a two-week daily MBI, enhanced psychological engagement with the mindfulness practice and led to transient reductions in alcohol craving compared to placebo [252]. Although still early, these findings support the rationale for integrating MBIs into PAT and underscore their potential to strengthen both preparation and integration phases.

This potential is already being realised in clinical protocols using classic psychedelics. For example, the **Yale Psilocybin Depression Manual (YPDM)** explicitly incorporates MBCT, recognising that psychedelic experiences often evoke mindfulness-related qualities such as decentering, psychological openness, and self-transcendence [288]. The manual proposes that formal mindfulness training may strengthen these emergent capacities, enhance emotional regulation, and offer a structured framework for translating psychedelic insights into long-term psychological change [295]. Other protocols, though not explicitly framed as mindfulness-based, also embed MBI principles. The Imperial College ACE manual, for instance, incorporates breath awareness, somatic scanning, and acceptance-based guidance to support participants in remaining grounded and receptive during difficult moments - approaches closely aligned with mindfulness mechanisms [296]. Together, these developments reflect a growing recognition that mindfulness training can play a critical role in PAT, not only by helping individuals navigate the acute effects of psychedelics with greater emotional stability and openness, but also by providing a scaffold for integrating profound experiential material into lasting personal transformation.

While MBIs in PAT primarily emphasise distress tolerance and present-moment awareness, they represent only a narrow subset of broader contemplative traditions [297]. Traditional meditation practices (particularly those from Buddhist, Vedantic, and other contemplative lineages) extend beyond short-term emotion regulation to cultivate sustained attentional stability, perceptual refinement, and systematic cognitive training [298, 299]. Given that both meditation and psychedelics disrupt self-referential processing and alter conscious perception [300, 301], meditation-based preparation may not only help individuals navigate the psychedelic experience itself, but also influence how they interpret and integrate its content. However, empirical research remains limited on whether pre-psychedelic meditation training enhances subjective or neurophysiological responses to psychedelics, or whether it improves outcomes beyond general sense of psychological preparation. Further investigation is needed to identify whether specific meditation-based approaches uniquely optimise psychedelic readiness, and how they interact with pharmacologically induced states. These questions - particularly around meditation's role in modulating baseline psychological traits, shaping psychedelic content, and facilitating long-term integration - are explored in more depth in **Chapter 4**.

While second- and third-wave cognitive-behavioural approaches show considerable promise for integration into PAT, designating them as the “default psychotherapeutic model” [192] may be premature. To date, no controlled trials have directly compared CBT-based frameworks with alternative psychotherapeutic approaches in the context of psychedelics, and much of the existing literature draws on theoretical alignment or qualitative accounts rather than rigorous efficacy data [302]. Critics have cautioned that imposing structured cognitive-behavioural frameworks onto psychedelic experiences may constrain the therapeutic process, potentially shaping how patients interpret, integrate, or even access certain insights [302]. More broadly, the longstanding assumption that CBT represents the “gold standard” of psychotherapy has come under increasing scrutiny. Meta-analyses suggest that its superiority over other models is often overstated [303, 304], and growing evidence supports the efficacy of psychodynamic approaches - long dismissed as unscientific - on par with CBT, with some studies suggesting longer-lasting therapeutic gains [252, 305, 306]. Nonetheless, these developments highlight the need for epistemic openness when considering which therapeutic frameworks may best complement psychedelic treatment [189].

Table 1.1. Concepts from cognitive-behavioural approaches relevant to psychedelic preparation

Approach	Concept	Description	Relevance to psychedelic preparation
Second-wave approaches			
CBT	Structured session format	A consistent framework guiding each session (e.g., agenda setting, review, interventions, summary, and homework)	Enhances predictability and containment, helping participants feel grounded ahead of uncertain and potentially intense psychedelic experiences.
	Psychoeducation	Providing clients with information about their condition, treatment rationale, and what to expect from therapy.	Supports informed consent, manages expectations, and increases participant confidence in the therapeutic process.
	Self-monitoring	Encouraging ongoing tracking of thoughts, emotions, and behaviours to build awareness between sessions.	Promotes psychological insight and emotional regulation, offering tools that can enhance preparation and post-session integration.
Third-wave approaches			
DBT	Pre-treatment and commitment strategies	Early sessions aimed at building commitment to therapy goals and increasing motivation.	Strengthens engagement and readiness, helping participants approach the psychedelic experience with greater intentionality.
	Therapy-Interfering Behaviour (TIB)	Identifying and addressing behaviours that may disrupt the therapy process.	Increases awareness of avoidance or resistance patterns, allowing facilitators to support engagement and safety during preparation.
	Skills training	Teaching practical emotion regulation, interpersonal effectiveness, distress tolerance, and mindfulness skills.	Equips participants with coping strategies to manage emotionally intense or destabilising experiences during and after psychedelic sessions.
ACT	Psychological flexibility	The ability to remain open to experience while pursuing valued goals, even in the presence of difficult thoughts or feelings.	Enhances adaptive responding to altered states, supporting therapeutic engagement and resilience in the face of challenging material.
	Acceptance over avoidance	Encouraging willingness to experience discomfort rather than attempting to control or suppress it.	Promotes surrender and reduces experiential resistance - key mechanisms for navigating difficult psychedelic content.
	Values clarification	Helping individuals identify and commit to personally meaningful values.	Anchors psychedelic insights in real-life purpose and motivation, facilitating meaningful integration and behaviour change.
MBI	Present-moment awareness	Training attention to stay focused on immediate experience with non-judgmental awareness.	Strengthens attentional stability and helps participants remain centred during the disorienting effects of psychedelics.
	Non-reactivity	Cultivating the ability to observe thoughts and emotions without immediate reaction or judgment.	Supports emotional equanimity and reduces impulsive or defensive responses during challenging psychedelic states.
	Breath and body awareness	Directing attention to physical sensations and the breath as anchors for awareness.	Provides somatic grounding techniques useful for calming anxiety and sustaining presence during all phases of the psychedelic process.

Given that psychedelics often induce profound shifts in consciousness, emotion, and self-concept, therapeutic approaches that engage with unconscious material may offer distinct advantages over those solely focused on cognitive restructuring [302]. Future research should directly compare different psychotherapeutic frameworks within PAT, evaluating not only symptom reduction but also integration of experience, meaning-making processes, and sustained psychological transformation. Of particular importance is identifying which specific therapeutic mechanisms - whether psychoanalytic processes (e.g., transference work, exploration of unconscious material), second-wave cognitive approaches (e.g., cognitive restructuring, exposure techniques), or third-wave interventions (e.g., mindfulness practice, psychological flexibility) - most effectively support the psychedelic experience across preparation, dosing, and integration phases. This nuanced understanding will help establish evidence-based protocols without prematurely dismissing therapeutic models that, while less easily standardised within conventional research paradigms, may offer equal or superior clinical utility for particular populations or conditions.

1.4.4 Non-directive

The non-directive approach to preparation in PAT is based on the principle that the psychedelic experience itself is the primary agent of therapeutic change [307]. Unlike structured psychotherapeutic models that often engage participants in interpretive or cognitive interventions, non-directive facilitation seeks to create conditions in which individuals can engage with their experiences in an open-ended manner, without external shaping of their psychological trajectory [174]. Facilitators in this model aim to create psychological safety by being attentive and compassionate, without applying content-driven interpretive frameworks. The rationale is that deep insights and emotional breakthroughs arise naturally when individuals feel secure enough to explore their inner landscape. Introducing a therapeutic framework (e.g., CBT) is seen as potentially priming participants toward predetermined goals, rather than allowing their intrinsic aims to emerge naturally with the support of compassionate facilitation.

The **Yale Program for Psychedelic Science (YPPS)** trial on PAT for **obsessive-compulsive disorder (OCD)** provides a structured example of non-directive preparation in a clinical setting [307]. The YPPS manual formalises a process that prioritises psychological safety while deliberately avoiding priming participants with specific psychotherapeutic frameworks or interpretations. Preparatory sessions focus on building rapport, discussing expectations, reviewing personal history, and providing psychoeducation on psychedelic effects, yet facilitators are explicitly instructed not to introduce interpretive frameworks or suggest specific psychological outcomes. Unlike structured psychotherapy models that incorporate cognitive restructuring, such as CBT-integrated approaches, YPPS facilitators engage in "empathetic witnessing," ensuring that participants feel supported without being steered toward predefined narratives. This support can include gentle "Socratic questioning", encouraging participants to reflect on their emotional and cognitive patterns without imposing therapeutic agendas or interpretive structures. While facilitators refrain from interpreting, they remain fully present, creating a supportive and open environment. This active non-directiveness differs from passivity; facilitators intentionally balance presence and non-intervention, avoiding reassurances or directives while ensuring participants feel psychologically supported.

One central justification for non-directive PAT is the concept of "inner healing intelligence" - the idea that individuals possess an innate capacity for psychological healing that unfolds naturally under the right conditions, minimising the need for structured intervention [308]. Popularised by Grof and adopted by models such as those developed by **Multidisciplinary Association for Psychedelic Studies (MAPS)**, this framework assumes that psychedelics catalyse a self-organising therapeutic process [308, 309]. However, its empirical basis remains weak. A recent RCT at Imperial College London [310] attempted to measure the phenomenon using a single-item scale asking participants to rate the extent to which they experienced an "inner healer" during their session. Scores were significantly higher in the high-dose group[16] and correlated with reductions in depressive symptoms [311], but the construct itself remains conceptually and methodologically vague. Recent developments in cognitive science and philosophy raise further concerns Psychedelics are known to elicit powerful feelings of insight: experiences that feel emotionally profound and self-validating, even when their content is inaccurate [189, 312]. These so-called "false insights" are often accompanied by a strong noetic quality (a sense of obvious truth) which can give rise to epistemically fragile beliefs [313, 314]. From a predictive processing perspective, these moments may reflect a destabilisation of top-down priors and overweighting of bottom-up signals, producing a compelling illusion of coherence [315–317]. In this light, reports of an "inner healer" may reflect the misattribution of this felt clarity to a latent healing force, rather than evidence of an autonomous therapeutic mechanism. Moreover, the inner healer construct overlaps conceptually with known mediators of PAT efficacy, such as emotional breakthroughs and mystical-type experiences, further muddying its status. Without a coherent theoretical model or robust measurement strategy, inner healing intelligence risks becoming a psychologically

[16] The high-dose and low-dose groups referenced here are derived from a Phase II, double-blind, randomised, controlled trial comparing psilocybin with escitalopram for moderate-to-severe major depressive disorder (Carhart-Harris et al., 2021). The high-dose group received two separate doses of 25 mg of psilocybin 3 weeks apart, while the low-dose group received two separate doses of 1 mg of psilocybin alongside daily escitalopram for 6 weeks. Both groups received psychological support throughout the trial.

appealing but epistemically ambiguous concept; one that may reflect the power of suggestibility and post hoc meaning-making as much as any self-directed therapeutic process.

While non-directive facilitation is often justified on the basis that psychedelic experiences are inherently self-organising, its role in preparatory sessions remains unclear. Preparation is typically aimed at fostering a sense of safety, setting intentions, and providing information that can help individuals feel more grounded and supported during their experience. However, the assumption that all participants will be able to self-regulate effectively may overlook those with complex psychological histories, trauma, or difficulties with trust and containment. For these individuals, structured guidance during preparation may be essential. Without a clear framework for when and how to introduce such support, non-directive approaches risk leaving participants underprepared for the intensity of psychedelic states. The lack of standardised protocols specifying whether preparation sessions are limited to supportive listening or permitted to include directive techniques leaves both participants and facilitators vulnerable to inconsistency and ethical uncertainty. As Richard and Levine (2025) argue, “monitors may have applied techniques or interventions beyond the scope of psychological support due to the absence of clear provisions for what should or should not be implemented in a particular trial” [318]. To protect participant wellbeing and maintain treatment fidelity, clearer criteria are needed to delineate when passive facilitation is appropriate and when structured intervention is warranted.

In the absence of structured content or therapeutic models, non-directive facilitation places the therapeutic relationship at the centre of containment. This places considerable demands on facilitators’ emotional attunement, interpersonal sensitivity, and real-time responsiveness - demands that may exceed what is feasible or appropriate in many clinical contexts. While strong facilitator-participant relationships are associated with positive therapeutic outcomes [319], not all participants are equally able to access relational safety. Individuals with relational trauma or difficulties with boundaries may struggle to engage with or benefit from such a model. For them, structured therapeutic tools can offer an alternative stabilising framework. Moreover, over-reliance on the relational container complicates standardisation and reproducibility in clinical trials. Without clear definitions of what relational support entails, facilitators may drift into psychotherapeutic techniques without adequate training, undermining both safety and consistency. It is therefore essential to establish defined relational roles and boundaries to prevent inappropriate role expansion and to ensure that interpersonal support remains within facilitators’ scope of competence.

Non-directiveness is often positioned as a safeguard against external influence in PAT. Yet in practice, it may be more of an aspirational ideal than an achievable stance. Even seemingly neutral facilitator behaviours (e.g., reflective listening, eye contact, the pacing of questions, the phrasing of preparatory language etc.) can subtly shape participant expectations and interpretations. As Richard and Levine (2025) note, “the integration of microskills at all levels of the hierarchy is indeed a form of psychosocial intervention”, meaning that even ‘supportive’ behaviours carry intersubjective weight. Rather than eliminating external influence, non-directiveness may simply displace it into subtler, less accountable forms. Without explicit parameters for what constitutes directive versus non-directive behaviour, models that promote non-directiveness risk inconsistency across therapists, sessions, and sites. This creates both epistemic problems and practical barriers to evaluating fidelity in clinical research. A more rigorous examination of how facilitation shapes participant experience is needed to determine whether non-directiveness can function as a viable and reproducible therapeutic stance.

Moving forward, research must investigate when non-directive preparation enhances therapeutic depth and when it risks leaving participants uncontained. This requires clarifying its underlying assumptions, defining the limits of facilitator neutrality, and identifying which populations may benefit most from a structured approach. Preparation sessions are especially vulnerable to drift, where communication unintentionally shifts from passive support to subtle forms of direction [318]. Given the heightened suggestibility induced by psychedelics, even neutral facilitation may implicitly direct experience [287], raising both ethical and methodological concerns. If non-directive models are to be widely adopted, they must be grounded in clear protocols and observable communication behaviours, ensuring that facilitators remain within their remit and participants are adequately supported. Moreover, the field must critically assess whether foundational concepts like ‘inner healing intelligence’ reflect unique therapeutic mechanisms or merely repackage expectancy effects [288, 289] and interpersonal dynamics [205, 290, 291]. Ultimately, the challenge is not whether non-directiveness has value, but how to define its appropriate role, establish safeguards against implicit influence, and ensure that flexibility does not come at the cost of rigour, safety, or clarity.

1.5 Systematic review of psychedelic preparation protocols

The diverse theoretical frameworks reviewed above highlight the range of psychological and therapeutic approaches employed in psychedelic preparation. While each model offers distinct advantages, their application in clinical settings varies considerably. Some trials formally integrate structured therapeutic interventions, while others adopt more implicit preparatory methods that do not align neatly with any single framework. To systematically characterise the methodological diversity of psychedelic preparation, we conducted a focused systematic review of clinical trials assessing preparation protocols for full-dose classical psychedelics[17]. Rather than providing an exhaustive account, the review presented in this thesis aimed to exemplify varying components of preparation within the field. To ensure relevance and clarity, we applied strict inclusion criteria, prioritising studies that involved the administration of classical psychedelics to adults with diagnosed mental health conditions, combined with assisted psychotherapy - EBT or non-directive psychological support - in controlled therapeutic settings, reporting clinical outcomes. We excluded studies primarily focused on neuroimaging or feasibility alone.

Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we performed a literature search across Web of Science and Ovid platforms (MEDLINE, EMBASE, PsycINFO) in November 2024. The primary aim was to identify the specific parameters and components of preparation used in these studies and to evaluate the quality of reporting on preparation protocols. After removing duplicates and screening for eligibility, eight studies met the inclusion criteria from an initial pool of 3,353 records (see **Appendix A1.1** for complete methodology, search strategy, and PRISMA flow diagram of study selection).

Analysis of the eight included trials revealed substantial methodological heterogeneity (**Table 1.2**) (see **Appendix A1.2** for full study design and outcome information table). Most of the included studies focused on depression, specifically Major Depressive Disorder (MDD) and Treatment-Resistant Depression (TRD) and employed a range of therapeutic frameworks. Most trials used non-directive approaches described as 'psychological support', while a few explicitly applied structured EBTs such as ACT. Preparation protocols also showed significant variation across studies. The number of preparation sessions ranged from one to four, with total preparation time spanning from one to eight hours, conducted over a period ranging from one to 42 days. The content of these sessions commonly included rapport building, psychoeducation, intention setting, and orientation to study procedures. Some studies also incorporated specific elements like

[17] This systematic review was conducted in collaboration with MSc student Abigail Major (UCL).

relaxation training or surrender guidance. However, the theoretical basis for preparation was often not clearly defined, reflecting a broader inconsistency in how preparatory interventions are conceptualised and delivered in PAT. Facilitator qualifications also varied substantially, ranging from licensed psychiatrists to graduate students. The use of manualised procedures was inconsistent, with some studies adhering to a structured manual while others did not specify any formal guidance. This reflects a broader inconsistency in the training and accreditation of facilitators involved in PAT, indicating a need for clearer standards to ensure consistency and safety in practice.

To assess the reporting quality of preparation protocols, we developed and applied a modified version of the **Template for Intervention Description and Replication (TIDieR)** checklist [320]. Our adaptation incorporated a graduated scoring system (0-3) to evaluate reporting completeness across key domains, with additional items specific to PAT preparation (see **Appendix A1.3** for the modified TIDieR checklist scoring system). The assessment revealed considerable variability in reporting practices, with total scores ranging from 19 to 33 out of a possible 42 points (mean = 24.43, SD = 5.26) (**Fig. 1.2c**). While some domains demonstrated relatively strong reporting quality, including session procedures and risk management frameworks, critical areas showed substantial deficiencies (**Fig. 1.2a**). Notably, documentation of cultural and accessibility adaptations, materials and resources, and standardised preparedness assessments was particularly poor (mean scores ≤ 1), highlighting significant gaps in protocol transparency and replicability. Of particular concern was the inconsistent reporting of preparation-integration alignment and implementation fidelity, elements considered crucial for establishing evidence-based practices in PAT. Individual study scores across items are shown in **Fig. 1.2b** (see **Appendix A1.4** for the full TIDieR-based quality assessment table).

Table 1.2. Comparison of preparation protocol elements across psychedelic clinical trials

Author	Primary diagnosis	Therapeutic Model	Drug	Number of prep. sessions	Duration of each prep. session (hrs)	Total duration of prep. (hrs)	Total prep. period (days)	Prep. delivery mode	Reported prep. components	Facilitator credentials (N)	Manual (Y/N)
Davis et al. (2021) [321]	MDD	Non-directive ('supportive psychotherapy'[18])	Psilocybin	2	-	8	14	In-person	Psychoeducation (verbal), rapport building, patient history, study orientation, coping techniques (surrender), environmental familiarisation[19]	Study clinicians[20] (2)	N
Schneier et al. (2023) [322]	BDD[21]	Non-directive ('psychological support')	Psilocybin	4	-	≥4	28	In-person	Psychoeducation, relaxation techniques	Psychotherapists[22] (2)	N[23]
Carhart-Harris et al. (2016) [4]	TRD	Non-directive ('psychological support')	Psilocybin	1	~4	~4	6	In-person	Rapport building, patient history, psychoeducation, study orientation	Psychiatrists (2)	N[24]
Sloshower et al. (2023)	MDD	Evidence-based ('manualised ACT-based psychotherapeutic support')	Psilocybin	1	2	4	28	In-person	Psychoeducation, rapport-building, expectations, patient history, intentions, study orientation, safety briefing, boundary setting, coping techniques (surrender), grounding techniques (diaphragmatic breathing), mindfulness practice	Study clinician and therapist[25] (2)	Y

[18] Details of supportive psychotherapy reported elsewhere (Johnson et al., 2008)
[19] Preparatory components reported elsewhere (Johnson et al., 2008)
[20] Backgrounds in psychology, psychiatry, social work; education: BA-MD and medical degrees
[21] Body Dysmorphic Disorder; non-delusional type
[22] Both assisting and lead therapists were recruited as psychiatrists, master's-level qualified psychologists, nurses, diploma-level cognitive behavioural therapists, or doctorate-level mental health specialists. The therapist-training program (Tai et al., 2021) had four components: an online learning platform, in-person training, clinical training, and ongoing individual mentoring and webinars. Therapists were required to complete the first three components of the training program before they could lead sessions independently and to engage in the fourth component to continue their professional development
[23] Manualised supportive procedures developed for psilocybin depression studies (Tai et al., 2021)
[24] Although not explicitly described in this protocol, the ACE (Accept-Connect-Embody) manual was retrospectively attributed to this trial [5]
[25] Therapists were licensed clinicians (psychiatrists, psychologists, psychiatric nurses, or social workers) with 5+ years of clinical experience. All had specialised training in psilocybin-assisted ACT therapy, including pre-readings, videos, four day-long training sessions, and an intensive retreat led by a peer-reviewed ACT trainer. Experience with psychodynamic and cognitive-behavioural therapies was beneficial, as was familiarity with altered states of consciousness. Training incorporated resources from MAPS, CIIS, and ACT-specific supervision. Therapist present for all preparatory sessions, study psychiatrist (male) was present for *most*

Goodwin et al. (2022) [6]	TRD	Non-directive (‘psychological support’)	Psilocybin	≥3	-	≥3	21-42	Hybrid[26]	Rapport building, psychoeducation, study orientation	Study clinicians (2)	Y[2]
Raison et al. (2023) [7]	MDD	Non-directive (‘psychological support’)	Psilocybin	>1	-	~6-8	1-6	Hybrid[27]	Rapport building, environmental familiarisation, patient history, intentions, expectations	Study clinicians[28] (2)	Y[29]
von Rotz et al. (2023) [8]	MDD	Non-directive (‘psychological support’)	Psilocybin	2	-	2	-	In-person	Rapport building, psychoeducation, study orientation, intentions, patient history, expectations, coping techniques (openness), ground rules	Study clinician[30] (1)	N
Carhart-Harris et al. (2021) [9]	MDD	Non-directive (‘psychological support’)	Psilocybin	1	~3	~3	~7	In-person	Rapport building, expectations, relaxation techniques, study orientation	Study clinicians[31] (2)	N[1]

Note. Major Depressive Disorder (MDD); Treatment Resistant Depression (TRD); Body Dysmorphic Disorder (BDD); psychedelic preparation (prep.); hybrid (in-person and online delivery method)

[26] All participants undergo an in-person preparatory session before receiving access to a digital study platform (Longboat) for psychoeducation
[27] Additional preparatory sessions may be conducted remotely, if necessary
[28] Lead Facilitators were doctoral-level psychotherapists with experience in the psychological treatment of MDD (PhD, PsyD, MD or DO). Co-Facilitators held a minimum of a bachelor’s degree in a mental health field. Both Lead and Co-Facilitators had training to identify safety issues during sessions
[29] Facilitators trained on study-specific Usona Facilitator Training Manual, not accessible upon request
[30] Study therapist is a trained clinician (either a physician or psychologist)
[31] One of the pair was a clinical psychologist, psychotherapist, or psychiatrist, and the other could be an equivalent grade clinician or trainee; both with experience of providing psilocybin treatment in the context of research studies, including clinical trials

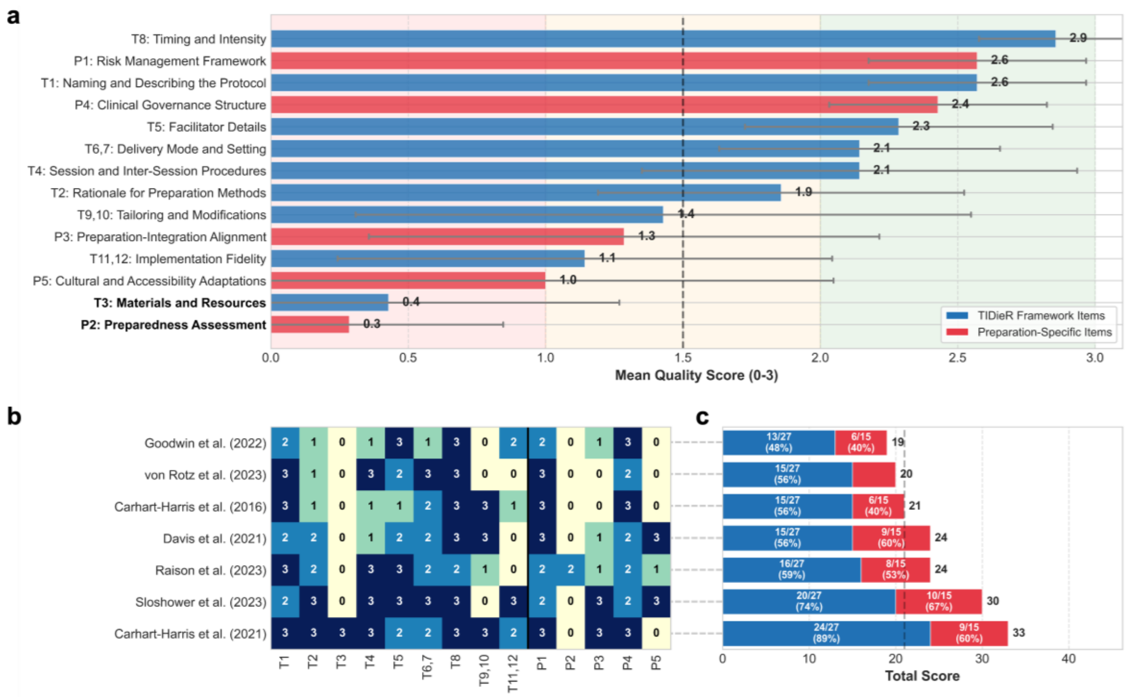


Figure 1.2. Quality of reporting for PAT preparation protocols assessed using a modified TIDieR checklist

(a) Horizontal bar chart of mean quality scores (0-3) for TIDieR framework items (blue) and preparation-specific items (red), highlighting areas of strong and weak reporting. T denotes standard TIDieR framework items, while P represents additional items specific to psychedelic-assisted therapy preparation, included in the modified checklist. (b) Heatmap showing the scores for each study across individual checklist items. (c) Stacked bar chart illustrating total scores by study, divided into TIDieR and preparation-specific items. Total scores range from 19 to 33 out of 42, indicating variability in reporting completeness across studies.

Our analysis of psychedelic preparation protocols identifies key challenges that should be addressed as the field advances. The wide variation in session structure, content, duration, and theoretical frameworks reflects deeper uncertainties about what constitutes effective preparation [16]. While research highlights the influence of pre-session psychological states on therapeutic outcomes [117, 119, 120, 122], many protocols lack clear empirical foundations. This gap is reflected in our TIDieR analysis, which revealed poor reporting of essential elements, making it difficult to assess their theoretical basis or effectiveness. Currently, no studies have systematically isolated the impact of specific preparation components on clinical outcomes. However, this challenge is not unique to PAT. Psychotherapy research has long struggled to identify active therapeutic ingredients, largely because experimental component studies require extensive resources and complex methodologies [325, 326]. In conventional psychotherapy, researchers have addressed this by applying statistical methods to large datasets from numerous completed trials, allowing them to identify which therapeutic elements correlate with better outcomes [327–329]. Unfortunately, PAT research has not yet generated sufficient standardised data to apply these approaches effectively. As more clinical trials with consistent measures are completed, these analytical methods may help identify which preparation components are most beneficial. Until then, establishing evidence-based guidelines remains difficult due to inconsistent outcome reporting across studies. As PAT moves toward clinical application, preparation must become a rigorously studied process. Achieving this will require better documentation, standardisation, and eventually, the application of advanced analytical methods to optimise therapeutic impact.

1.6 Preliminary feasibility testing of a digital psychedelic preparation protocol

While these challenges have been identified in clinical settings, a similar issue exists within psychedelic research: the lack of widely available, standardised preparation protocols specifically designed for non-clinical studies. This gap became particularly evident when developing a preparation protocol for a non-clinical DMT study at UCL's **Understanding Neuroplasticity Induced by Tryptamines (UNITy)** Lab in 2020. Unlike PAT, where preparation is therapist-led and tailored to clinical populations, we needed to find a way to prepare healthy volunteers for a controlled psychedelic experience in a research setting, without therapist facilitation.

To address this, we designed a structured six-day digital preparation protocol that adapted key preparation principles for self-directed use (see **Fig. 1.3**). The intervention (*UNITy-Prep*) consisted of five core modules - psychoeducation, breathwork, meditation, body scanning, and visualisation exercises - followed by a final day dedicated to journaling and reflection. Each 30-minute daily session provided structured guidance while ensuring consistency across participants. While clinical PAT preparation emphasises therapeutic alliance and individualised support, our digital format prioritised accessibility and standardisation, making it well-suited for research contexts where controlled delivery is essential. This pilot study tested the feasibility of this approach and gathered initial user feedback, offering insights into its practical implementation and limitations. The findings from this study directly informed the development of a more comprehensive digital intervention, which is explored in subsequent chapters (**Chapters 3, 5**).

To evaluate the feasibility of *UNITy-Prep* and identify areas for refinement, we collected initial feedback from early participants (N=11) in the ongoing trial. All participants completed the full six-day intervention (100% completion rate), indicating strong adherence. To assess perceived usefulness, participants rated each module's helpfulness on a five-point scale. Meditation received the highest mean rating (M = 4.45), followed by visualisation (M = 4.18) and breathwork (M = 4.09), while psychoeducation (M = 3.45) and body scanning (M = 3.27) were rated slightly lower. Notably, over 90% of participants rated meditation as "Very helpful" or "Extremely helpful," and no module was rated as "Not at all helpful," suggesting that each component contributed meaningfully to preparation for the DMT experience. These findings provided valuable insights into participant engagement and informed refinements to later iterations of the intervention.

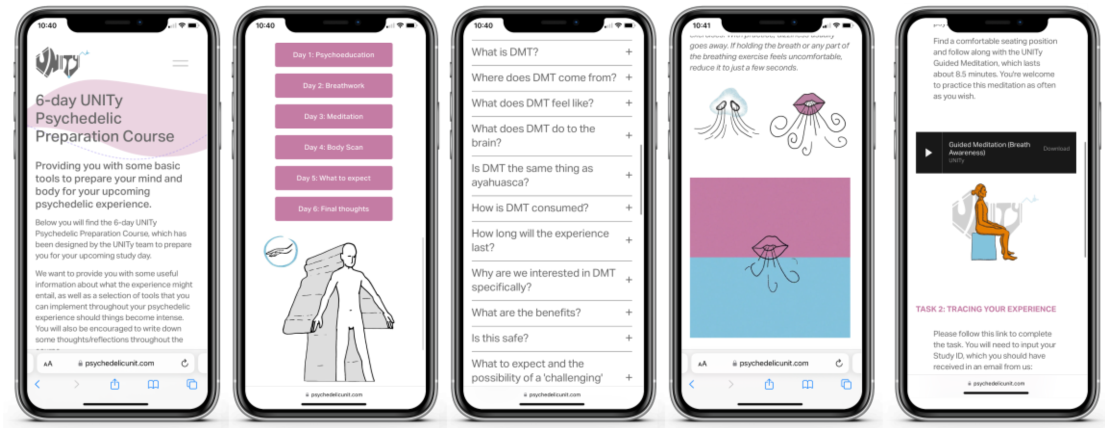


Figure 1.3. UNITy-Prep: digital psychedelic preparation protocol interface
Screenshot array from the UNITy 6-day digital psychedelic preparation course ('UNITy-Prep'), designed to standardise and enhance psychedelic readiness. The interface features the landing page, daily module menu, DMT information section, breathwork exercises, and guided meditation. This digital format ensures consistent content delivery, structured psychoeducation, and guided experiential practices to support preparation in research settings.

Qualitative feedback was collected to understand participants' experiences with the protocol in more detail (**Table 1.3**). When asked about the most helpful components, participants most frequently highlighted breathing techniques (n=5, 45.5%) and meditation practices (n=5, 45.5%). The DMT visualisation, psychoeducation, and specific coping strategies were each mentioned by three participants (27.3%), with particular emphasis on their value for setting expectations and managing challenging experiences. When identifying least helpful aspects, the body scan exercises were most frequently mentioned (n=4, 36.4%), with participants noting personal difficulties engaging with this practice. Two participants (18.2%) found the technical/scientific information challenging to contextualise. Individual participants also reported challenges with meditation and breathwork format, though one participant explicitly stated nothing was unhelpful, and one provided no response. Regarding potential improvements to the protocol, while the largest group (n=5, 45.5%) indicated the protocol was complete and needed no additions, several suggestions for enhancement emerged. These focused on expanding existing elements rather than adding new components, with equal numbers of participants (n=3, 27.3%) requesting more meditation/visualisation content and additional guidance around intention-setting. One participant suggested including more contextual information about the study environment and mechanisms of action.

Table 1.3. Participant feedback from the 6-day UNITy-Prep pilot

Theme	N (%)	Illustrative Quote
Most helpful		
Breathwork	5 (45.5)	“The breathwork provided the most practical tool to use during dosing” (P2)
Meditation	5 (45.5)	“The guided meditation was pretty effective and calmed my nerves a lot” (P5)
Visualisation	3 (27.3)	“The audio [for the DMT visualisation] was a nice summary of what to expect” (P4)
Psychoeducation	3 (27.3)	“Having clear concise info on DMT and its effects, as well as the purpose of the study” (P6)
Coping strategies	3 (27.3)	“The tools to take into the session, like the 4/6 breathing, asking ‘what do you have to show me’ and ‘in and through’” (P7)
Body awareness	2 (18.2)	“I liked being forced to recognise where I hold tension in my body in the body scan” (P8)
Least helpful		
Body scan	4 (36.4)	“I personally struggle with the whole body scan side of things, but I can understand that others value this” (P4)
Psychoeducation	2 (18.2)	“The more detailed scientific info on day 1 (because it doesn't really mean anything to me)” (P7)
Meditation	1 (9.1)	“I really don't enjoy meditation. I find it really hard to see thoughts come and go and not either grasp or control them” (P11)
Breathwork	1 (9.1)	“Breathwork, would have been nice to have a video like the ones in the Calm app” (P10)
No issues	2 (18.2)	“None” (P1)
Areas for improvement		
Meditation/ visualisation	3 (27.3)	“I wish the meditation was a bit longer. It felt very rushed. The content was great but longer pauses to experience the breath, or sound, or thoughts would have been very helpful” (P2)
Intention-setting	3 (27.3)	“More guidance on what an intention is and how to choose it... maybe some examples would be good” (P7)
Nothing missing	5 (45.5)	“Very thorough and comprehensive!” (P3)
Context	1 (9.1)	“I guess knowing who will be in the room with me, maybe something about how drugs work” (P10)

Note. Percentages based on total sample (N=11); participants could mention multiple themes.

While this initial pilot demonstrated feasibility and highlighted promising directions for psychedelic preparation, it also revealed critical methodological and theoretical gaps in the field. Although the high engagement rates and qualitative feedback suggested the digital format was acceptable to participants, two fundamental limitations emerged. First, the absence of validated instruments to measure psychedelic preparedness meant we could not quantitatively assess intervention efficacy or track changes in readiness - a crucial methodological limitation for the field. Second, while participant feedback provided valuable insights, particularly regarding the value of experiential components, the development of a robust digital intervention requires systematic co-production with stakeholders and adherence to established intervention development frameworks. These limitations informed a comprehensive research programme presented in this thesis.

1.7 Thesis objectives and structure

The overarching aim of this thesis is to advance evidence-based approaches to psychedelic preparation by developing and validating both measurement tools and digital interventions. To achieve this, the research follows a sequential structure, where each chapter builds upon the findings of the previous one (**Fig. 1.4).**

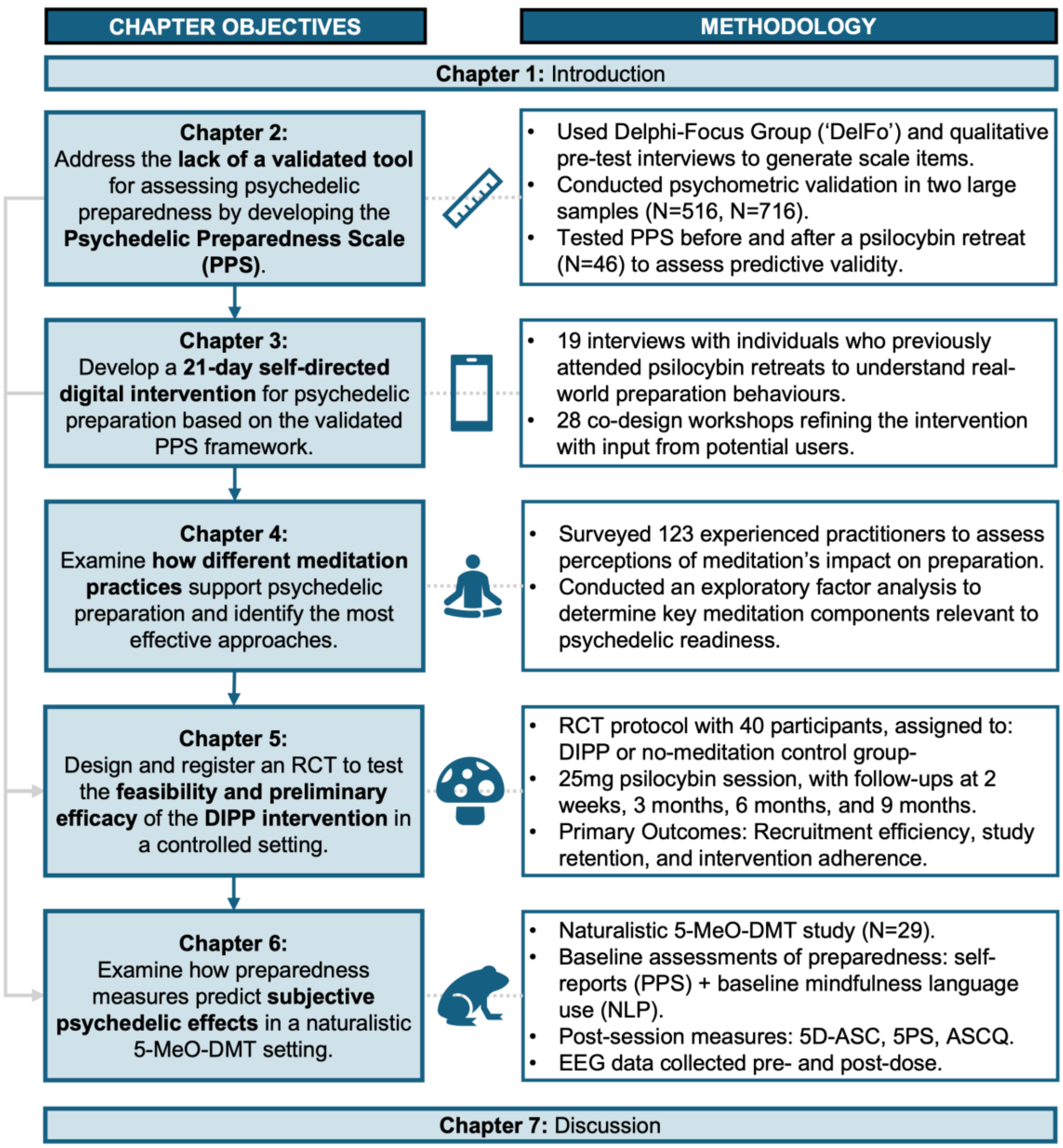


Figure 1.4. Structure of the thesis

Note. Psychedelic Preparedness Scale (PPS); Digital Intervention for Psychedelic Preparedness (DIPP); Randomised Controlled Trial (RCT); 5-Dimensional Altered States of Consciousness Rating Scale (5D-ASC); 5-MeO-DMT Phenomenology Scale (5PS); Altered Self Consciousness Questionnaire (ASCQ); Natural Language Processing (NLP); Electroencephalography (EEG).

First, **Chapter 2** addresses the lack of psychometrically validated tools by developing the Psychedelic Preparedness Scale (PPS), providing a structured measure of key preparedness dimensions. Building on the PPS framework, **Chapter 3** details the development of the 21-day Digital Intervention for Psychedelic Preparedness (DIPP), an evidence-informed, self-led intervention aligned with four identified preparedness factors. Based on participant feedback in Chapter 3 that identified meditation as a crucial element of preparation, **Chapter 4** systematically evaluates various meditation practices, highlighting those most suitable for integration into preparation protocols. **Chapter 5** presents a registered randomised controlled trial protocol designed to assess the feasibility and preliminary efficacy of the DIPP intervention. The trial involves participants completing the DIPP program before receiving a single 25 mg psilocybin session, comparing a meditation-based approach against a music-based control condition. Finally, **Chapter 6** extends this research into a naturalistic setting, examining how explicit (PPS) and implicit (linguistic markers) measures of preparedness predict subjective experiences with 5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT). Together, these chapters form a coherent trajectory from foundational measurement development to systematic intervention design and controlled evaluation, culminating in an ecologically valid investigation of psychedelic preparedness.

CHAPTER 2

Development and psychometric validation of a novel scale for measuring 'Psychedelic Preparedness'

"Hoping for the best, prepared for the worst, and unsurprised by anything in between."

— *Angelou, M. (1969). I Know Why the Caged Bird Sings.*

2.1 Abstract

Preparing participants for psychedelic experiences is essential to ensure safety and maximise potential benefits. However, no validated measure currently exists to assess how well participants are prepared for these experiences. To address this need, **Chapter 2** presents the development, validation, and testing of the Psychedelic Preparedness Scale (PPS). Using a novel iterative **Delphi-focus group methodology ('DelFo')**, followed by **Qualitative Pre-test Interviews (QPIs)**, we incorporated the perspectives of expert clinicians/researchers and of psychedelic users to generate items for the scale. Psychometric validation of the PPS was carried out in two large online samples of psychedelic users (N = 516; N = 716), and the scale was also administered to a group of participants before and after a 5–7-day psilocybin retreat (N = 46). Exploratory and confirmatory factor analysis identified four factors from the 20-item PPS: Knowledge-Expectations, Intention-Preparation, Psychophysical-Readiness, and Support-Planning. The PPS demonstrated excellent reliability (ω = 0.954) and evidence supporting convergent, divergent and discriminant validity was also obtained. Significant differences between those scoring high and low (on *psychedelic preparedness*) before the psychedelic experience were found on measures of mental health/wellbeing outcomes assessed after the experience, suggesting that the scale has predictive utility. By prospectively measuring modifiable pre-treatment preparatory behaviours and attitudes using the PPS, it may be possible to determine whether a participant has generated the appropriate mental 'set' and is therefore likely to benefit from a psychedelic experience, or at least, less likely to be harmed.

2.2 Introduction

Psychedelic preparedness, as outlined in **Chapter 1**, refers to the psychological state preceding a psychedelic session that enhances safety and facilitates personally meaningful experiences. While research increasingly acknowledges the importance of preparation in shaping psychedelic outcomes [16] and highlights the predictive power of pre-psychedelic states [119, 122], existing measures are only able to assess the immediate pre-session state (or *set*) rather than preparedness itself. The absence of a validated psychedelic preparedness measure limits researchers' ability to systematically examine how preparatory practices influence psychedelic experiences and prevents clinicians from objectively evaluating readiness or refining preparation protocols based on empirical evidence. To address this need, **Chapter 2** details the development and validation of the Psychedelic Preparedness Scale (PPS), a psychometrically rigorous instrument designed to assess psychological readiness for psychedelic experiences.

Unlike physical properties, which can be measured with standardised units, psychological constructs - such as psychedelic preparedness - are inherently latent[32] [330, 331]; they cannot be directly observed but must be inferred from patterns in test responses, questionnaires, or behavioural assessments [332]. As a result, developing a psychometrically sound measure of psychedelic preparedness requires a structured, multi-phase process integrating theoretical grounding, empirical validation, and iterative refinement [333–335]. A widely accepted framework for scale development includes three primary phases: item development, scale construction, and scale evaluation [335, 336], each consisting of structured steps to ensure reliability and validity (**Fig. 2.1**). The item development phase involves 1) defining the construct and its theoretical domains and 2) generating and refining items to ensure content validity through expert and target population review. The scale construction phase includes 3) pre-testing items for clarity and comprehension, 4) administering the survey to an appropriate sample, 5) refining items using statistical techniques such as **exploratory factor analysis (EFA)** and item-total correlations, and 6) identifying latent factors to confirm the underlying structure. The scale evaluation phase consists of 7) testing dimensionality using **confirmatory factor analysis (CFA)**, 8) assessing reliability (e.g., internal consistency and test-retest reliability), and 9) establishing validity, including construct, criterion, and discriminant validity. By systematically following these best practices, we aimed to develop the PPS as a theoretically grounded, empirically validated, and methodologically rigorous instrument, enhancing its utility for both research and clinical applications.

[32] In psychometrics, a latent variable is a construct that cannot be directly observed or measured. Instead, it is inferred from a set of observable indicators, such as responses to questionnaire items or patterns in behavioural data. The term 'latent' comes from the Latin word *'latere'*, meaning 'to lie hidden', reflecting the idea that latent variables are not directly measurable but manifest through measurable outcomes.

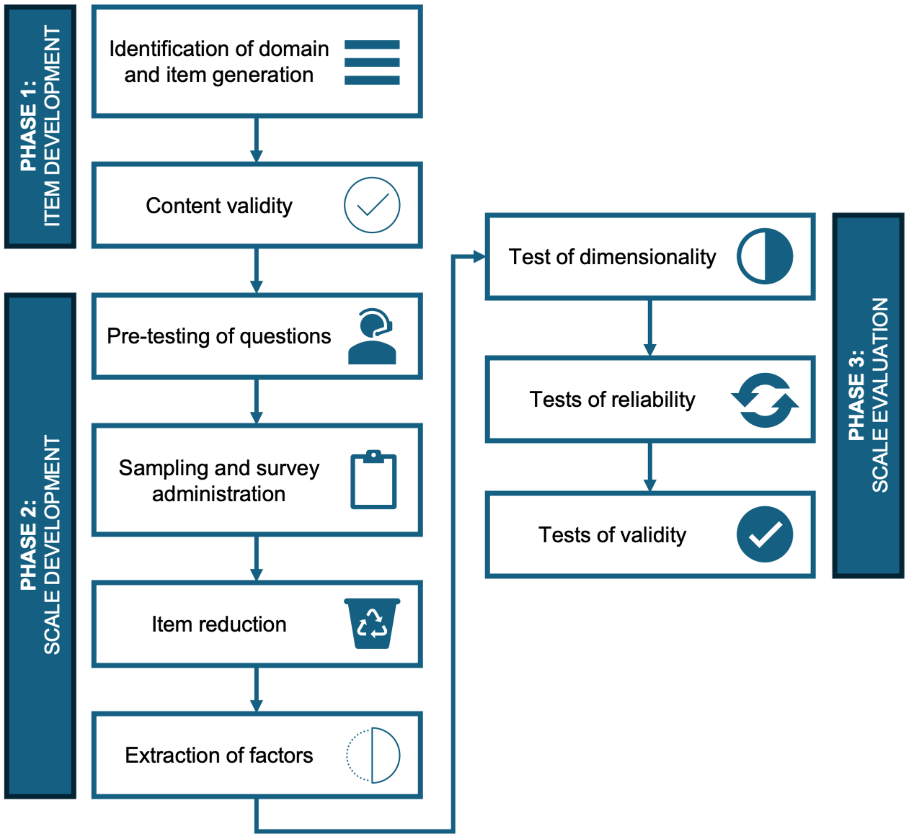


Figure 2.1. Phases of scale development and validation

A three-phase framework for developing and validating a psychometric scale, adapted from Boateng et al. (2018). Phase 1 (Item Development) involves defining the construct, generating items, and ensuring content validity. Phase 2 (Scale Development) includes pre-testing, survey administration, item refinement, and factor extraction. Phase 3 (Scale Evaluation) assesses dimensionality, reliability, and validity to establish the measure's psychometric robustness. This structured approach ensures methodological rigour in developing the Psychedelic Preparedness Scale (PPS).

A common limitation in scale development is the overreliance on researcher (or 'expert') input which, while valuable, may fail to capture the full complexity of the construct being measured [337]. This issue is particularly relevant for psychedelic preparedness, where existing theoretical frameworks are limited, and much of the knowledge base comes from experiential rather than empirical sources. Excluding stakeholders from item development risks incomplete domain sampling [338] and may compromise content validity, especially when items prioritise theoretical constructs over real-world practices [339, 340]. Moreover, when items fail to align with participants' lived experiences, both response and ecological validity can be diminished, potentially undermining the scale's interpretability and relevance [341, 342]. To address these limitations, we integrated perspectives from academic researchers, clinical practitioners, and individuals with direct experience of PAT. This comprehensive approach enhanced both construct validity and practical utility, responding to recent calls for broader stakeholder engagement in psychedelic research [343, 344].

This chapter details the development and validation of the PPS through a series of three interconnected studies:

- **Study 2.I**: Scale development - We employed expert consultation and the Delphi-focus group (DelFo) method, complemented by Qualitative Pre-test Interviews (QPIs), to generate and refine scale items, ensuring strong content validity.
- **Study 2.II**: Scale validation - We assessed the psychometric properties of the PPS through exploratory and confirmatory factor analyses, alongside tests of reliability and validity in a large, diverse sample of participants.
- **Study 2.III**: Scale implementation - We evaluated the PPS as a predictive measure in participants attending a psilocybin retreat, examining its test-retest reliability and its ability to predict acute and long-term psychedelic outcomes.

This work advances the study of psychedelic preparation by providing a validated measure that captures key aspects of psychological readiness. The PPS offers a foundation for future research on how preparation influences outcomes and can inform tailored approaches to optimising psychedelic experiences across diverse settings.

2.3 Methods

The UCL Research Ethics Committee approved all procedures (ID: 9437/001). Participants gave electronic informed consent after reviewing the study details. Data collection was conducted online.

2.3.1 Participants and recruitment

All participants were English-proficient adults (18+). Recruitment methods varied by study and are detailed in the following sections.

Study 2.I: Scale development

The scale development process in **Study 2.I** consisted of three phases: preliminary consultation, 'DelFo' method, and QPIs. For the preliminary consultation phase, six experts in psychiatry, psychology, and philosophy who specialise in psychedelic research helped develop the initial scale items. No demographic data was collected from these experts. The DelFo method involved two groups of participants. The first group, termed 'expert judges', comprised seven researchers and clinicians with expertise in psychedelics. These individuals were recruited via the authors' professional network and were required to be actively involved in psychedelic research or psychedelic-assisted psychotherapy practice. Notably, none of these judges were involved in the preliminary consultations. The second group, termed 'lived experience judges', consisted of eight individuals with experience of PAT. These participants were recruited through advertisements on social media platforms and were invited to attend all three focus group rounds. Detailed participant characteristics for both groups can be found in **Appendices A2.3** and **A2.4,** respectively. For the QPIs, an additional purposive sample of six lived experience participants was recruited through collaborating psilocybin retreat centres. All participants in this phase were required to have previously attended a 5–7-day psilocybin retreat. Participant characteristics for this group are provided in **Appendix A2.5.**

Study 2.II: Scale validation

Study 2.II involved two large, self-selected groups of participants with experience of psychedelic use for the validation of preparedness items generated in **Study 2.I.** The first group, Sample A, consisted of 518 participants whose data was used for the initial extraction of factors (EFA). A subset of Sample A (N = 296) completed a follow-up survey after two weeks to assess the test-retest reliability of the PPS. These follow-up responses were not included in the factor analyses. The second group, Sample B, comprised 718 participants whose data was used for tests of dimensionality (confirmatory factor analysis; CFA). For subsequent tests of reliability and validity, a pooled sample of 1236 participants were analysed.

Study 2.III: Scale implementation

For **Study 2.III**, 46 participants were recruited through collaborating retreat centres. These individuals were enrolled in 5-7-day residential psilocybin retreats and were invited to join the study prior to their arrival. Eligibility criteria included willingness to complete surveys before and after the retreat. Participants were included in the data analysis only if they fully completed all relevant questionnaires at both timepoints.

2.3.2 Procedures

Study 2.I: Scale development

Preliminary consultation phase

The preliminary consultation phase involved online feedback sessions aimed at gathering views on the definition of psychedelic preparedness, its subdomains, and the items to be considered for inclusion in the scale. Based on the feedback from these consultations, the research team conducted a rapid thematic analysis, generating 56 items across 10 subdomains of preparatory behaviours and attitudes, including *Education, Intention Setting, Expectation Management, Psychological Mindedness, Emotional Readiness, Willingness to Surrender, Psychophysical Robustness, Safety/Security, Preparedness for Change,* and *Preparatory Practices*, along with three additional items addressing *preparatory efficacy* [345, 346]. This resulted in a total of 59 items that were used in the subsequent DelFo and QPIs for methodological refinement of the scale. Each phase of the consultation process involved distinct participants with no overlap between groups.

DelFo method

The novel DelFo method was developed to evaluate the initial items for relevance, representativeness, and technical quality, combining iterative input from expert judges in multiple Delphi rounds and lived experience judges in interspersed focus group discussions (**Fig. 2.2**). Over four rounds of consultation [347, 348], participants with lived experience provided feedback, with expert judges rating 59 items developed during the preliminary phase using a 4-point Likert scale (1 = strongly agree, 4 = strongly disagree) and providing free-text responses to suggest changes or clarify their ratings. After each Delphi round, responses were shared with the lived experience judges in focus groups led by author RM, encouraging reflection and new ideas [349, 350]. This iterative process allowed for items to be revised, added, or removed based on evolving feedback, culminating in 51 items for further psychometric evaluation. The focus groups, held via

Microsoft Teams and lasting 60-90 minutes, used auto-transcription and audio recordings for accuracy, while the Delphi rounds provided individualised surveys, allowing participants to see their previous responses and the group's consensus (% agreeing/disagreeing). The process ensured that differences in status, knowledge, and power between experts and lived experience participants did not hinder creativity, and feedback from focus groups was incorporated into each subsequent Delphi round to refine the scale content.

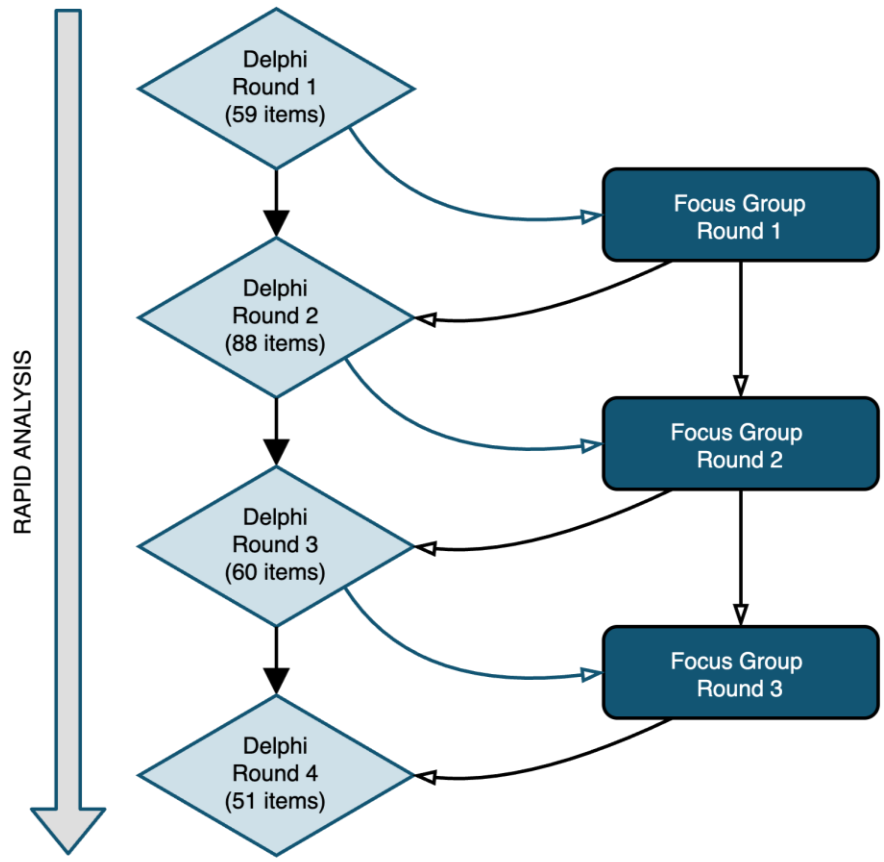


Figure 2.2. The 'DelFo' method: integrating Delphi rounds with focus groups

Flow diagram illustrating the Delphi-Focus Group (DelFo) method used for item evaluation. Expert judges participated in four iterative Delphi rounds, rating items for relevance, representativeness, and technical quality, while lived experience judges provided feedback in interspersed focus group discussions. The number of items evaluated in each Delphi round is shown in the diamonds. This iterative process allowed for continuous refinement, ensuring a balanced integration of expert assessment and stakeholder insights.

Qualitative Pre-test Interviews (QPIs)

The insights from the DelFo method informed a series of QPIs [351] designed to evaluate whether the survey questions accurately reflected psychedelic preparedness and produced valid measurements. This approach treated participants as "co-experts" and employed a "think-aloud" method, where participants verbalised their thoughts as they reviewed each survey item [352]. Six participants with previous experience in PAT (see **Appendix A2.5** for participant characteristics) participated via Microsoft Teams. During the interviews, participants provided real-time feedback on the clarity and relevance of each question, allowing for modifications to grammar, phrasing, and word choice to enhance understanding. This iterative process aimed to identify ambiguities, refine the survey items, and ensure that responses reflected participants' experiences accurately. Revisions continued until saturation was reached, ensuring that the survey items were refined and improved to enhance their validity and reliability.

Study 2.II: Scale validation

Participants accessed the survey via an online link, where they first reviewed an information sheet about the study and provided informed consent. They then completed a structured online survey, which included 41 psychedelic preparedness items developed in **Study 2.I**, along with the **Mystical Experience Questionnaire (MEQ)** [353], **Challenging Experience Questionnaire (CEQ)** [354], **Emotional Breakthrough Inventory (EBI)** [68], **Post-Traumatic Growth Inventory Short Form (PGTI-SF)** [355], **Centrality of Event Scale (COES)** [356], and **Short Warwick-Edinburgh Mental Wellbeing Scale (SWEMWBS)** [357] scales. For the 41 preparedness items, participants were instructed to reflect on their most significant psychedelic experience and rate their agreement with each statement on a 7-point Likert scale from "not at all" to "completely" (see **Appendix A2.23** for retrospective PPS). The same scale and instructions were applied to the 10 'preparedness efficacy' items (**Appendix A2.7**). Importantly, participants were not asked to specify the psychedelic substance involved in their most significant experience, as the study aimed to assess psychedelic preparedness in a general sense across various substances. This broader focus allowed for the exploration of preparedness without limiting the findings to specific psychedelic drugs, though it is acknowledged that different substances may influence preparation in distinct ways, a limitation not addressed in the current study. In the re-test condition, participants received email reminders to complete the survey at the second time point. Anonymity was maintained by avoiding the collection of personally identifying information, aside from email addresses required for follow-up. No IP addresses or other data that could identify participants were collected, ensuring privacy throughout the process.

Study 2.III: Scale Implementation

To evaluate the PPS as a prospective measure (i.e., prior to a planned psychedelic experience), it was administered to a sample of 46 participants one day before they participated in a psilocybin ceremony (see **Appendix A2.22** for prospective PPS). The PPS was repeated two weeks after the ceremony to replicate the reliability findings reported in **Study 2.II**. In addition to the PPS, participants completed the **11**

Dimensions Altered States of Consciousness (11D-ASC) [358] and **Depression, Anxiety, and Stress Scale (DASS-21)** [359] scales to further assess criterion validity.

2.3.3 Measures

Emotional breakthrough

The Emotional Breakthrough Inventory (EBI) [68] assesses, retrospectively, episodes of catharsis or emotional release following a psychedelic experience. It is a 6-item scale scored on 0 to 100 **visual analogue scale (VAS).** Here, EBI scores are presented as a single total, summed score ranging from zero to 600.

Mystical experience

The Mystical Experience Questionnaire (MEQ) [353] is a 30-item scale scored on a 6-point Likert scale (1 = none, not at all; 6 = extreme, more than any other time in my life). It consists of four factors which measure different dimensions of the mystical-type experience: 'mystical', 'positive-mood', 'transcendence of time and space' and 'ineffability'. In the current study, we present data in the form of a single total MEQ score ranging from 30 to 180.

Challenging psychedelic experience

The Challenging Experience Questionnaire (CEQ) [354] is a 26-item scale scored on a 6-point Likert scale (1 = none, not at all; 6 = extreme, more than any other time in my life). It consists of seven factors which measure different dimensions of challenging aspects of the psychedelic experience: 'fear', 'grief', 'physical distress', 'insanity', 'isolation', 'death', 'paranoia'. Here, we present data in the form of a single total CEQ score ranging from 26 to 156.

Post-psychedelic growth

The Post-Traumatic Growth Inventory Short Form (PGTI-SF) [355] is a 7-item scale that assesses positive self-related changes ('growth') experienced by individuals following a traumatic event. While the scale was developed and has been used to assess growth following traumatic events, a review of the items of the PGTI suggest that it also has broader relevance, including for participants who have experienced positively valanced transformative events. We therefore minimally adapted it for use in studying the effects of psychedelic experiences (**Appendix A2.1**). Despite the items being identical to the PGTI-SF, to distinguish its use in the context of psychedelic growth from its common use to assess posttraumatic growth, we refer to the scale here as the **Post-Psychedelic Growth Inventory (PPGI)**. Respondents rate their beliefs on a

7-point Likert scale (1 = strongly disagree; 7 = strongly agree), with items including changes in priorities, spiritual matters, closeness with others, and personal strength (e.g., “I have changed my priorities about what is important in life”, “I have a better understanding of spiritual matters”, “I have a greater sense of closeness with others”, “I discovered that I'm stronger than I thought I was” etc.,). Here, we present data in the form of a single total PPGI score ranging from 7 to 49.

Centrality of psychedelic experience

The 10-item Centrality of Event Scale (COES) [356] is a validated measure of how much a specific experience becomes central to personal identity, a turning point in one's life story, and a reference point for everyday inferences. Respondents rate statements such as “The experience permanently changed my life” and “The experience was a turning point in my life” on a 7-point Likert scale (1 = strongly disagree; 7 = strongly agree). Although traditionally used to assess growth following traumatic events, it was minimally adapted for use in studying the effects of psychedelic experiences, in line with the PPGI justification above (**Appendix A2.2**). Here, we present data in the form of a single total COES score ranging from 7 to 70.

Change in wellbeing

The Short Warwick-Edinburgh Mental Wellbeing Scale (SWEMWBS) [357] is a 7-item measure of wellbeing. For this study, the instructions of the SWEMWBS were slightly adapted to specifically capture data related to changes in wellbeing following psychedelic experiences. Participants were asked to select the answer that best represented how they had felt since their most significant psychedelic experience, and the items were modified to include indications of change (e.g., “I've been feeling more optimistic about the future”, “I've been feeling more useful”, “I've been feeling more relaxed”, etc). Each item was rated on a 7-point Likert scale (1 = definitely disagree; 7 = definitely agree), and a total SWEMWBS score was calculated for each participant, ranging from 7 to 49.

Romantic attachment style

The Experiences in Close Relationship Scale-Short Form (ECR-S) [360] is a 12-item scale scored on a 7-point Likert scale (1 = strongly disagree; 7 = strongly agree), which provides data on two continuous scales concerning the extent to which participants show attachment dimensions: anxiety and avoidance. For the purposes of this chapter, the instructions of the ECR-S were slightly adapted to specifically capture data related to changes in romantic attachment style following psychedelic experiences, by asking participants how they experienced romantic relationships before the stated psychedelic experience. As only the scores related to the anxiety attachment dimension were included (e.g., “I needed a lot of reassurance that I am loved by my partner”, “I find that my partner(s) don't want to get as close as I would like”, “My desire to be very close sometimes scares people away" etc.,), we refer to this scale as the ECR-SAn. A total ECR-SAn score was calculated for each participant, ranging from 7 to 42.

Extraversion

The Big Five Inventory (BFI) [361] is a 44-item scale scored on a 5-point Likert scale (1 = strongly disagree; 5 = strongly agree), which measures an individual on the Big Five Factors (dimensions) of personality [362]. As only the 8 items related to Extraversion were included (e.g., "Is talkative", "Is full of energy", "Generates a lot of enthusiasm" etc.,), we refer to this scale as the **BFI-Ex**. A total BFI-Ex score was calculated for each participant, ranging from 8 to 40.

Altered states of consciousness

The 11 Dimensions Altered States of Consciousness (11D-ASC) [358] was used to assesses the acute effects of psilocybin experiences on 11 dimensions of consciousness, including 'experience of unity', 'spiritual experience', 'blissful state', 'insightfulness', 'disembodiment', 'impaired control and cognition', 'anxiety', 'complex imagery', 'elementary imagery', 'audio-visual synaesthesia', and 'changed meaning of percepts'. Items contain statements (e.g., "I felt I was in a wonderful other world"), which can be answered on a continuous scale ranging from "No, not more than usual" (0) to "Yes, much more than usual" (100), where 0 is considered to resemble a sober state. Separate mean subscale scores were calculated, ranging from 0-100. The mean score of all the questions gives the global-ASC score.

Emotional distress

The Depression, Anxiety, and Stress Scale (DASS-21) [359] was used to assess symptoms of depression, anxiety, and stress. The DASS-21 consists of 21 items rated on a 4-point Likert scale (1 = did not apply to me at all, 4 = applied to me very much, or most of the time). Separate total scores were calculated for each subscale. The total score of each subscale can range from zero to 21.

2.3.4 Statistical analysis

Descriptive statistics for each study are presented as frequencies (and %). All statistical analyses were conducted using the most current version of Python at the time of analysis (Python 3.12).

Study 2.I: Scale development

In the Delphi procedure, consensus was pragmatically defined as the majority of participants either agreeing/strongly agreeing or disagreeing/strongly disagreeing with the inclusion of an item [349, 363].

After each round, the number of items in each sub-domain and the percentage of items where consensus was achieved were calculated. Qualitative analysis of the focus groups and QPIs followed a rapid thematic analysis approach, where data collection and preliminary analysis occurred in tandem [345, 346]. This iterative process helped shape subsequent focus groups and QPIs, refining the interview guides to capture emerging insights.

Study 2.II: Scale validation

Factor structure

The 41-item scale was subjected to EFA to determine the optimal number of factors and items to retain. Sample adequacy was assessed using the **Kaiser-Meyer-Olkin (KMO)** measure and Bartlett's test of sphericity, ensuring the data were suitable for factor analysis. The number and composition of factors were determined by common psychometric heuristics, including a visual inspection of the scree plot [364], the 'Kaiser rule' [365], and tests such as optimal coordinates, parallel analysis, and the acceleration factor test [366]. Oblique (oblimin) rotation was used to allow for intercorrelated factors, enhancing interpretability. Subscales were defined based on the extracted factors, with items assigned to factors based on their loading patterns. To ensure clarity and simplicity in interpretation, two criteria were applied: (1) each item demonstrated a factor loading of ≥ 0.3, and (2) cross-loadings on other factors were <0.2 [367, 368].

Dimensionality

After identifying the items to retain based on loadings and cross-loadings from the EFA, tests of dimensionality were conducted on a separate dataset (Sample B) to validate the identified factor structure. CFA was applied to several structural models: (1) the hypothesised 4-factor model derived from the EFA; (2) a hierarchical 4-factor model, where the covariance between first-order latent variables was explained by a second-order latent construct labelled "Psychedelic Preparedness"; (3) a 3-factor model based on the highest factor covariance in the hypothesised model; and (4) a 2-factor model derived from the highest factor covariance in the 3-factor model. The fit of models 2-4 was compared to the hypothesised 4-factor model. Goodness of fit was evaluated using the model chi-square statistic as an absolute measure of fit, though, given its sensitivity to sample size, additional indices were also used, including the **Comparative Fit Index (CFI)**, **Tucker-Lewis Index (TLI)**, **Root Mean Square Error of Approximation (RMSEA)**, and **Standardised Root Mean Square Residual (SRMR)** [369, 370]]. Criteria such as CFI/TLI values ≥ 0.95 (good fit) and ≥ 0.90 (adequate fit) were applied to assess the models. The likelihood ratio test ($\Delta\chi^2/\Delta df$) was used to compare model fits [371], and changes in RMSEA (ΔRMSEA) were also calculated to facilitate model comparison [372]. A full description of these model evaluation methods and their rationale can be found in **Appendix A2.8**.

Reliability

Internal consistency and construct reliability were assessed using McDonald's ω and 95% **confidence intervals (CI)**, both at the factor and scale levels, for the model with the best fit. McDonald's ω was chosen over Cronbach's α due to the violation of tau-equivalence, a key assumption for α [373]. Test-retest reliability was evaluated through Spearman's rho (ρ), **intra-class correlation (ICC)**, and Bland-Altman plots. Spearman's rho was employed due to non-normal distribution of the total PPS scores, as indicated by the Shapiro-Wilk test (Shapiro-Wilk statistic = 0.967, $p < 0.001$). This non-normality was further supported by visual inspection of histograms and Q-Q plots (**Appendix A2.10**). Bland-Altman plots were used to visually assess agreement between measurements taken on two different days, providing insight into any systematic discrepancies between test and retest scores (**Appendix A2.9**).

Validity

The construct validity of the PPS was assessed by examining correlations between the total and subscale PPS scores and a single-item measure of overall preparedness ["Please [drag the slider to] describe how prepared you felt overall for your psychedelic experience (1 = not at all prepared; 5 = completely prepared)"]. To establish convergent and divergent validity, correlations were examined between PPS scores and validated measures expected to align positively with psychedelic preparedness, such as the EBI and MEQ, and negatively with the CEQ. Discriminant validity was evaluated by assessing correlations between PPS scores and unrelated measures, including the **Experiences in Close Relationships Scale-Anxiety (ECR-SAn)** and the **Big Five Inventory-Extraversion (BFI-Ex)**. Criterion validity (i.e., predictive validity) was examined by investigating how total PPS scores correlated with the 10-item 'preparation efficacy' measure, as well as by exploring correlations between PPS scores and changes in three outcome measures: PPGI, COES, and perceived changes in well-being following the psychedelic experience (SWEMWBS). To further demonstrate the impact of preparation level on outcomes, participants were categorised into 'Low Preparation' (PPS total scores below the median) and 'High Preparation' (PPS total scores above the median). Two-sample t-tests were then used to compare the mean scores of each relevant outcome measure (EBI, MEQ, CEQ, PPGI, COES, SWEMWBS) between these two groups.

Study 2.III: Scale implementation

Reliability and validity

Internal consistency and construct reliability were assessed using the same methods as in **Study 2.II**, applying McDonald's ω to evaluate reliability. To assess criterion validity, correlations were examined between the prospective total PPS scores and the 'global ASC' scores, which represent the average score across all 11D-ASC dimensions. Additionally, correlations were analysed to evaluate changes in the three subscales of the DASS-21. To further demonstrate the effect of psychedelic preparation on outcomes, participants were categorised into 'High Preparation' and 'Low Preparation' groups, following the same median-split method used in **Study 2.II**. Two-sample t-tests were then conducted to compare the global-ASC scores, the mean scores of each 11D-ASC subscale, and changes in DASS-21 subscale scores between these two groups.

2.4 Results

2.4.1 Scale development

DelFo method and QPIs

Table 2.1 provides a summary of how the number of items in each subdomain evolved across the four rounds of the DelFo procedure. Consensus on item inclusion steadily improved with each round. In Round 1, consensus was achieved for 66.1% of the items (39 of 59), and by Round 4, this had increased to 92.2% (47 of 51 items). Notably, 100% consensus was reached for seven subdomains, while the lowest consensus was observed in the Intention Setting domain, with 66.7% agreement by Round 4.

Feedback from the QPIs led to additional modifications, particularly regarding grammar and word choice, for four items (see **Appendix A2.6** for details). These changes were implemented to improve clarity and ease of understanding.

	Number of items in each sub-domain				Number of items where consensus was achieved (%)			
Sub-domain	**R1**	**R2**	**R3**	**R4**	**R1**	**R2**	**R3**	**R4**
Education	4	5	6	5	3 (75%)	4 (80%)	5 (83.3%)	4 (80%)
Intention Setting	6	9	5	3	5 (83.3%)	6 (66.7%)	4 (80%)	2 (66.7%)
Expectation Management	6	8	4	4	5 (83.3%)	7 (87.5%)	4 (100%)	4 (100%)
Psychological Mindedness	0	6	3	3	0 (0.0%)	5 (83.3%)	3 (100%)	3 (100%)
Emotional Readiness	8	9	5	4	5 (62.5%)	8 (88.9%)	4 (80%)	3 (75%)
Willingness to Surrender	6	8	3	3	4 (66.7%)	7 (87.5%)	3 (100%)	3 (100%)
Psychophysical Robustness	5	7	4	3	3 (60%)	6 (85.6%)	3 (75%)	3 (100%)
Safety/Security	5	7	4	4	4 (80%)	7 (100%)	4 (100%)	4 (100%)
Prepared for Change	6	8	7	6	3 (50%)	8 (100%)	6 (85.7%)	6 (100%)
Preparatory Practises	10	11	9	6	6 (60%)	9 (81.8%)	8 (88.9%)	5 (83.3%)
Preparation Efficacy	3	10	10	10	1 (33.3%)	10 (100%)	10 (100%)	10 (100%)
Totals	59	88	60	51	39 (66.1%)	77 (87.5%)	54 (90%)	47 (92.2%)

Table 2.1. Summary of item changes by subdomain across DelFo rounds

Note. Rx = Round

Study 2.I conclusion

Following the completion of the DelFo and QPI procedures, a total of 51 items were finalised for inclusion (**Appendix A2.7**). A subsequent psychometric evaluation was conducted in **Study 2.II** to validate these items for both prospective and retrospective versions of the scale. Notably, the ten items related to 'preparedness efficacy' (e.g., "My preparation impacted my experience"), which are applicable only in a retrospective context, were excluded from the scale and treated as a separate measure.

2.4.2 Scale validation

Demographic

Demographic characteristics of participants in Sample A (N = 518) and Sample B (N = 718) are summarised in **Appendix A2.11**. Participants in both samples were predominantly male (55.6% in Sample A, 43.7% in Sample B) and White (82.8% in Sample A, 80.5% in Sample B), with mean ages of 33.72 (SD = 12.81) and 37.24 (SD = 12.64) years, respectively. Educational attainment was high, with over 70% holding an undergraduate or postgraduate degree. Lifetime psychedelic use varied, with a substantial proportion reporting more than 20 lifetime occasions (35.3% in Sample A, 42.2% in Sample B). Religious affiliation differed notably between samples, with 52.8% of Sample B identifying as spiritual compared to 6.2% in Sample A. Further details are provided in **Appendix A2.11**.

Factor structure

An EFA using **maximum likelihood (ML)** estimation was conducted on the 41 original preparedness items (excluding the 10 'preparation efficacy' items) from the Sample A dataset (N = 518). Sample A was deemed suitable for factor analysis, as indicated by a high KMO measure of sampling adequacy (0.913) and a significant Bartlett's test of sphericity ($\chi^2(820) = 11{,}257.648$, $p < 0.001$) [72]. Visual inspection of the scree plot (**Appendix A2.12**), along with parallel analysis and optimal coordinate estimates, suggested a 4-factor solution, which was used for extracting factor loadings. Item loading patterns (**Appendix A2.13**) showed that 14 items had significant cross-loadings (> 0.2) and 7 items had factor loadings below 0.30, leading to their removal. The EFA was repeated (**Appendix A2.14**), and the final version of the 'Psychedelic Preparedness Scale' included 20 items with satisfactory loading patterns. The four factors explained 56.53% of the total variance, with the first factor accounting for 16.04%, the second 15.65%, the third 12.51%, and the fourth 12.33%. Based on the content of the items that loaded onto each factor, the factors were labelled to represent sub-domains of psychedelic preparedness: **Knowledge-Expectation (KE)**, **Intention-Preparation (IP), Psychophysical-Readiness (PR)**, and **Support-Planning (SP).**

Dimensionality

The 4-factor structure (Model 1) identified from the EFA was tested through a CFA using a separate dataset from Sample B (N = 718). Although the chi-square test was significant ($\chi^2(66, N = 718) = 611.973$, $p < 0.001$) [67, 68], other fit indices indicated an acceptable model fit. The CFI was 0.936, the TLI was 0.925, the RMSEA was 0.062 (95% CI = 0.057 - 0.067), and the SRMR was 0.054. Standardised factor loadings for this model are presented in **Fig. 2.3**.

CFA was also conducted on three nested models which were compared to the hypothesised 4-factor model (**Table 2.2**). Models 2 and 3 showed acceptable fit. However, the hypothesised 4-factor model showed lowest RMSEA values, and a lower likelihood ratio test ($\chi2$/df) result relative to all other models, which was considered more favourable (**Appendix A2.8**),

Table 2.2. Model fit indices for nested structural models of the PPS

	Model	RMSEA (95% CI)	SRMR	CFI	TLI	X^2 (df)	$\Delta X^2/\Delta df^a$	$\Delta RMSEA^b$
1	4-factor model	0.062 (0.057-0.067)	0.054	0.936	0.925	611.973 (164)	-	-
2	Hierarchical 4-factor model	0.064 (0.059-0.069)	0.055	0.929	0.919	658.682 (166)	+46.709/+2	+0.002
3	3-factor model	0.064 (0.058-0.069)	0.059	0.930	0.921	651.600 (167)	+39.627/+3	+0.002
4	2-factor model	0.082 (0.077-0.087)	0.061	0.883	0.869	982.354 (169)	+370.384/+5	+0.020

Note. The model with the best fit is shown in bold. N = 718. RMSEA, root mean square error of approximation; CI, confidence interval; SRMR, standardised root mean squared residual; CFI, Comparative Fit Index; TFI, Tucker-Lewis Fit Index; $\chi2$, Chi-square; df, degrees of freedom. [a] Likelihood ratio test, shown as a change in $\chi2$/df values relative to the parent model i.e., the hypothesised 4-factor model (top row). [b] Change in RMSEA value relative to the parent model i.e., the hypothesised 4-factor model (top row).

Figure 2.3. Confirmatory Factor Analysis (CFA) model of the PPS

Structural representation of the four-factor model (Model 1) of the Psychedelic Preparedness Scale (PPS) tested using confirmatory factor analysis (CFA) in Sample B (N = 718). Circles represent latent factors: Support-Planning, Intention-Preparation, Psychophysical-Readiness, and Knowledge-Expectation. Squares represent observed items, one-way arrows indicate factor loadings, and two-way arrows indicate covariances between factors. Standardized factor loadings demonstrate the relationships between observed indicators and latent constructs.

Reliability

The 20 items from the PPS showed excellent total scale reliability (McDonald's omega (ω) = 0.945, 95% CI =0.940-0.949), as did all sub-scales in the hypothesised 4-factor model: KE (ω=0.890, 95%CI=0.880-0.900), IP (ω=0.865, 95%CI=0.854-0.877), PR (ω=0.828, 95%CI=0.813-0.844), and SP (ω=0.799, 95%CI=0.782-0.817) (Appendix A2.15). A sub-sample (N = 296) from sample A was used to estimate the test-retest reliability of the PPS. The Bland-Altman plot was used to visually inspect the test–retest scores. As displayed in Appendix A2.9, 25 (8.45%) of the 296 within-subject test-retest difference scores were outside of the 95% CI [-29.28, 33.458]. There was a mean difference (t_1-t_2) on total PPS scores of 2.091 between test occasions (95% CI = 0.261-3.922). The test and retest reliability metrics in these 296 participants suggested good reliability ($\rho = 0.77$, $p < 0.001$, ICC = 0.76). Test-retest reliabilities for the four separate factors were also indicative of good reliability: KE ($\rho = 0.77$, $p < 0.001$, ICC = 0.79), IP ($\rho = 0.77$, $p < 0.001$, ICC = 0.74), PR ($\rho = 0.77$, $p < 0.001$, ICC = 0.62), and SP ($\rho = 0.77$, $p < 0.001$, ICC = 0.70).

Validity

In Sample A (N = 518), total PPS scores were moderately (positively) correlated with the single item rating of overall preparedness (Spearman's rho = 0.549, $p < 0.001$), supporting construct validity of the multivariate PPS. In the pooled sample (N = 1236), correlation coefficients between total PPS, its subscales and other validated measures are displayed in **Table 2.3**, demonstrating convergent and discriminant evidence. Results revealed a strong positive correlation between the total PPS score and the overall preparation efficacy score ($r = 0.81$, $p < 0.001$). PPS totals were also moderately correlated with all three 'criterion' variables (PPGI: ($r = 0.51$, $p < 0.001$, COES: $r = 0.59$, $p < 0.001$, SWEMWBS: $r = 0.59$, $p < 0.001$), demonstrating criterion validity (see **Fig. 2.3** for relevant scatterplots).

Table 2.3. PPS convergent, divergent and discriminant validity

					Convergent		Divergent[b]	Discriminant[a]	
	PPS Total	**KE**	**IP**	**PR**	**MEQ**	**EBI**	**CEQ**	**ECR-SAn**	**BFI-Ex**
PPS Total	-				0.55*	0.43*	-0.42*	-0.05	0.01
KE	0.87*	-			0.55*	0.48*	-0.41*	-0.03	0.16
IP	0.88*	0.73*	-		0.57*	0.42*	-0.49*	-0.01	0.24
PR	0.82*	0.69*	0.81*	-	0.55*	0.43*	-0.41*	-0.06	0.01
SP	0.82*	0.82*	0.61*	0.71*	0.53*	0.45*	-0.41*	-0.02	0.05

*Note. Correlation coefficients between the PPS, total and PPS subscales scores and validated secondary measures. Coefficients are Pearson's r. * sig at p < 0.001. KE = Knowledge-Expectations; IP = Intention-Preparation; PR = Psychophysical-Readiness; SP = Support-Planning. [a]Data for these surveys was only collected in Sample B (N = 718). [b]Data for this measure was collected from all 518 participants in Survey A and 457 participants in Survey B, making a total sample of N = 975.*

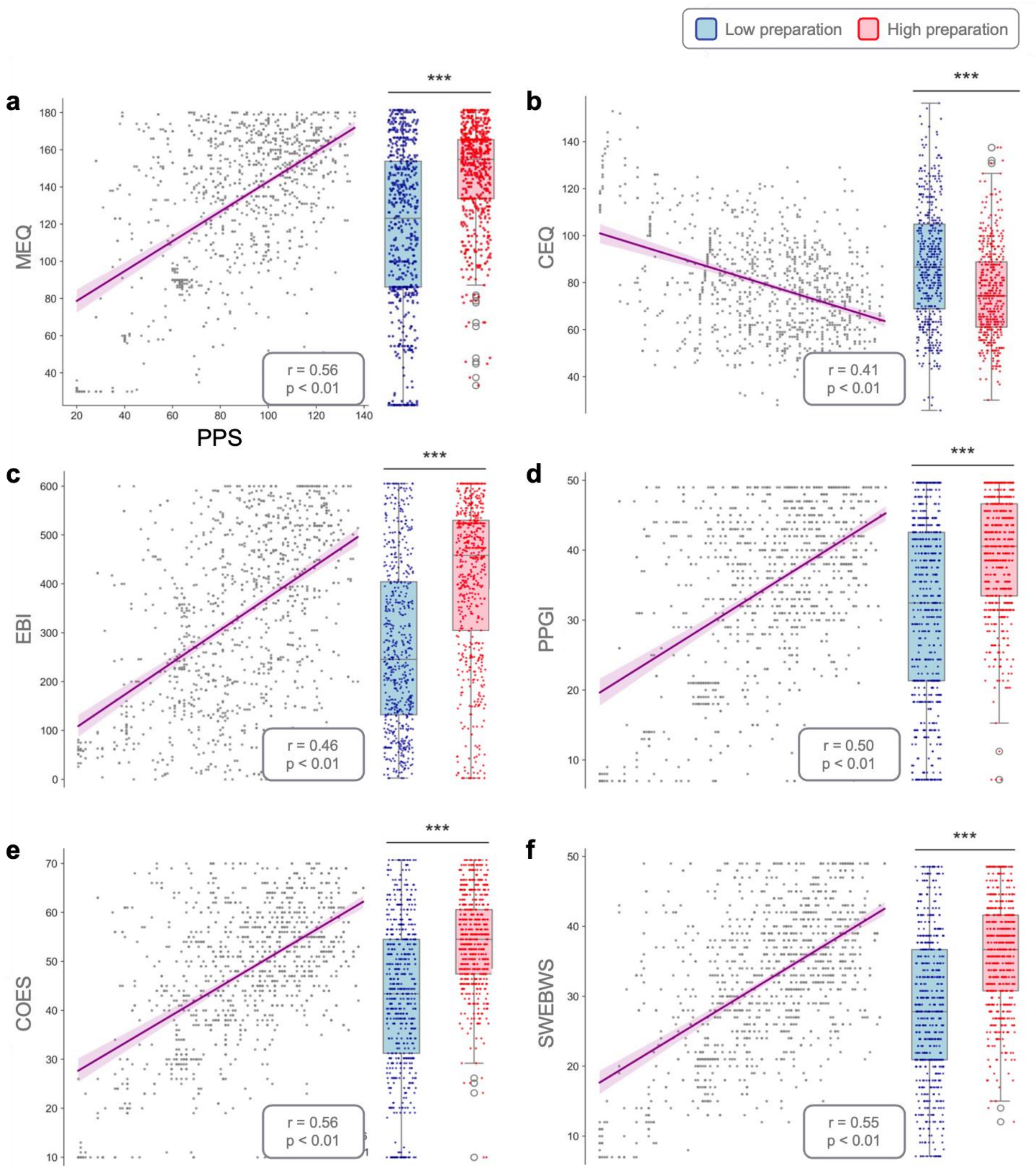


Figure 2.4. Relationship between psychedelic preparation and outcomes

Scatter plots and box plots illustrating the association between total Psychedelic Preparedness Scale (PPS) scores and six outcome measures: (a) Mystical Experience Questionnaire (MEQ); (b) Challenging Experience Questionnaire (CEQ); (c) Emotional Breakthrough Inventory (EBI); (d) Post Psychedelic Growth Inventory (PPGI); (e) Centrality of Events Scale (COES); and (f) Short Warwick and Edinburgh Wellbeing Scale (SWEBWBS). The box plots compare high (upper 50th percentile) and low (lower 50th percentile) preparation groups, showing significant differences across all outcomes.

Descriptive statistics for high and low preparation groups on the MEQ, CEQ, EBI, PPGI, COES, and SWEBWBS outcomes can be found in **Appendix A2.16**. Independent t-tests were conducted to compare the mean scores of the high (upper 50^{th} %ile) and low (lower 50^{th} %ile) preparation groups on each outcome.

Results showed significant differences between the high and low preparation groups on all six criterion variables (**Fig. 2.4**). Specifically, the high preparation group had significantly higher mean scores on the MEQ ($t(1234) = 14.654$, $p = <.001$, EBI ($t(1234) = 11.945$, $p = <.001$), PPGI ($t(1234) = 14.437$, $p = <.001$), COES ($t(1234) = 17.235$, $p = <.001$), and SWEBWBS ($t(1234) = 16.663$, $p = <.001$), and lower scores on the CEQ ($t(972) = -8.647$, $p = <.001$) than the low preparation group.

Study 2.II conclusion

Study 2.II provides strong evidence for the psychometric properties of the PPS, demonstrating its reliability and validity as a measure of psychedelic preparedness. The exploratory and confirmatory factor analyses supported a clear four-factor structure, representing distinct sub-domains of psychedelic preparedness: KE, IP, PR, and SP. The PPS showed excellent internal consistency, test-retest reliability, and strong convergent, discriminant, and criterion validity. The scale's ability to predict both acute and post-acute psychological effects induced by psychedelics highlights its potential utility in research and clinical settings.

2.4.3 Scale implementation

Demographic

The demographic characteristics of participants in the Retreat Survey can be found in **Appendix A2.17**.

Reliability

The retrospective PPS scores were used to estimate the test–retest reliability of the prospective PPS scores. The Bland-Altman plot method was used to visually inspect the test-retest reliability after 2 weeks (**Appendix A2.18**). Like the results obtained in **Study 2.I**, 6.52% (3/46 participants) of the within-subject test–retest difference scores were outside of the 95% CI [-22.62, 28.32]. There was a mean difference (t1-t2) of 2.848 between the days (95% CI = -1.01, 6.71). Spearman's rho (ρ) and intraclass correlation coefficients ($ICC_{2,1}$) obtained in this smaller ecological sample were also similar to those reported for Study 2.I for the total PPS ($\rho = 0.71$, $p < 0.001$, ICC = 0.71) and the sub-domains of preparation: KE ($\rho = 0.71$, $p < 0.001$, ICC = 0.81), IP ($\rho = 0.71$, $p < 0.001$, ICC = 0.62) PR ($\rho = 0.71$, $p < 0.001$, ICC = 0.58), and SP($\rho = 0.71$, $p < 0.001$, ICC = 0.54).

Validity

Total PPS score was significantly correlated with global-ASC score ($r = 0.56$, $p < .001$), and changes in total DASS-21 scores (depression: $r = -.0.45$, $p = .002$; anxiety: $r = -.53$, $p < .001$; stress: $r = -.56$, $p < .001$) (**Appendix A2.24** for scatter plots).

Results showed significant differences between the high (upper 50^{th} %ile) and low (lower 50^{th} %ile) preparation groups on global-ASC score (t(44) = 2.106, p = 0.041) (**Appendix A2.24** for bar charts), and eight of the eleven 11D-ASC outcomes (**Appendix A2.19**). Specifically, the high preparation group had significantly higher mean scores on the experience of unity (t(44) = 4.719, p = <.001, spiritual experience (t(44) = 3.545, p = <.001), blissful state (t(44) = 3.117, p = 0.003), insightfulness (t(44) = 3.358, p = 0.002), disembodiment (t(44) = 4.375, p = <.001), and lower mean scores on the anxiety (t(44) = -2.348, p = 0.023) and elemental imagery (t(44) = -3.432, p = 0.001) than the low preparation group (see **Appendix A2.20** for radar plot).

Results showed significant differences between the high and low preparation groups on change scores of all three measures of psychological distress from the DASS-21 (**Appendix A2.24** for bar charts). Specifically, the high preparation group had significantly greater reductions in Depression (t(44) = -3.526, p = <.001, Anxiety (t(44) = -3.202, p = .003), and Stress (t(44) = -3.162, p = 0.003) scores, than the low preparation group (**Appendix A2.21**).

Study 2.III conclusion

Study 2.III provides preliminary evidence for the utility of the PPS as a prospective measure of psychedelic preparedness. The study demonstrates that the PPS, when administered prior to a psilocybin retreat, can predict both the acute subjective effects of the psychedelic experience and the subsequent changes in psychological well-being. The test-retest reliability of the prospective PPS scores was found to be good, with results similar to those obtained in **Study 2.II.** This finding suggests that the PPS is a stable measure of psychedelic preparedness, even when administered in an ecologically valid setting. The prospective PPS scores showed significant correlations with the global ASC score and changes in DASS-21 scores, providing evidence for the criterion validity of the scale. Furthermore, when participants were divided into high and low preparation groups based on their PPS scores, significant differences were observed in the global ASC score, several dimensions of the ASC, and changes in DASS-21 subscale scores. These findings suggest that higher levels of psychedelic preparedness, as measured by the PPS, are associated with more positive acute subjective effects and greater improvements in psychological well-being following the psilocybin experience.

2.5 Discussion

Chapter 2 introduces and validates the PPS, an original self-report measure. In **Study 2.I**, our novel DelFo method was used to develop the questionnaire items, and subsequent QPIs were employed to reach consensus on structure and content. In **Study 2.II**, the 20-item PPS demonstrated good reliability and validity and was able to predict both acute and post-acute psychological effects induced by psychedelics. **Study 2.III** further confirmed these findings, revealing the PPS to be an effective prospective as well as retrospective tool for measuring preparedness and estimating responses to psychedelics (see **Appendix A2.22** and **A2.23** for prospective and retrospective PPS).

The results of our studies provide compelling evidence for the existence of a measurable psychological state of psychedelic preparedness, which is predictive of positive acute and long-term outcomes associated with psychedelic use. Our study used robust scale development and psychometric validation methodology, revealing four distinct underlying factors of psychedelic preparedness: KE, IP, PR, and SP. The 4-factor model of the PPS exhibited superior goodness of fit in comparison to the second-order model; nonetheless, the hierarchical model still demonstrated adequate fit and may offer enhanced clinical convenience for implementation in research and clinical settings. Notably, the hierarchical model provides simplified scoring, interpretation, and representation of the overarching constructs, along with flexibility in its application. For instance, the PPS could serve as a valuable screening tool to identify individuals who may require additional preparation or support prior to undergoing psychedelic interventions, thereby functioning as a pre-intervention assessment to pinpoint areas of preparedness that necessitate attention. Furthermore, the PPS could serve as an outcome measure to evaluate the effectiveness of psychedelic preparedness interventions or to compare the efficacy of different preparation protocols. As such, future research endeavours should continue to explore the potential applications of the PPS and its role in the development of individualised treatment plans in clinical settings, as well as investigate the relative influence or interaction of each factor in predicting acute and long-term effects of psychedelics.

The present study makes a unique and comprehensive contribution to the field in part by employing a methodology that emphasises **Patient and Public Involvement (PPI)**[33]**.** PPI is a critical but often overlooked aspect of measure development processes [376–378]. However, despite challenges posed by paternalistic beliefs that may hinder collaboration with individuals who have lived experience [379], involving end-users in research activities can empower these individuals, foster trust in the research, and

[33] Although other definitions are acknowledged, for the purposes of this study, PPI is defined as the "active involvement of patients, service users, carers or family members in activities done *with* or *by*, rather than *to*" them [374, 375]

optimise the research process [380]. When done systematically and thoughtfully, PPI can significantly enhance the credibility and impact of research, promoting accountability, transparency, and relevance [381]. Despite the establishment of recent guidelines for PPI strategy in psychedelic science [337], the lack of patient/public collaborators acknowledged in this field is still evident. In this chapter, we aimed to address this issue by incorporating PPI into our scale development process, allowing us to test clinical and theoretical tenets of psychedelic preparedness [16, 174], while also identifying gaps in our understanding of the acceptability and feasibility of the scale, among end-users who would actually be using it [380, 382]. This approach aligns with the principles of **Community-Based Participatory Research (CBPR)**, which promotes equitable partnerships between researchers and communities, emphasising the value of local knowledge and expertise [383]. Accordingly, the consensus-focused ambition of this chapter, which incorporated stakeholder perspectives in a co-production fashion, represents a significant contribution to the field of psychedelic research.

There are several limitations to this study. Firstly, the validation of the PPS is limited by a self-selection bias for all three studies. Study participants were predominantly **WEIRD (white, educated, industrialised, rich, democratic)** [384] reflecting a pervasive problem in psychedelic research [161]. We encourage future studies to conduct a validation and analysis of PPS scores in ethnically, geographically, and culturally diverse settings. Secondly, the high attrition rate in the retreat study meant only 46 participants completed the before and after surveys, which could have created attrition bias effects. Participants who dropped out of the study may have had different experiences and outcomes compared to those who completed the study, potentially affecting the results. It is important for future research to address potential attrition bias by carefully monitoring and accounting for participant dropout rates. Furthermore, it should be noted that while participants in the survey studies were permitted to have used a variety of psychedelics, the retreat studies exclusively focused on psilocybin. This limitation may restrict the generalisability of the findings to other types of psychedelics, as there could be potential variations in the impact of preparation on acute and long-term effects depending on the specific substance used. Lastly, the present article provides no specific examination of the validity and clinical utility of the PPS in and between different clinical populations. To address these issues, future research should systematically investigate the role of preparedness for different types of psychedelics in different neuropsychiatric conditions, allowing for a more comprehensive understanding of potential between-psychedelic effects and their implications. Broader limitations surrounding measuring psychedelic preparedness are discussed in **Chapter 7**.

Conclusion

This chapter provides compelling evidence for the existence of a measurable psychological state of psychedelic preparedness that predicts both acute and longer-term outcomes of psychedelic use. The development and validation of the PPS represent a significant advance in operationalising this construct. Through rigorous methodology and integration of PPI, the PPS captures four distinct factors of preparedness, offering both clinical utility and research value. While not a standalone diagnostic tool, the PPS may be used to identify individuals who require additional support prior to psychedelic intervention and to evaluate the efficacy of preparatory protocols. These findings contribute to growing evidence that a positive and intentional preparatory context enhances therapeutic outcomes and underscore the importance of developing evidence-based approaches to support this critical pretreatment state. Future research should explore the PPS across diverse populations, substances, and clinical settings to expand our understanding of how preparedness shapes the psychedelic experience and its enduring effects

CHAPTER 3

Development of a Digital Intervention for Psychedelic Preparation (DIPP)

"Science is the belief in the ignorance of experts."

— *Feynman, R.P. (1999) The Pleasure of Finding Things Out.*

3.1 Abstract

This chapter describes the development of a self-directed, digital intervention for psychedelic preparation. Drawing on elements from the UK **Medical Research Council (MRC)** framework for developing complex interventions, the design was informed by a four-factor model of psychedelic preparedness (**Chapter 2**), using a person-centred approach. Our mixed-methods investigation consisted of two studies. The first involved interviews with 19 participants who had previously attended a 'high dose' psilocybin retreat, systematically exploring their preparation behaviours and perspectives on the proposed intervention. The second study engaged 28 attendees of an ongoing psilocybin retreat in co-design workshops, refining the intervention protocol using insights from the initial interviews. The outcome is a co-produced 21-day digital course (**Digital Intervention for Psychedelic Preparation [DIPP]**), that is organised into four modules: **Knowledge-Expectation (KE), Psychophysical-Readiness (PR), Support-Planning (SP)**, and **Intention-Preparation (IP)**. Fundamental components of the course include daily meditation practice, supplementary exercises tied to the weekly modules, and mood tracking. DIPP provides a comprehensive and scalable solution to enhance psychedelic preparedness, aligning with the broader shift towards digital mental health interventions.

3.2 Introduction

Despite the current ubiquity of clinician-guided preparatory sessions, the potential utility of self-directed preparation strategies to enhance individuals' readiness for psychedelic experiences has not yet been investigated. While a trusting therapeutic relationship seems to be a crucial prerequisite for psychedelic treatment [319], extensive contact with a clinician in the preparation phase is resource-intensive and poses a significant challenge to the scalability and accessibility of psychedelic therapy [385]. By contrast, the use of digital technologies to deliver structured and standardised self-directed strategies allows for extensive, tailored and convenient psychedelic preparation outside the clinical setting [386].

Results from **Chapter 2**, which established a four-factor model of psychedelic preparedness, together with preliminary findings from the UNITy DMT trial presented in **Chapter 1**, suggest that a substantial portion of psychedelic preparation strategies can be standardised and delivered remotely or digitally. These include strategies aimed at enhancing (i) individuals' understanding of psychedelic substances and clarification of their expectations regarding potential immediate and long-term effects (Knowledge-Expectation [KE]), (ii) the extent to which individuals are mentally and physically ready to navigate the psychedelic experience (Psychophysical-Readiness [PR]), (iii) the introspective inquiry integral to a participant's decision to engage with psychedelics (Intention-Preparation) [IP], and ensuring (iv) a safe and supportive environment in the post-psychedelic stage (Support-Planning [SP]). These standardised preparation components could be systematically delivered through digital platforms while still allowing flexibility to accommodate individual participants' needs, preferences, and pace [387, 388].

As the healthcare sector increasingly integrates technology to enhance well-being and mental health, many services traditionally delivered face-to-face are being reimagined in the digital realm and have been shown to be non-inferior to more resource intensive in-person delivery [389, 390]. As such, the use of web- and app-based technology, be it standalone or adjunctive, offers advantages for the delivery of self-directed psychedelic preparation interventions, such as improved accessibility, flexibility, anonymity, and cost-effectiveness [391–395]. Moreover, the use of digital interventions has shown to be pivotal in empowering participants in the management and delivery of therapeutic services [396–398], by allowing them to take an active role in the management of their own health [388]. While recent initiatives have recognised the potential of digital tools in monitoring outcomes associated with psychedelic use [399], no published or publicly available digital interventions specifically target the preparation phase of psychedelic therapy. This significant gap presents an opportunity to develop standardised digital tools that could enhance the efficiency and accessibility of psychedelic therapies while reducing demands on both participants and service providers.

While there is a growing body of evidence demonstrating the effectiveness of digital interventions in alleviating or preventing symptoms of mental health [385, 400–403], suboptimal user engagement poses a significant challenge in translating these benefits to real-world applications [395, 404, 405]. Recognising the need to promote better engagement with digital interventions, several studies have emphasised the necessity of taking a person-centric approach to digital intervention design [406–410]. The rationale for involving relevant stakeholders from the start, and indeed working closely with them throughout, is that they can help to identify priorities, understand challenges, and find solutions that enhance the likelihood of successful implementation [411–416]. Although recent guidelines in psychedelic science [337] have advocated for a person-centric approach and have emphasised the inclusion of patients and the public more broadly to enhance the credibility and impact of research while promoting accountability, transparency, and relevance [381], the inclusion of such perspectives is still noticeably lacking in the field [417].

In light of the recognised potential of digital and remotely-delivered psychosocial interventions within psychedelic science and therapy [399, 418–420], the purpose of **Chapter 3** was to develop and refine a self-directed DIPP using a person-centred, mixed-methods approach. Aligned with the four-factor model of psychedelic preparedness (**Chapter 2**), DIPP's content and structure were developed through a phased process involving two studies:

- Initial intervention development (**Study 3.I**): This phase aimed to identify essential components for psychedelic preparation by conducting qualitative interviews with psilocybin retreat participants. The insights obtained were crucial in determining the foundational elements and thematic structure of DIPP, ensuring the intervention's relevance to actual user experiences.
- Intervention component refinement (**Study 3.II**): Building upon the findings from **Study 3.I**, this phase involved iterative feedback through co-design workshops with psilocybin retreat attendees. This step was key to refining DIPP's components, enhancing its user-centeredness and implementation across varied contexts.

While DIPP has been tailored to be suitable for both clinical and retreat contexts (and potentially adaptable for non-therapeutically oriented research studies), the data collection efforts focused on psilocybin retreat participants. This population was selected as they were more readily accessible for the purposes of this research. The insights derived, however, are expected to be translatable across other clinical and non-clinical settings.

The intervention was structured following the UK MRC framework for complex interventions [411, 416, 421] which delineates four stages: *Development*, *Feasibility and Pilot Testing*, *Evaluation*, and *Implementation*. Within this Chapter, the focus was on the *Development* stage, prioritising the early assessment of feasibility and acceptability through qualitative methods, as recommended by the MRC [422–424]. The description of our intervention follows the TIDieR checklist [320] and the **GUIDance for the rEporting of Intervention Development (GUIDED)** framework [425] (**Appendix A3.4, A3.5**). **Chapter 4** outlines the protocol designed to assess the feasibility of DIPP, focusing on the *Feasibility and Pilot Testing* stage.

3.3 Methods

All research was performed in accordance with the Declaration of Helsinki and all procedures were reviewed by, and received approval from, the UCL REC (ID: 9437/001). All studies were performed in line with relevant guidelines and regulations [426–431].

3.3.1 Participants and recruitment

Initial intervention development (Study 3.I)

Participants were recruited through collaborating psilocybin retreat centres. While there are some differences in the structure and content of each retreat centre's program, the centres were selected to be as similar as possible in program structure and types of support offered. For additional contextual information on collaborating psilocybin retreat centres, see **Appendix A3.1**. Information about the study was disseminated to potential participants by email, outlining the study's aims and containing a hyperlink to an information sheet detailing the study protocol. The inclusion criteria specified that participants must be over the age of 18, have experienced a 'significant change' as a result of a psilocybin retreat, and be proficient in English. Informed consent was acquired electronically, verifying each participant's understanding and agreement to the study's terms. Nineteen participants met inclusion criteria and completed the study.

Intervention component refinement (Study 3.II)

Participants were recruited in-person on the final day of retreats at one of the collaborating retreat centres. During one of the final sessions, study details were presented to potential participants. Consenting participants attended a co-design workshop at the end of the retreat. Cumulatively, these sessions included 28 participants and took place in three separate workshops.

3.3.2 Procedures

Initial intervention development (Study 3.I)

A total of 19 participants were interviewed via video conferencing (Microsoft Teams), approximately three months after their retreat experience (range: 1-9 months). These semi-structured interviews were designed to thoroughly explore different aspects of participant preparation.

The interview was divided into three sections, each targeting a specific dimension of preparation. The first section focused on participants' preparatory activities, asking them to reflect on what they did to prepare and the outcomes they perceived from these efforts. The second section explored their views on the effectiveness of specific preparation techniques, identifying any challenges they faced during the process and soliciting suggestions for areas where additional guidance could enhance the experience. The final section invited participants to provide feedback on a proposed preparatory intervention. They were asked to evaluate its potential usefulness, suggest key features and components, recommend elements to omit based on their experiences, and share preferences for how the intervention should be delivered and its ideal duration.

Intervention component refinement (Study 3.II)

Three co-design workshops were held in person at the *Buena Vida* retreat, with each workshop involving participants from three consecutive, independent retreats. Detailed methodology for these workshops can be found in **Appendix A3.2**. The primary goal was to collaboratively generate and refine the activities or components to be included in the initial version of the intervention protocol. This process built upon insights from the qualitative interviews conducted in **Study 3.I**, as well as the four-factor framework for psychedelic preparation outlined in **Chapter 2**. Participants were encouraged to use these findings as a foundation to identify and prioritise components for the intervention, while also noting any missing elements.

The workshops balanced structured discussions, interactive exercises, prioritisation activities, and individual reflection to promote idea generation and consensus building. Each session lasted approximately 90 minutes.

- Workshop 1 focused on identifying and prioritising key components of the psychedelic preparation intervention. Participants used a dot-voting technique to indicate priority components. A **priority score (P1)** was calculated by dividing the total number of priority votes by the total number of participants, with a P1 score of 1.00 indicating full consensus on a component's priority.
- Workshop 2 aimed to refine this list, using a similar voting process to assign **updated priority scores (P2)** to each component. After voting, participants assessed the feasibility of including each priority component in the digital intervention. The **feasibility score (F2)** for each component was calculated by dividing the number of feasibility votes by the total number of participants, with an F2 score of 1.00 indicating unanimous agreement on both the component's critical importance and its feasibility. Components were then ranked based on their F2 scores to streamline the selection of elements considered both essential and feasible for inclusion.
- Workshop 3 had two main objectives: to evaluate each component for its potential **Benefits, Barriers, Risks, and Outcomes (BBRO),** and to collaboratively develop solutions for any challenges identified during this assessment.

3.3.3 Statistical analysis

Descriptive statistics

Demographic data was collected in numerical or categorical forms. Quantitative data from both **Study 3.I** and **Study 3.II** is presented descriptively as counts (or %) and means.

Interview-based thematic analysis (Study 3.I)

Thematic analysis [426, 427] was conducted using qualitative analysis software NVivo 14 to identify key methods and outcomes related to participants' preparatory experiences. Recorded interviews were transcribed using Microsoft Teams live transcription feature, and all transcriptions were cross-checked for accuracy against the original recordings. Collaborative coding, combining inductive and deductive approaches, was conducted by RM and two undergraduate research assistants (MK[34], and MM[35]). The qualitative data underwent **Structured Tabular Thematic Analysis (ST-TA)** [432], a process that converts qualitative responses into numeric codes to facilitate a frequency and percentage distribution analysis of different themes, thereby creating a quantitative summary of the data. The data were analysed using Python (Version 3.12).

The theoretical framework guiding this analysis was based on the four-factor model of psychedelic preparedness developed in **Chapter 2**. The four factors/themes consisted of KE, IP, PR, SP. Notably, the occurrence of a preparatory activity within a particular theme or subtheme was determined by its unique role as identified by participants, resulting in some activities being associated with multiple themes. For instance, the activity 'Journaling' falls under both PR subtheme 2.2 ('Present-moment awareness'), and IP subtheme 3.2 ('Intentions'). The thematic structure and the corresponding activities for each subtheme is illustrated in **Fig. 3.1**.

Meditation and yoga practices were commonly reported across various subthemes. Previous research has classified these practices according to their primary objectives and methodologies, giving rise to various proposed typologies [433–437]. While acknowledging their limitations, we adopted gross categorisation systems for both meditation and yoga practices. For meditation, we used the categories of **focused-attention (FA), open-monitoring (OM), compassion and loving-kindness (CLKM)**, and **self-transcendence (ST)** [438]. For yoga, we employed **power yoga (PY)** and **meditative-stretch yoga (MSY)** taxonomy [439, 440].

[34] BSc student Maisha Khan (UCL)
[35] BSc student Larisa Morometescu (UCL)

Workshop-based thematic analysis (Study 3.II)

The primary data sources from all three workshops was participant feedback, collected as written field notes and the products of written tasks performed by participants throughout the workshops [374, 441]. Field notes and participant written material were reviewed and subjected to a rapid thematic analysis by lead author and LM[36] [345, 346]. This commenced with initial coding, whereby distinct labels representing core ideas were assigned to sections of the notes. These codes were then grouped into broader themes. Qualitative responses were converted systematically into numeric codes and a process of ST-TA [432] was employed, as in **Study 3.I.**

[36] BSc student Larisa Morometescu (UCL)

3.4 Results

3.4.1 Initial intervention development

Demographic

The sample consisted of 19 participants who completed qualitative interviews, with a mean age of 42.37 years (SD = 12.37). Participants had attended their psilocybin retreat an average of 3.16 months prior (SD = 2.09) and reported engaging in preparation for an average of 17.68 days (SD = 11.29), spending approximately 37.63 minutes per day (SD = 18.06) on preparation. Most participants were female (63.2%) and White (73.7%), with most holding an undergraduate (42.1%) or postgraduate (52.6%) degree. Nearly two-thirds (63.2%) had no prior psychedelic experience before the retreat. Most attended retreats in Mexico (63.2%), while the remainder attended in the Netherlands (36.8%). Further demographic details are provided in **Appendix A3.8**.

Thematic analysis

The thematic analysis revealed four primary themes in participants' preparatory activities, aligned with the four-factor model of psychedelic preparedness established in **Chapter 2**. Through inductive analysis, each primary theme yielded distinct sub-themes that captured specific preparatory behaviours and practices. A comprehensive visualisation of this thematic framework, including the specific activities associated with each subtheme, is presented in **Fig. 3.1**. The complete thematic analysis, including supporting participant quotations and detailed analytical documentation, is provided in **Appendix A3.7**.

The most effective preparation strategies reported by participants were meditation (including various mindfulness techniques), reading psychedelic literature, and journaling. Other approaches included expert consultations, intention-setting, breathwork, and embodiment practices (**Figure 3.2a**). Primary hurdles in preparation were information overload and time constraints, followed by challenges with intention-setting and motivation (**Figure 3.2b**). Looking toward future psychedelic experiences, participants predominantly planned to increase their focus on meditation and intention-setting practices, with additional emphasis on journaling, breathwork, and lifestyle adjustments (**Figure 3.2c**). Participants identified several areas where they desired more guidance, particularly regarding coping strategies and understanding the range of potential experiences. Additional guidance needs included intention-setting methods, integration resources, and technical information about substances (**Figure 3.2d**).

Most participants (79%) recommended implementing a structured psychedelic preparation program (**Figure 3.3a**). The most endorsed components for inclusion were educational resources, meditation guidance, intention-setting support, and journaling prompts. Additional recommended features ranged from community sharing to movement practices (**Figure 3.3b**). Key elements to avoid included unrealistic expectations, inflexible approaches, and information overload (**Figure 3.3c**). Regarding delivery preferences, most participants favoured an online format, with some suggesting a hybrid approach that includes offline options (**Figure 3.3d**). Participants recommended a program duration of approximately three weeks, with daily sessions averaging 36 minutes (**Figure 3.3e**)

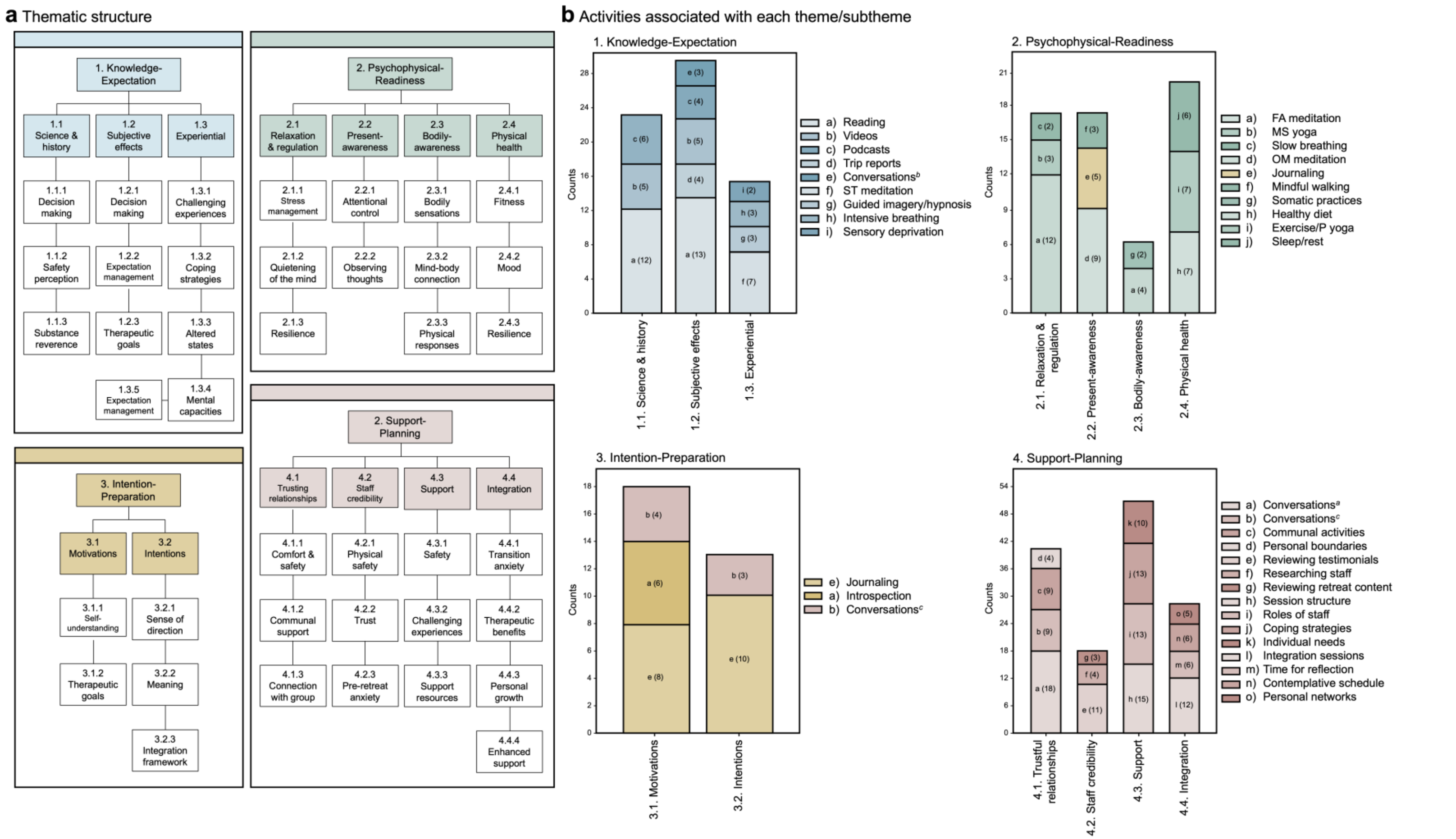


Figure 3.1. Thematic structure of psychedelic preparation

Thematic analysis of participants' preparatory activities, categorized into four primary themes: (1) Knowledge-Expectation, (2) Psychophysical-Readiness, (3) Intention-Preparation, and (4) Support-Planning. (a) A hierarchical framework illustrates the subthemes within each category, capturing specific preparatory behaviours and practices. (b) Bar charts display the distribution of activities associated with each subtheme, highlighting the methods participants engaged in, such as reading, meditation, journaling, conversations, and physical practices. Further details, including supporting participant quotations, are available in Appendix A3.7.

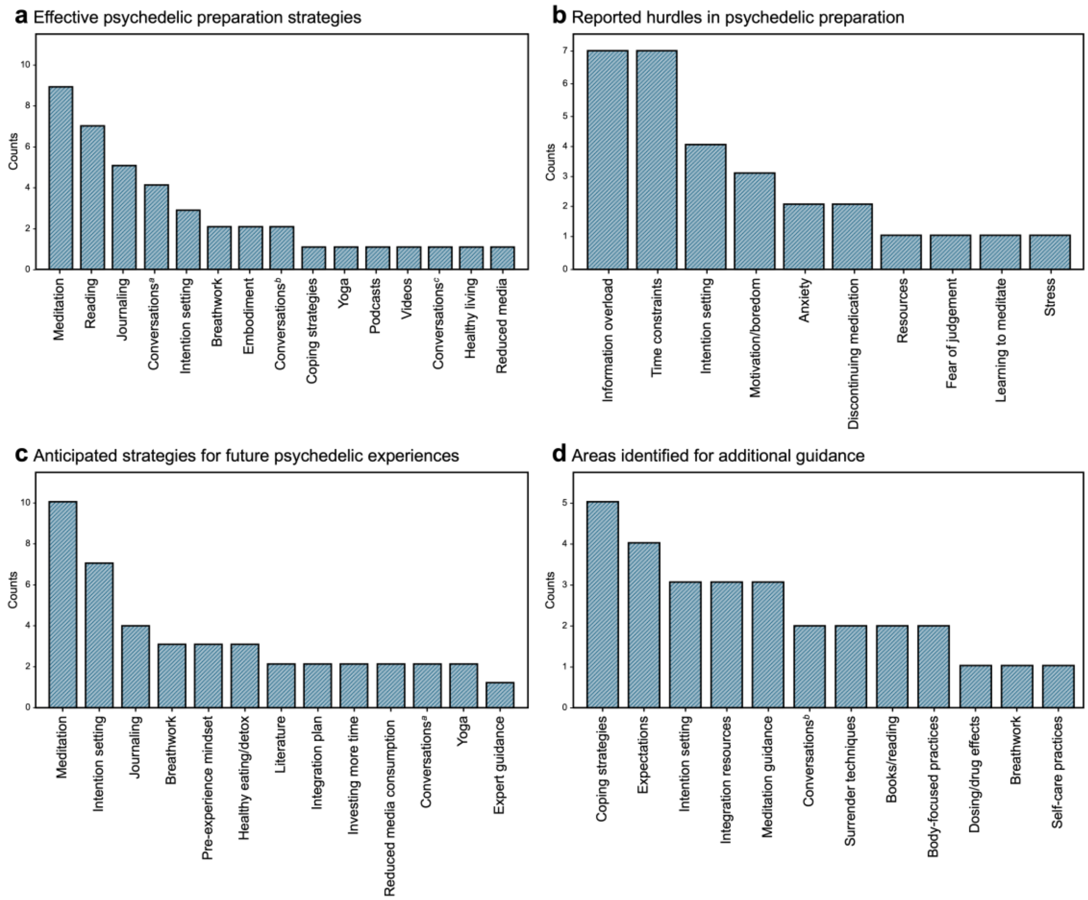


Figure 3.2. Participant-reported strategies, challenges, and guidance needs for psychedelic preparation

Frequency of participant responses in four key domains related to psychedelic preparation: (a) Effective strategies, (b) Reported hurdles, (c) Anticipated strategies for future experiences, (d) Areas identified for additional guidance. Note. 'Conversations' are categorised as: (a) with experts, (b) with experienced others, and (c) with family/friends.

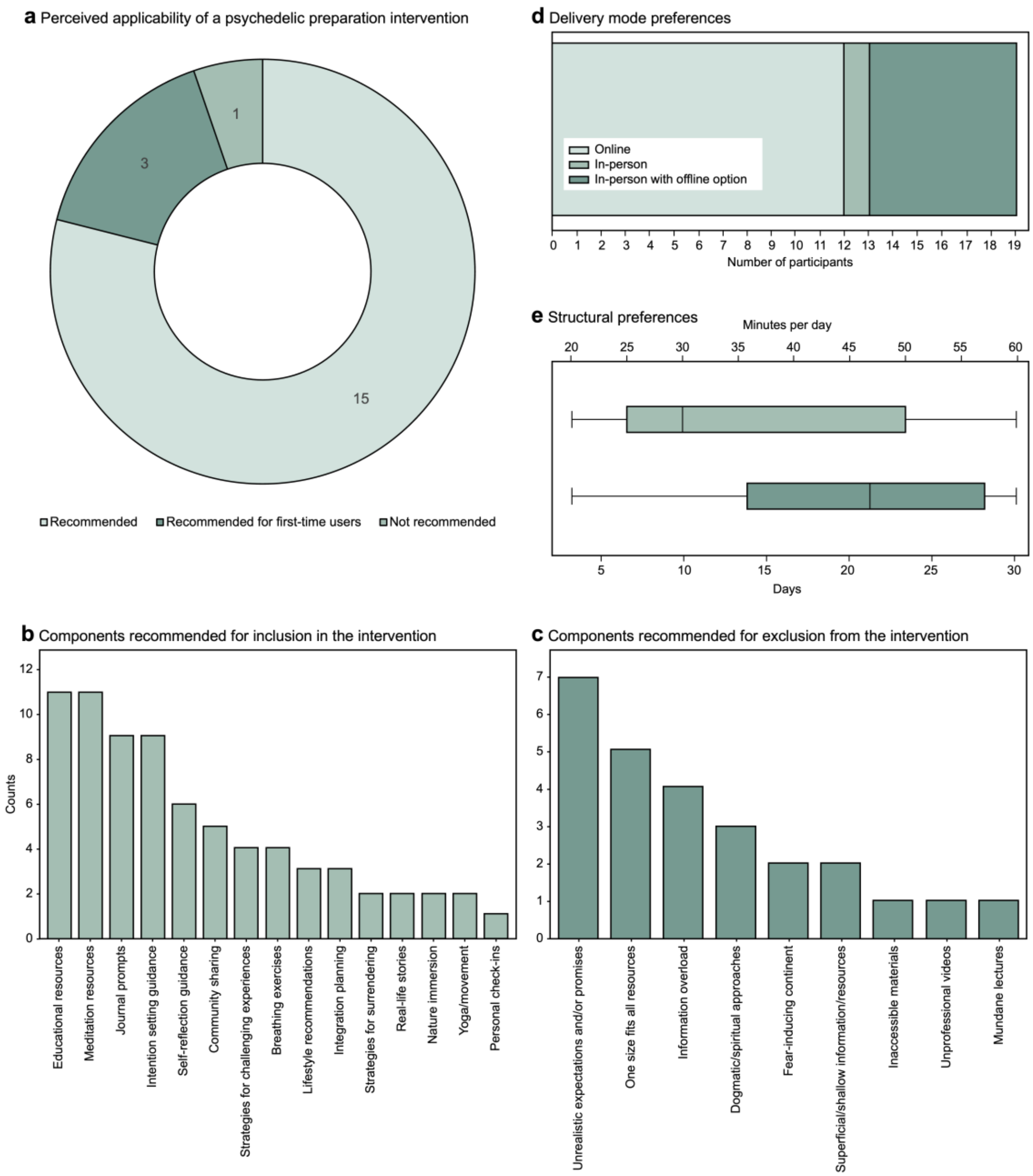


Figure 3.3. Participant preferences for a psychedelic preparation intervention

Summary of participant preferences regarding the design and structure of a psychedelic preparation intervention: a) Pie chart showing perceived applicability of a psychedelic preparation intervention (the numbers in the rings refer to the number of participants endorsing each of the three responses); b) Bar chart displaying components recommended for inclusion in the intervention (note: participants could endorse >1 component); c) Bar chart displaying components recommended for exclusion from the intervention; d) Stacked horizontal bar chart displaying delivery mode preferences among participants; e) Box plots displaying structural preferences, in terms of course duration in days (bottom axis) and time commitment in minutes per day (top axis).

3.4.2 Intervention component refinement

Demographic

The sample consisted of 28 participants who took part in the co-design workshops, with mean ages ranging from 46.11 years (SD = 8.33) in Workshop 1 to 51.88 years (SD = 14.32) in Workshop 3. Most participants were female in Workshops 1 (70.0%) and 2 (77.8%), while Workshop 3 had a more even gender distribution (55.6% male). Most participants were White (66.7-80.0%) and held an undergraduate (44.4-66.7%) or postgraduate (30.0-55.6%) degree. A large proportion of participants identified as not religious (66.7-70.0%). Prior psychedelic experience varied, with 33.3–60.0% having never used psychedelics before, and 20.0–22.2% reporting limited experience (1-5 occasions). Further demographic details are provided in **Appendix A3.8**.

Workshop 1: Development of a prioritised list of components

Workshop 1 provided valuable insights into the essential components of the program through both individual and group-based activities. During the initial ideation phase, participants independently generated 31 unique components. Many of these components demonstrated substantial overlap with the primary elements identified in **Study 3.I**, though participants often used different terminology. For example, what participants in this workshop termed "Connecting with retreat leaders" closely paralleled the "Personal check-ins" component from **Study 3.I** (see **Appendix A3.3** for a complete mapping of these relationships).

Through subsequent group discussions, participants consolidated these initial ideas into 21 consensus components. These components were then subjected to a prioritisation exercise using dot voting, wherein participants indicated their preferred elements on a standardised voting form. This process revealed seven highest-priority (P1) components: Reading assignments (0.9), Meditation (0.8), Journaling (0.7), Abstinence from alcohol/drugs (0.7), Carving out time post-retreat (0.7), Dietary guidance (0.7), and Grounding techniques (0.6). **Table 3.3** presents the complete list of components along with their corresponding prioritisation scores.

Workshop 2: Refinement prioritised components

Prior to Workshop 2, we consolidated several related components from Workshop 1 to streamline the evaluation process. This consolidation merged three community-focused activities ("Group discussions", "Group sharing", and "Connecting with retreat guests") into a single component called "Community building & shared experiences". Similarly, "Carving out time" and "Creating an integration plan" were combined into “Planning integration”, while “Panel discussions” and “Lecture series” were unified under “Expert-led educational sessions”. These consolidated components were then presented visually for participant evaluation.

The subsequent two-step dot voting procedure assessed both priority and feasibility of 17 distinct components. This evaluation revealed seven components with the highest feasibility (F2) scores: Reading assignments (0.89), Grounding techniques (0.89), Abstinence from alcohol/drugs (0.89), Journaling (0.67), Planning integration (0.56), Meditation (0.44), and Resource list (0.44). **Table 3.3** provides comprehensive details of both priority (P2) and feasibility (F2) scores for all components.

Workshop 3: Evaluation of potential BBROs

Following the prioritisation exercise, participants worked in subgroups to conduct an in-depth analysis of the highest-ranked components (as determined by F2 scores from Workshop 2). Each subgroup performed a structured evaluation examining four key BBRO dimensions: potential benefits, implementation barriers, associated risks, and ideal outcomes. These analyses were then synthesised through a facilitated group discussion, during which participants collaboratively developed strategies to mitigate identified risks and overcome potential barriers. **Table 3.4** summarises the key findings from this analytical process.

Table 3.3. Prioritisation and ranking of intervention components conducted in Workshop 1 and 2

#	Component (theme)	Workshop 1 (n=10)	Workshop 2 (n=9)	
		P1	P2	F2
1	Reading assignments (KE)	0.90	0.89	0.89
2	Grounding techniques (PR)	0.60	0.89	0.89
3	Abstinence from alcohol/drugs (PR)	0.70	0.89	0.89
4	Journaling (IP)	0.70	0.67	0.67
5 6	Carving out time after the retreat (SP) Creating an integration plan (SP)	0.70 0.50	0.56[a]	0.56
7	Meditation (PR)	0.80	0.67	0.44
8	Resource list (SP)	0.30	0.44	0.44
9	Dietary guidance (PR)	0.70	0.22	0.22
10	Yoga (PR)	0.50	0.22	0.22
11	Connecting with retreat leaders (SP)	0.30	0.67	0.22
12 13	Panel discussions (KE) Lecture series (KE)	0.20 0.10	0.22[b]	0.22
14	Physical exercise routines (PR)	0.50	0.11	0.11
15	Nature walks (PR)	0.60	0.22	0.11
16	Quizzes (KE)	0.10	0.11	0.11
17	Holotropic breathwork (KE)	0.50	0.33	0.00
18	Hands-on workshop (KE)	0.30	0.11	0.00
19 20 21	Connecting with retreat guests (SP) Group sharing (IP) Group discussions (KE)	0.40 0.30 0.30	0.22[c]	0.00

Note. In Workshop 1, a 'priority score' (P1) was calculated by dividing the total number of priority votes for each component by the number of voters; a score of 1.0 signifies unanimous priority consensus. In Workshop 2, a similar 'priority score' (P2) was determined, along with a 'feasibility score' (F2), which was derived by dividing the feasibility votes by the total number of participants; a score of 1.0 denotes unanimous criticality and feasibility consensus. KE: Knowledge-Expectation, PR: Psychophysical-Readiness, IP: Intention-Preparation, SP: Support-Planning [a] 'Carving out time after the retreat' and 'Creating an integration plan' were combined into 'Planning integration'. [b] 'Panel discussions' and 'Lecture series' were combined into 'Expert-led educational sessions'. [c] 'Connecting with retreat guests', 'Group sharing', and 'Group discussions' were combined into 'Community building & shared experiences'.

Table 3.4. Thematic breakdown of the top components from Workshop 3 (n=9)

	Small group discussions			Group brainstorm	
Component (theme)	**Benefits**	**Barriers**	**Risks**	**Ideal outcomes**	**Solutions**
Reading assignments (KE)	Increased understanding of psychedelic experiences. Encourages independent research. Provides foundational knowledge for discussions.	Potential information overload. Difficult for non-regular readers. Quality and credibility of sources.	Misinterpretation of text. Over-reliance on a single source. Becoming overly critical.	Foundational understanding. Prepared for informed discussions.	Curate concise and vetted reading lists with diverse sources. Provide FAQs for each reading to prevent misinterpretations.
Grounding techniques (PR)	Offers stabilisation during and after intense experiences. Provides tools for emotional and mental regulation.	Lack of familiarity with techniques. Scepticism about efficacy. Difficulty in accessing resources.	Ineffectiveness for some individuals. Ignoring other necessary interventions.	Efficient self-regulation. Enhanced mindfulness. Equipping participants with tools for during the psychedelic experience and post-retreat life.	Introducing various techniques. Provide resources or references for continued practice.
Abstinence from alcohol/drugs (PR)	Pure experience without influences. Resets body chemistry. Clarity and focus. Eliminates counteractive effects.	Potential withdrawal symptoms. Social pressures. Breaking habits.	Abrupt cessation complication. Mood disturbances. Non-compliance. Overcompensation post-retreat.	Substance-free entry. No drug interactions. Clear-headed participation. Healthier lifestyle approach.	Educate on the benefits of temporary abstinence. Provide a support community for those struggling.
Journaling (IP)	Personal reflection. Intention setting, experience and emotion tracking. Encourages self-awareness. Post-retreat review tool.	Maintaining consistency is difficult. Time commitment. Over-analysing experiences.	Overthinking negatives. Misinterpreting writings. Overly self-critical behaviour.	Personal journey record. Regular introspection. Tool for post-retreat reflection. Enhance personal accountability.	Provide structured templates or prompts. Regularly remind participants about the purpose and benefits.

Table 3.4 (continued)

Component (theme)	Benefits	Barriers	Risks	Ideal outcomes	Solutions
Planning integration (SP)	Provides dedicated time for processing experiences. Ensures intentional reflection and assimilation of retreat learnings. Reduces the risk of post-retreat overwhelm. Enhances long-term benefits and application of retreat insights.	Managing daily commitments with integration time. Potential lack of discipline in following through with plans. Distractions from daily life and routines. Potential for feeling isolated in the process.	Inadequate time leading to suppressed or unresolved emotions. Misguided or misunderstood integration techniques. Potential for neglecting daily responsibilities. Over-isolation or excessive introspection.	Well-structured post-retreat period maximising benefits. Seamless transition from retreat to daily life, retaining retreat insights. Enhanced personal growth and understanding from the retreat. Continuous integration of retreat learning into daily life.	Provide structured post-retreat guidance. Organise follow-up group sessions for continued support. Offer resources for effective daily-life integration.
Meditation (PR)	Emotional regulation. Mindfulness. Reduces pre-retreat anxiety.	Lack of experience. Achieving focus difficulty. Time commitment. Environmental distractions.	Unresolved traumas surfacing. Misunderstanding purpose. Becoming overly introspective.	Calm mindset. Familiarity with thoughts. Handle disturbances.	Offer beginner-friendly guided sessions. Start with short sessions and progressively increase. Offer support for surfacing traumas and misunderstood objectives.
Resource list (SP)	Provides attendees with credible, trustworthy preparation material. Makes research easier. Standardised information disseminated to attendees.	Overwhelming volume of resources. Inconsistency in quality or relevance of resources. Potentially biassed or one-sided material.	Misinterpretation or misinformation. Over-reliance on a singular source. Information overload.	Informed and well-prepared attendees. Cultivation of a culture of continuous learning. Encouragement of diverse perspectives.	Periodically update and vet resources. Provide summaries or overviews for each resource. Encourage participants to seek multiple perspectives.

Note. KE: Knowledge-Expectation, PR: Psychophysical-Readiness, IP: Intention-Preparation, SP: Support-Planning

3.5 Discussion

This chapter outlines the co-production process used to develop the core components of DIPP. **Study 3.I** began by identifying specific preparatory behaviours and strategies aligned with the four superordinate themes presented in **Chapter 2**: KE, IP, PR, SP. Participants reported using a range of strategies, with meditation, journaling, and reading cited most frequently. Key challenges included information overload, time constraints, and difficulties with intention-setting. Looking ahead to future sessions, participants expressed a clear desire for more structured guidance - particularly around coping strategies and managing expectations. When asked about the ideal format for a preparatory programme, participants overwhelmingly favoured a structured, digital approach incorporating psychoeducational content, regular meditation practices, and intention-setting support. A three-week duration was considered optimal by most. In **Study 3.II**, a series of co-design workshops were conducted to iteratively refine the intervention's content. In Workshop 1, participants generated an initial list of components, which were then prioritised in Workshop 2 based on feasibility. Key elements included: 'Reading assignments' (KE), 'Grounding techniques' (PR), 'Abstinence from alcohol and drugs' (PR), 'Journaling' (IP), 'Planning for integration' (SP), 'Meditation' (PR), and the inclusion of a 'Resource list' (SP). In Workshop 3, subgroups assessed each component's benefits, barriers, risks, and outcomes (BBRO). Together, the findings from both studies informed the development of a full prototype intervention. A description of the intervention is presented below in accordance with the first six items of the TIDieR checklist [320] (see **Appendix A3.5**), with the remaining items to be addressed following pilot evaluation.

DIPP is a 21-day, self-guided digital programme designed to cultivate psychological readiness for high-dose psychedelic experiences. It was developed in accordance with the UK MRC framework for complex interventions and is grounded in the four-factor model of psychedelic preparedness established in **Chapter 2**. The programme comprises four thematic modules: three delivered sequentially (KE, PR, SP), and one running throughout (IP). DIPP also provides daily meditation training, including 21 individually designed meditation scripts developed in collaboration with meditation experts DK[37] and AL[38]. These scripts were carefully recorded, edited, and produced by the lead author to ensure quality and consistency (see **Fig. 3.4a**). The inclusion of meditation reflects strong and consistent support across both studies for its role in enhancing psychedelic preparation. This aligns with prior research suggesting that meditation may mitigate difficult psychedelic experiences and promote adaptive capacities such as acceptance, presence, and self-compassion [289–291, 442] (see **Chapter 4** for elaboration). Each module includes structured, self-paced

[37] Doug Kraft (Harvard Meditation Programme)
[38] Andrew Litchy (Harvard Meditation Programme)

activities supported by an online resource library (SP) and is introduced through a digital handbook, designed by AC[39] **(Fig. 3.5**, see **Appendix A3.9** for the full handbook). Participants are encouraged to abstain from alcohol and recreational drug use for the duration of the programme and to maintain regular routines around sleep, diet, and physical activity (PR). A short daily mood check-in is integrated to support psychological monitoring across the three-week period. See **Fig. 3.4b** for interface screenshots of the DIPP web app. Full module content and delivery structure are detailed in **Appendix A3.6**.

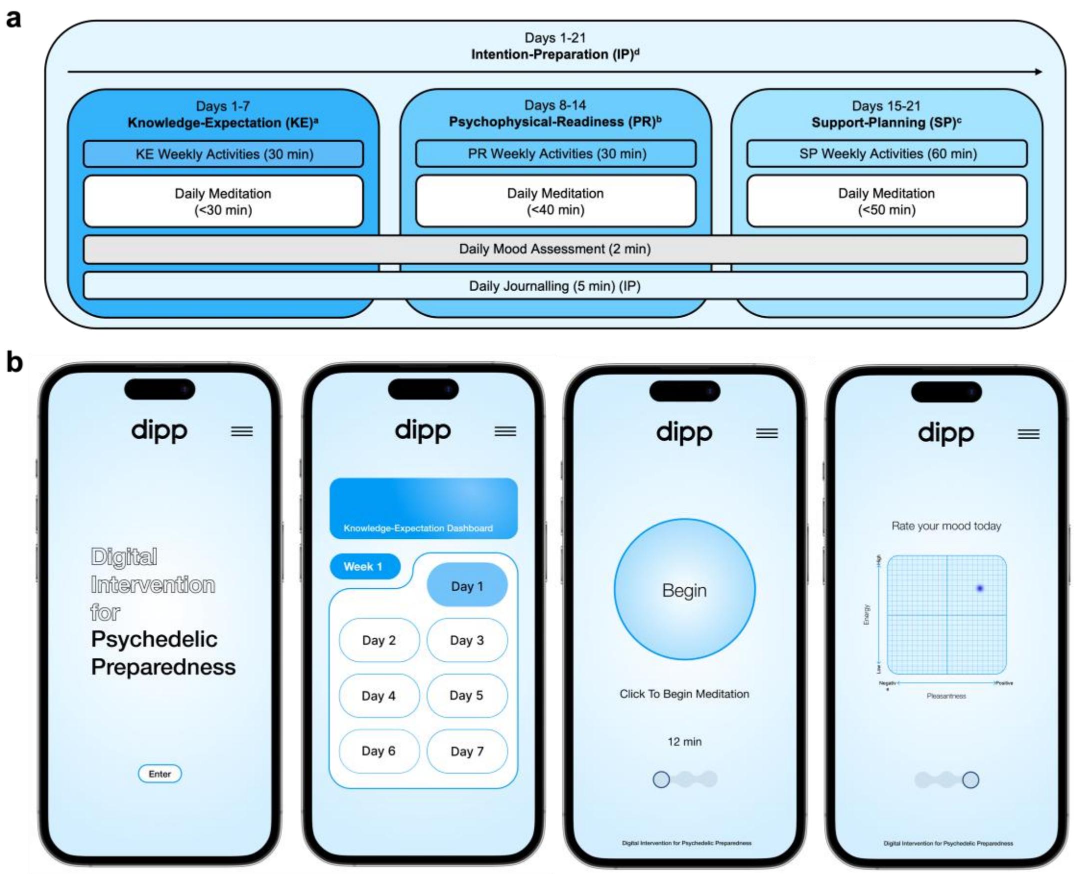


Figure 3.4. Structure and mobile interface of the DIPP

(a) Overview of the 21-day program structure, organised around the four-factor model of psychedelic preparedness: Knowledge-Expectation, Psychophysical Readiness, Intention-Preparation, and Support-Planning. Daily activities include guided meditation, mood tracking, and journaling, while weekly activities progressively introduce content relevant to each preparation factor. (b) Screen images from the DIPP mobile application, showing from left to right the home screen, KE dashboard, meditation interface, and mood tracking tool.

[39] Ariel Castro (UCL)

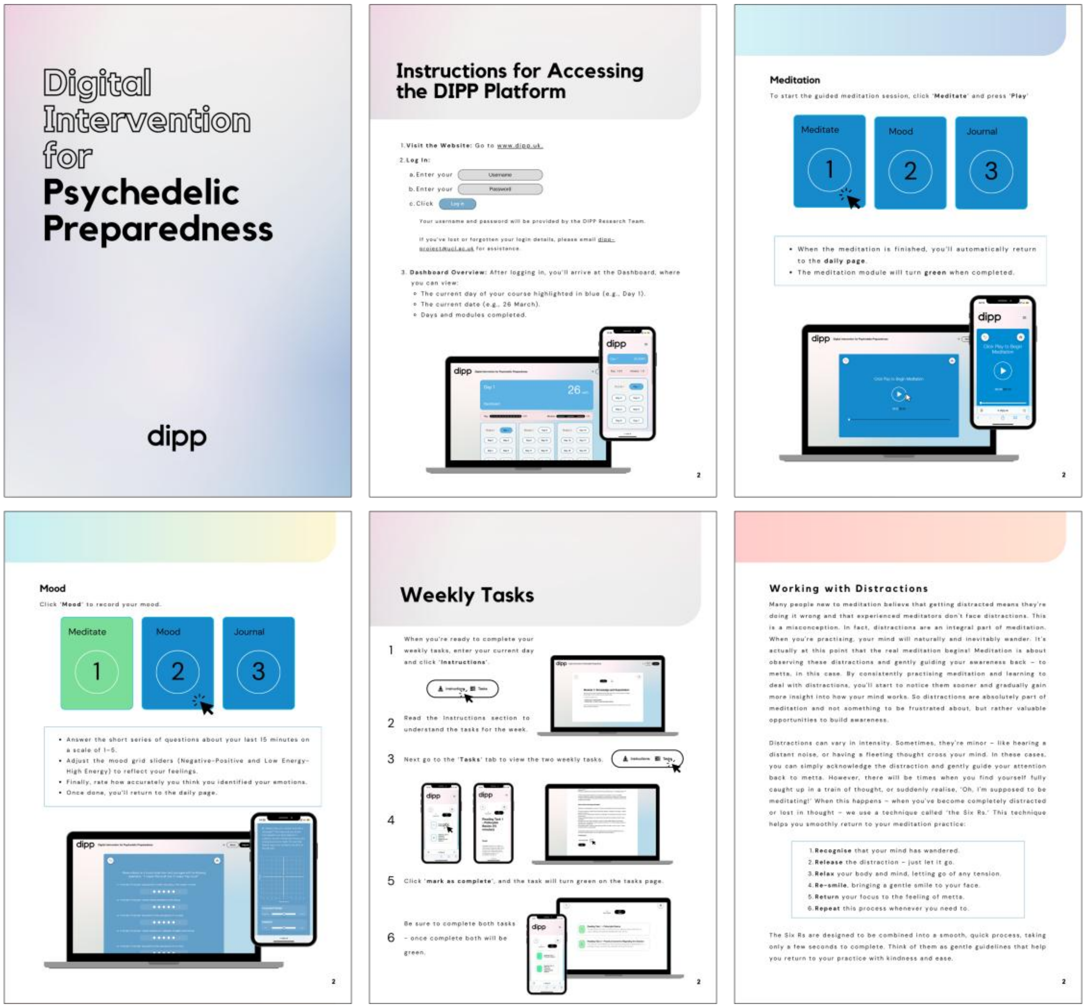


Figure 3.5 Sample pages from the DIPP handbook

These sample pages from the DIPP handbook illustrate how participants are guided through the digital platform, including instructions for completing daily and weekly tasks and orienting to weekly meditation practices. The handbook supports self-paced engagement with the programme and introduces each module's core components. See Appendix A3.9 for the full handbook.

In line with UK MRC guidance on complex intervention development, the design of DIPP was informed by continuous stakeholder engagement across both studies. This participatory approach enriched the contextual relevance of the intervention by integrating the lived experiences, priorities, and practical insights of future users. Stakeholders were not only consulted but actively involved throughout the development process, ensuring that the intervention's structure, content, and delivery aligned with genuine user needs rather than theoretical assumptions alone [405, 443, 444]. This collaborative model exemplifies best practice in co-production, bridging the gap between conceptual frameworks and real-world utility. The iterative nature of the process - marked by feedback loops, component refinement, and feasibility testing - reflects the dynamic and responsive approach advocated by the MRC [411]. While the current work privileges experiential expertise to shape the intervention's foundation, the next critical step lies in evaluating whether these components lead to measurable improvements in psychological outcomes relative to credible control conditions. As we move into pilot testing (**Chapter 5**), sustained stakeholder involvement will continue to play a key role in refining, implementing, and ultimately validating the intervention.

The DIPP intervention was designed with versatility in mind. The framework is intended to support preparation across a range of user groups, including individuals engaging in clinical treatment, retreat-based use, and even some forms of non-clinical or personal psychedelic exploration. It is also structured to be broadly compatible with a variety of psychedelic substances. However, effective implementation requires thoughtful adaptation. While the overall delivery format and the core components (e.g., meditation practice, intention-setting, and integration planning) can remain largely consistent, certain elements must be tailored to the specific psychedelic and context in question. In particular, the KE module must be precisely aligned with the pharmacology, psychological effects, and safety considerations of the relevant compound. For example, preparatory information for a psilocybin session would differ in both tone and content from that designed for 5-MeO-DMT. By maintaining consistent structure across modules while allowing for customisation of content, DIPP offers a flexible yet grounded framework that can be adapted to the diverse needs of psychedelic users and facilitators.

Limitations and future directions

While stakeholder engagement strengthened the intervention's practical and contextual relevance, the sampling strategy introduces important limitations. Participants in both **Study 3.I** and **Study 3.II** were predominantly White (**Study 3.I**: 73.7%; **Study 3.II**: mean 67.42%), highly educated, and, in many cases, had limited or no previous experience with psychedelics - reflecting broader trends in PAT research, where minoritised ethnic groups and lower-income populations remain markedly underrepresented [161, 445]. In **Study 3.I**, participants were selected based on reporting a 'significant change' following their retreat experience - a criterion intended to explore the perceived relevance of preparation strategies among those who felt they had benefited. However, this introduces a risk of confirmation bias [446], whereby individuals with positive or transformative experiences may retrospectively overstate the efficacy of preparatory elements, while those with less impactful, neutral, or negative experiences were systematically excluded. Additionally, participants in **Study 3.II** were recruited from a high-end psilocybin retreat, representing a relatively privileged, self-selecting group with the financial means and motivation to pursue non-clinical psychedelic experiences. Together, this demographic and experiential homogeneity narrows the scope of perspectives feeding into intervention development, potentially limiting the cultural sensitivity, accessibility, and generalisability of the resulting programme. To build more equitable and inclusive preparation protocols, future research must prioritise stakeholder diversity - not only in terms of demographics but also in lived experience with psychedelics - ensuring that interventions are responsive to the needs, expectations, and outcomes of the broader psychedelic community.

Despite the limitations in sampling diversity, the participatory structure of the co-design workshops (**Study 3.II**) contributed valuable experiential insights and user-informed refinement of the intervention. These workshops fostered collaborative engagement and helped translate preliminary findings from **Study 3.I** into a structured, context-sensitive programme. By drawing on the shared retreat experiences of participants, the workshops promoted a sense of mutual understanding and psychological safety, enabling rich, experience-based discussions. However, group-based formats are not without challenges [447, 448]. As noted in participatory design literature, workshop settings can sometimes be influenced by group dynamics, with more outspoken individuals unintentionally shaping the direction of discussion or discouraging dissenting views [449, 450]. Furthermore, collective brainstorming can promote convergent thinking, where consensus is prioritised over conceptual diversity [451–453]. To minimise these risks, workshops were structured to include a balance of individual reflection, small-group interaction, and full-group dialogue. Participants were encouraged to contribute freely, and the value of diverse perspectives was explicitly stated at the outset of each session. The familiarity among participants, who had attended the same retreats, appeared to facilitate respectful dialogue without clear dominance. These measures helped ensure that the co-design process remained inclusive, iterative, and grounded in a wide range of participant insights, contributing meaningfully to the development of a user-centred, theoretically grounded intervention.

While these workshops meaningfully shaped the development of a user-centred, theoretically grounded intervention, it is vital to acknowledge the uncertainties that remain. Key aspects of the intervention (e.g., its intensity, optimal delivery modes, material specificity, and procedural details) require further calibration (see **Chapter 7**, **Section 7.2.2** for further discussion). Additionally, the most appropriate setting for implementation, whether clinical, retreat-based, or independent, remains to be determined. These questions not only provide important directions for future research but also have immediate implications for practitioners seeking to integrate the intervention into real-world contexts. Awareness of these variables is essential for tailoring the programme to individual needs. Transparently recognising these uncertainties not only positions the intervention as a work in progress but also helps ensure that its ongoing evolution is guided by both empirical findings and practical insights.

Conclusion

This chapter introduced DIPP: a novel 21-day digital intervention designed to enhance psychedelic preparedness. Developed through a person-centred co-design process and grounded in the four-factor model of psychedelic preparedness (**Chapter 2**), DIPP weaves together thematic modules that address emotional, cognitive, and contextual dimensions of preparation. Core components - including daily meditation, intention-setting, and integration planning - reflect both participant feedback and insights from existing literature, with meditation emerging as a particularly promising tool for optimising psychedelic outcomes. While the intervention shows promise, its evaluation is shaped by the specific context of psilocybin retreats and a relatively homogenous sample. A key priority for future work will be to refine *what* meditation practices are most beneficial to train, moving beyond generic instruction to a more targeted, evidence-informed approach to cultivating specific competencies that support psychedelic preparation.

CHAPTER 4

Practitioner perspectives on meditation-based preparation for psychedelic experiences

> *"A human being is a part of the whole, called by us "Universe". [...] He experiences himself, his thoughts and feelings as something separated from the rest - a kind of optical delusion of his consciousness. […] Our task must be to free ourselves from this prison by widening our circle of compassion to embrace all living creatures and the whole of nature in its beauty. Nobody is able to achieve this completely, but the striving for such achievement is in itself a part of the liberation."*
>
> — *Einstein, A (1950). Letter to Dr. Robert S. Marcus.*

4.1 Abstract

Although meditation is a core component of DIPP and valued for enhancing psychedelic preparedness, its specific role and efficacy remain underexplored. To investigate this, we surveyed 123 experienced practitioners with substantial backgrounds in both meditation and psychedelic use. Respondents expected meditation to enhance acceptance and present-moment focus during psychedelic experiences while increasing oceanic boundlessness and reducing anxious ego-dissolution. Among practitioners with limited meditation (1-3 years) and psychedelic (1-20 sessions) experience, adherence to specific meditation traditions correlated with higher **PBMPP (Perceived Benefits of Meditation for Psychedelic Preparation)** scores. However, this trend reversed among highly experienced meditators (10+ years) with limited psychedelic experience, where non-adherents reported higher PBMPP scores. **Loving-kindness meditation (LKM)** was rated the most effective preparatory practice, surpassing approaches like **focused attention (FA).** Exploratory factor analysis identified three meditative components, with **Positive Emotional States (PES)** receiving the strongest endorsement for psychedelic preparation. These findings provide empirical groundwork for evidence-based meditation protocols in psychedelic preparation, and highlight the importance of considering psychedelic users' level of previous meditation experience in optimising such interventions

4.2 Introduction

Chapter 3 described the development of DIPP, a structured 21-day program designed to enhance and standardise self-directed preparation. Among the various strategies identified, participants consistently highlighted meditation as one of the most effective tools for preparing for a psychedelic experience. As a result, meditation was integrated as a central component of the intervention. Building on this foundation, the current chapter takes a closer look at meditation's role in psychedelic preparation. It explores practitioner perspectives on meditation-based approaches and investigates how factors such as meditation experience, adherence to a tradition, and specific techniques relate to perceived benefits for psychedelic use.

While meditation encompasses diverse contemplative practices, we focus here specifically on its 'mind-training' aspects, that is, systematic techniques for cultivating the focus and stability of attention and awareness. Meditation traditions provide an instructive model for cultural adaptation, demonstrating through the "cycle of meaning" [454] how practices can maintain their transformative essence while evolving across diverse cultural contexts [455–458] - a capacity particularly relevant for integrating traditional practices into contemporary therapeutic paradigms[40]. However, when meditation practices are divorced from their cultural and interpretive foundations (e.g., through commodification or de-contextualisation) they risk being reduced to superficial techniques focused solely on relaxation or, in perhaps the ultimate form of secular appropriation, recast as tools for workplace productivity, thereby diminishing their profound potential for personal transformation [459, 460]. This historical tension mirrors the challenges faced by contemporary PAT, where traditional practices must be integrated into modern paradigms without losing their depth or cultural significance [153]. Meditation's enduring capacity to navigate these challenges underscores its relevance as a model for designing preparation frameworks that respect and adapt ancient wisdom to meet the ethical, cultural, and practical needs of Western therapeutic settings.

The scientific exploration of meditation's therapeutic potential has followed a trajectory somewhat similar to that of psychedelic research, with both fields experiencing substantial growth in recent decades [461,

[40] The concept of the "cycle of meaning" as described by Laughlin (2018) highlights how meditation practices within traditional cultures are embedded in a feedback loop between individual experience and collective worldview. As Laughlin explains, *"most people accept and participate in accordance with the worldview they inherit from their culture's pool of knowledge. This participation results in real-life experiences that are in turn interpreted in terms of the cosmology, thus completing a semi-negative feedback loop which instantiates the cosmology in individual experiences and which also self-validates the truth of the people's system of knowledge"* [459]. This dynamic ensures that meditation practices retain their transformative essence while evolving to accommodate new experiences and interpretations.

462]. These parallel paths now converge meaningfully in what has been termed the "third wave" of meditation research [463], where investigation of advanced meditation, that is, skills, states, stages, and transformations that are the result of mastery and ongoing meditation practice [464–468], has revealed striking similarities with psychedelic experiences. Both approaches consistently give rise to phenomena such as self-transcendence and non-dual awareness [467–474], characterised by the dissolution of self-boundaries, profound experiences of unity, and transformative shifts in perception and emotional processing [94, 300, 301, 475, 476]. The parallels extend beyond phenomenological descriptions into shared neurobiological mechanisms, including modulation of the **default mode network (DMN)** [477–481][41], increased neural complexity [438, 482–485], and systematic changes in brain regions associated with self-referential processing, emotional regulation, and sensory integration [486, 487]. These convergent findings have catalysed growing interest in potential synergies between meditation and psychedelics [94, 289–291, 442, 488]. However, while some research has examined meditation's role during psychedelic sessions or in post-session integration [489–495], the systematic investigation of meditation as a preparatory tool for psychedelic experiences remains largely unexplored, representing a promising frontier for research.

Meditation may optimise the pre-psychedelic state through its influence on psychological states and traits linked to therapeutic outcomes. Empirical evidence demonstrates that pre-session psychological states - including anxiety levels, mood, and mindfulness - predict the quality and outcomes of psychedelic experiences [120, 122, 496]. Meditation reliably modulates these key variables [497–500], fostering psychological conditions associated with enhanced safety and therapeutic benefit in psychedelic sessions. Crucially, meditation can also lead to lasting changes in psychological traits - including absorption capacity (the ability to become fully immersed in experiences) [501–503], openness to experience (willingness to engage with novel ideas and experiences) [504–508], and acceptance (non-judgmental awareness of present-moment experiences) [509–513] - which have been shown to significantly predict mystical experiences during psychedelic sessions, with trait absorption being particularly influential [117, 120, 514]. Importantly, the relationship between states and traits appears cyclical: regular meditation practice strengthens trait characteristics that, in turn, facilitate deeper meditative states, creating a self-reinforcing cycle of psychological development [515–517]. The cultivation of these psychological capacities through

[41] While the DMN is frequently implicated in psychedelic studies, its role in therapeutic outcomes remains debated. Some researchers caution that the observed changes in DMN activity may not directly account for therapeutic effects, as these findings could reflect "*a by-product or epiphenomenon of psychedelics*" [480] rather than a mediating role. Additionally, the challenge of 'reverse inference' complicates attempts to link DMN modulation directly to therapeutic change. Furthermore, the potential for publication bias has been noted, with early influential studies shaping the trajectory of subsequent research and hypotheses. To advance understanding, researchers recommend well-designed longitudinal studies that distinguish acute from lasting effects, as well as comparative analyses between experienced and naïve psychedelic users [480].

meditation practice suggests its potential role in establishing both immediate readiness and longer-term psychological resilience for psychedelic experiences. However, questions remain about optimal preparation periods and practice intensity needed to develop these beneficial traits, highlighting the need for systematic research into meditation-based preparation protocols.

In addition to enhancing the pre-state, meditation may serve as a valuable tool for psychedelic preparation by reconfiguring the architecture of subjective experience. Through sustained practice, meditators may develop greater skill in distinguishing direct experience from habitual mental patterns [461], gradually learning to recognise and adjust their mind's automatic predictions about reality - a capacity that predictive processing theory describes as the revision of hierarchical predictive models [518–520]. This refinement promotes an immediate, non-conceptual awareness that allows for more adaptive engagement with present-moment experiences [438, 521–525]. Such meditation-induced changes [526], share important neurocomputational parallels with psychedelic states, as evidence suggests that both experiences involve temporary relaxation of rigid mental models and increased neural complexity, implying common mechanisms in the modulation of predictive hierarchies [300, 483, 485]. However, while meditation typically cultivates this flexibility gradually, psychedelics can induce rapid shifts in predictive processing that may prove destabilising, potentially resulting in so-called 'ontological shock' - a fundamental disruption of core beliefs about reality and existence [13, 527]. While such destabilising experiences can also occur in intensive meditation practice, particularly when practitioners advance too quickly through contemplative stages [528–531], the gradual nature of most meditation training helps develop specific cognitive capacities that serve as protective factors: enhanced metacognitive awareness enables stable observation of changing mental states [532–534], while reduced self-referential processing [535–537] and increased tolerance for uncertainty facilitate skilful navigation of altered states of consciousness [538, 539]. This convergence between contemplative practices and neuroscientific understanding of predictive processing suggests meditation may offer valuable protective mechanisms when entering altered states of consciousness.

To translate the potential synergy between meditation and psychedelics into practical benefits, it is essential to identify which aspects of meditation are most valuable for preparation. This requires understanding not only how adherence to specific traditions shapes outcomes, but also distinguishing between various meditation 'practices' that provide structured methods (e.g., loving-kindness, open monitoring), the meditative 'elements' that constitute these practices (e.g., equanimity, non-discriminatory awareness), and the underlying psychophysiological 'processes' (e.g., emotion regulation, body awareness) [433, 438, 540, 541]. Each of these components plays a distinct yet interconnected role: practices provide structured methodological frameworks, meditative elements constitute the fundamental building blocks of these practices, and these processes are thought to represent the underlying mechanisms through which they affect mind and body. The significance of these elements extends beyond experienced practitioners; their accessibility to beginners, such as participants in clinical trials or the general population, is equally crucial. For those new to meditation, the ability to easily understand and engage with these practices is just as important as the theoretical depth of awareness they could cultivate. Therefore, it is imperative that these individuals have the time, resources and motivation required to develop a mindfulness practice that is therapeutically meaningful in this context. By examining how these aspects of 'mind-training' interact and manifest across practitioner experience levels, we can develop more targeted preparatory protocols that enhance psychedelic-assisted therapy outcomes while maximising benefits and minimising risks across diverse populations.

Given the current paucity of empirical research on the utility of meditation as a preparatory tool for psychedelic experiences, a valuable approach is to draw on the first-person insights of individuals with substantial experience with both meditation and psychedelic use [542, 543]. These individuals can provide nuanced perspectives on how meditation might enhance psychedelic preparation, including identifying which aspects of the experience benefit most. Perceptions of meditation's utility may be shaped by meditation experience, prior psychedelic experiences, and whether practitioners adhere to specific contemplative traditions. Such adherence might involve following established traditions (e.g., *Theravāda* Buddhism, Sufism etc.,) which provide philosophical frameworks and approaches that inform how meditation is understood and practiced. Importantly, contemporary meditation practices often diverge from their traditional contexts, where techniques (e.g., *Vipassana*, *Murāqabah* etc.,) are typically integrated into broader systems of philosophical inquiry, ritual, and mind transformation. In contrast, Western adaptations may isolate these practices from their cultural frameworks, potentially altering both their implementation and perceived effectiveness. Clarifying whether adherence to a meditation tradition - regardless of the specific tradition - or the absence of such adherence shapes perspectives on meditation's role in psychedelic preparation is essential for developing evidence-based meditation protocols. However, it is important to acknowledge that individual experiences are highly contextual, shaped by personal, cultural, and situational factors, even within traditional frameworks. In this context, as research evolves, a pluralistic and iterative approach that incorporates both empirical data and dialectical engagement with meditation and psychedelic practitioners will be essential. This challenging process holds the potential to develop robust frameworks that address the variability in user experiences and bridge the gap between controlled research and real-world applications in this rapidly evolving field [337].

Chapter 4 seeks to address current gaps by exploring the perspectives of individuals experienced in both meditation and psychedelic use, with the goal of shaping evidence-based meditation protocols for psychedelic preparation. Through a comprehensive survey we examined: (a) the perceived benefits of meditation training for psychedelic preparation, specifically focusing on how these benefits were influenced by three factors: meditation tradition adherence, lifetime meditation experience, and lifetime psychedelic use; (b) the anticipated impact of meditation on various aspects of the psychedelic experience, assessed using standardised scales; (c) the perceived helpfulness of specific meditation practices, importance of meditative elements, and relevance of psychological processes for psychedelic preparation; and (d) participant recommendations for designing a meditation program tailored to psychedelic sessions. By drawing on the insights of this uniquely qualified group, we aim to provide empirically grounded data to inform future research and contribute to the development of evidence-based preparation protocols.

4.3 Methods

This study was conducted in accordance with the Declaration of Helsinki and approved by the UCL REC (ID: 19437/001). All participants provided informed consent via a secure online platform after reviewing comprehensive study information. Participation was voluntary and uncompensated, and participants were informed of their right to withdraw at any stage of the study without penalty.

4.3.1 Participants and recruitment

Experienced meditators with prior psychedelic experience were recruited through social media platforms (Twitter/X, Reddit, LinkedIn), direct referrals, and word of mouth. Eligibility criteria required participants to have maintained a regular meditation practice, defined as meditating at least three times per week for a minimum of 30 minutes per session, over the past year; self-identified as having experienced a high-dose session with a classic psychedelic substance (e.g., psilocybin, **lysergic acid diethylamide (LSD)**, **N,N-Dimethyltryptamine (DMT**), **5-Methoxy-N,N-Dimethyltryptamine (5-MeO-DMT),** distinguishing such experiences from microdosing based on dosage (e.g., ≥100 µg LSD or ≥2 g psilocybin-containing mushrooms) and noticeable subjective effects, such as perceptual changes or altered states of consciousness; be 18 years of age or older; and demonstrate fluency in spoken and written English.

4.3.2 Procedures

Data collection occurred via an anonymous online survey (Qualtrics) from September 1, 2023, to March 31, 2024. The survey, requiring approximately 25-30 minutes to complete, comprised demographic items, assessments of meditation and psychedelic experience, and a series of randomised measures. These measures included scales assessing perceived benefits of meditation for psychedelic preparation, anticipated effects on mindfulness and altered states of consciousness, and preferences for meditation approaches and techniques. The survey evaluated the perceived impact of meditation on psychedelic experiences and gathered perspectives on developing structured meditation programs for psychedelic preparation.

4.3.3 Measures

Participant characteristics

Demographic information was collected on participants' age, gender, ethnicity, country of residence, education level, and religious affiliation. Participants provided exact details about their meditation experience, including the number of years of practice, weekly frequency of meditation, and the average duration of each session. For analysis purposes, the number of years of meditation practice was categorised into three levels: '1-3 years', '3-10 years', and '10+ years'. Participants were also asked whether they adhered to a specific meditation tradition, which was coded as a binary variable ('Adherence' or 'Non-adherence'). Similarly, participants reported their total number of full-dose psychedelic experiences with classic serotonergic psychedelics (e.g., psilocybin, LSD, DMT, **4-Bromo-2,5-dimethoxyphenethylamine (2C-B)**, ayahuasca, mescaline) or atypical psychedelics (e.g., salvia). Full doses were defined as those producing substantial alterations in consciousness, distinct from sub-perceptual microdoses. For analysis, psychedelic use was grouped into two categories: '1-20 occasions' and '20+ occasions'. The variables of meditation experience, meditation tradition adherence, and psychedelic experience were included as independent predictors in a three-way between-subjects **analysis of variance (ANOVA)** to examine their relationship with PBMPP total scores, as described in Section 4.3.4 (*Statistical analysis*).

Perceived benefits of meditation for psychedelic preparation

Seven items evaluated participants' perceptions of how a structured meditation course prior to a psychedelic session might influence the experience. Specifically, participants were asked whether meditation training would: (i) increase the likelihood of a positive psychedelic experience, (ii) enhance safety during the experience, (iii) facilitate the emergence of helpful insights, (iv) support smoother post-experience readjustment and integration, and (v) lead to lasting benefits. Additionally, participants were asked whether meditation training could (vi) help individuals access deeper meditative states during the psychedelic experience and (vii) reduce the likelihood of negative experiences. Responses were recorded on an 11-point Likert scale (0 = 'strongly disagree', 10 = 'strongly agree'). A composite PBMPP score was calculated as the mean of these seven items, with higher scores indicating stronger endorsement in meditation's beneficial effects on psychedelic experiences. This composite PBMPP score was used as the outcome variable in the three-way between-subjects ANOVA to examine the effects of meditation tradition, meditation experience, and psychedelic experience, as described in the Statistical Analysis section.

State mindfulness

We modified the 12-item **Cognitive and Affective Mindfulness Scale Revised (CAMS-R)** [544] to assess participants' endorsements about how pre-psychedelic meditation training might enhance specific mindfulness capabilities during a psychedelic experience. This modification was designed to focus on mindfulness as a set of cognitive and affective processes rather than as a meditation practice per se. The adapted scale maintained the original four factors: *Attention*, *Present-Focus*, *Awareness*, and *Acceptance*. Items were rephrased to reflect anticipated changes in these capacities during a psychedelic experience following meditation training. Participants were asked to rate their agreement with statements beginning with "Training in meditation before using a psychedelic would probably enhance someone's ability to…" Examples of items included: "... concentrate during the psychedelic experience" (Attention factor), "... describe their feelings in detail during the experience" (Awareness factor), "... accept uncontrollable aspects of the psychedelic experience" (Acceptance factor), and "... focus on the present moment during the experience" (Present-Focus factor). Responses were recorded on a 11-point Likert scale (0 = 'strongly disagree', 10 = 'strongly agree'), with an additional 'n/a' option for participants unable to answer. The complete set of items is available in **Appendix A4.1**.

Altered states of consciousness

Participants rated how pre-psychedelic meditation training might influence each of the five general dimensions derived from the Altered States of Consciousness Dimensions (5D-ASC) scale [545]. Rather than completing the full questionnaire, participants rated these summarised dimensions: (1) **Oceanic boundlessness (OBN)**: positive and enjoyable aspects of the psychedelic experience associated with the experience of boundary dissolution between oneself and the surroundings as well as the dissolution of time and space; (2) **Anxious ego-dissolution (AED)**: negative psychedelic experiences associated with depersonalisation and dissociation; (3) **Visionary restructuralisation (VRS)**: perceptual and imaginational alterations including visual phenomena; (4) **Acoustic alterations (AA)**: changes regarding auditory perceptions and acoustic hallucinations; and (5) **Vigilance reduction (VIR)**: the experience of clouded consciousness, sleepiness, or drowsiness. Ratings were made on a 11-point Likert scale (-5 = 'greatly decrease', +5 = 'greatly increase').

Meditation 'practices'

To assess how different types of meditation might prepare individuals for psychedelic experiences, we examined four fundamental categories of meditation practice: **focused attention (FA)**, **open monitoring (OM)**, **loving-kindness meditation (LKM)**, and **self-transcendence (ST)**. These categories represent distinct styles or approaches to meditation training, drawing from established research literature and recent systematic reviews [433, 438, 540]. Each practice was described to participants as follows: FA involves sustained voluntary attention to a selected target stimulus, requiring continuous monitoring of attention and active disengagement from distractors. OM cultivates moment-to-moment awareness of arising mental content without selective focus or conceptual engagement. LKM develops sequential positive emotional states beginning with self-compassion and extending outward, enhancing prosocial cognitive and affective processes. ST reduces self-referential processing, altering the perceived boundaries between self and non-self-experience. Participants rated how helpful they believed each practice would be for preparing someone for a psychedelic experience using an 11-point scale (0 = 'not at all helpful', 10 = 'extremely helpful'), with an option to indicate not applicable ('n/a').

Meditative 'elements'

While meditation practices represent different approaches to training, we also examined specific abilities that practitioners develop through these practices. Through literature review [433, 533, 546–550] and expert consultation with two experienced meditation practitioners (collaborators AL and DK, with over 60 years of combined teaching and research experience), we identified 18 key meditative elements. These meditative elements represent specific competencies that meditators can develop and apply: (1) observing attention, (2) positive emotion cultivation, (3) relaxation/tranquillity cultivation, (4) recognising and releasing distractions, (5) recognising interconnectedness of phenomena, (6) non-discriminatory awareness, (7) ongoing awareness, (8) insight, (9) equanimity, (10) empathy and compassion, (11) comfort with discomfort, (12) sense of humour, (13) curiosity, (14) one-pointed concentration, (15) visualisation, (16) mantra repetition, (17) body scan, and (18) noting. Participants rated how important they believed each meditative element would be for psychedelic preparation using an 11-point scale (0 = 'not at all important', 10 = 'extremely important'), with an option to indicate uncertainty ('n/a'). Detailed descriptions of each meditative element are provided in Appendix A4.1.

Meditation 'processes'

Beyond specific practices and meditative elements, we examined fundamental psychological processes that meditation training can influence [541]. Participants rated five key processes: (1) *Attention Regulation*: sustaining attention on the chosen object and returning attention whenever distracted; (2) *Body Awareness*: focusing on internal experiences such as breathing, emotions, or other body sensations; (3) *Emotion Regulation I*: approaching ongoing emotional reactions non-judgmentally, with acceptance; (4) *Emotion Regulation II*: being able to 'stay with' strong emotions and whatever is present in the field of awareness, letting oneself be affected without trying to escape or suppress them; and (5) *Change in Perspective on the Self*: detachment from identification with a static sense of self, seeing the activities of the mind and body as fleeting occurrences rather than as 'reality'. Participants rated how relevant they believed each process would be for psychedelic preparation using an 11-point scale (0 = 'not at all relevant', 10 = 'extremely relevant'), with an option to indicate uncertainty ('n/a').

Meditation training parameters

Open-ended responses were collected regarding ideal training duration (in days and daily meditation minutes). Binary (yes/no) questions assessed perspectives on online delivery and asynchronous instruction viability.

4.3.4 Statistical analysis

All analyses were conducted using Python 3.12.5. Where relevant, statistical tests were two-tailed with an $\alpha = 0.05$.

Descriptive statistics

We computed descriptive statistics for all variables: means, standard deviations, and 95% confidence intervals for continuous measures; frequencies and percentages for categorical variables. For recommended meditation training duration measures, we excluded potential outliers as data points exceeding 3 standard deviations from the mean [551].

Effects of meditation tradition, meditation experience, and psychedelic use on PBMPP scores

We conducted a three-way between-subjects ANOVA with PBMPP total scores as the dependent variable and meditation tradition adherence (adherent vs. non-adherent), meditation experience (1-3 years, 3-10 years, 10+ years), and psychedelic experience (1-20 occasions, 20+ occasions) as independent variables. Due to violations of the homogeneity of variance assumption, **heteroscedasticity-consistent (HC3)** standard errors were applied in the analysis [552]. Post-hoc comparisons of the model-derived **estimated marginal means (EMMs)** were performed using pairwise comparisons adjusted with HC3 standard errors. Simple effects of meditation tradition were tested at each combination of meditation experience and psychedelic experience. Assumptions of normality and homogeneity of variance were evaluated using both statistical tests and visual diagnostics (**Appendix A4.2**).

Expected influence of meditation training on CAMS-R and 5D-ASC factors

To examine differences between factors of the CAMS-R and dimensions of 5D-ASC, we conducted two separate one-way repeated measures ANOVAs. Assumptions of normality and sphericity were evaluated using Mauchly's test and visual diagnostics (**Appendix A4.2**). For both analyses, Mauchly's test indicated violations of sphericity (CAMS-R: $W = 0.829$, $p < .001$; 5D-ASC: $W = 0.452$, $p < .001$), thus Greenhouse-Geisser corrections were applied (CAMS-R: $\varepsilon = 0.901$; 5D-ASC: $\varepsilon = 0.749$). Post-hoc pairwise comparisons were conducted using paired t-tests with Bonferroni correction to control for multiple comparisons.

Perceived efficacy of meditation practices and processes for psychedelic preparation

To examine differences in perceived efficacy across meditation practices and meditation-related processes, we conducted two separate repeated measures ANOVAs. Assumptions of normality and sphericity were evaluated using both statistical tests and visual diagnostics (**Appendix A4.2**). Post-hoc pairwise t-tests were performed using Bonferroni correction to adjust for multiple comparisons.

Exploratory Factor Analysis (EFA) of meditative elements

To explore the underlying structure of the 18 meditative elements, we conducted an exploratory factor analysis (EFA) on the 18 items using maximum likelihood (ML) estimation with oblimin rotation. The primary aim was to identify coherent factor structures rather than reduce the data. One missing value was handled through listwise deletion. The Kaiser-Meyer-Olkin measure (KMO = 0.879) and Bartlett's test of sphericity ($\chi^2(153) = 1149.62$, $p < .001$) indicated that the data were suitable for factor analysis.

We evaluated factor solutions ranging from one to five factors using several criteria: parallel analysis, scree plot, fit indices, proportion of variance explained, and interpretability. Parallel analysis and the scree plot suggested a two-factor solution. However, after considering the fit indices, proportion of variance explained, and the interpretability of the factor loadings, we selected a three-factor solution. This solution provided a good balance between model fit, explained variance, and theoretical coherence (**Appendix A4.3**).

The three-factor structure was refined over four iterations. Items were considered for removal if they had low loadings (< 0.4) or problematic cross-loadings (primary loading ≥ 0.4, secondary loading ≥ 0.32, with a difference < 0.2 between them) [551, 553, 554]. This process was repeated until all retained items loaded strongly and uniquely onto a single factor, resulting in a final set of 12 items. For the final EFA model, we calculated factor loadings, communalities, proportion of variance explained, and factor correlations. Factor scores were computed using the mean of items loading on each factor. Internal consistency reliability was assessed using Cronbach's alpha. Descriptive statistics were calculated for each factor score.

4.4 Results

Participant characteristics

Our study sample consisted of 123 participants, predominantly male (66.67%), white (79.67%), and highly educated (79.68% with at least an undergraduate degree), with a mean age of 41.1 years (SD = 13.5). Participants reported a median of 7.4 weekly meditation sessions (SD = 4.6), each lasting an average of 46.4 minutes (SD = 33.4). The sample represented 24 countries, with 43.90% from the United States. Meditation experience varied: 1-3 years (37.40%), 3-10 years (24.39%), and over 10 years (38.21%). In terms of meditation tradition, 59.35% identified with one or more traditions, while 40.65% did not. All participants had prior psychedelic experiences, with 43.09% reporting over 20 lifetime experiences. Detailed participant characteristics are provided in **Appendix A4.4.**

4.4.1 Perceived benefits of meditation training for psychedelic preparation

Overall perceived benefits

Participants generally rated the potential benefits of meditation training for psychedelic preparation highly, with consistently strong PBMPP scores across all items (**Fig. 4.1a**). The highest ratings were for post-experience integration (M = 7.81, SD = 2.11) and increasing the likelihood of positive experiences (M = 7.50, SD = 2.24). Other perceived benefits, such as gaining helpful insights (M = 7.31, SD = 2.19), facilitating safer experiences (M = 7.34, SD = 2.50), accessing deeper meditative states (M = 7.26, SD = 2.41), and deriving lasting benefits (M = 7.28, SD = 2.19), all received similarly high ratings. While reducing the likelihood of negative experiences was rated slightly lower (M = 6.89, SD = 2.26), the scores still indicated a generally positive view of meditation's potential to mitigate negative outcomes.

Factors influencing perceived benefits

A three-way ANOVA revealed a significant interaction between meditation tradition, meditation experience, and psychedelic use on total PBMPP scores, $F(2, 111) = 3.987$, $p = 0.02$. Main effects and two-way interactions were observed, but these were best understood within the context of the higher-order interaction (see **Appendix A4.5** for full ANOVA results).

Post-hoc pairwise comparisons were conducted to explore the simple effects of meditation tradition across different combinations of meditation experience and psychedelic use. Among participants with least meditation (1-3 years) and psychedelic experience (≤20 lifetime occasions), adherents to a meditation tradition perceived the benefits of meditation for psychedelic preparation to be greater (higher PBMPP scores) compared to non-adherents (Estimate = -1.44, SE = 0.56, $t(111) = -2.59$, $p = 0.01$). Conversely, participants with the most meditation experience (≥10 yr) and relatively limited psychedelic experience (1-20 occasions), non-adherents had significantly higher PBMPP scores than adherents (Estimate = 1.38, SE = 0.68, $t(111) = 2.04$, $p = 0.04$). No significant differences were observed in other comparisons (see **Appendix A4.6** for detailed post-hoc comparisons). **Fig. 4.1b** visualises the interaction, highlighting how PBMPP scores vary across different levels of meditation experience and psychedelic use.

4.4.2 Expected influence of meditation training on CAMS-R and 5D-ASC factors

The analysis of expected benefits of meditation training on mindfulness factors during a psychedelic experience (CAMS-R) revealed significant differences between factors ($F(2.7, 329.75) = 40.20$, $p < .001$, ges = 0.06). Participants anticipated the greatest improvements in *Acceptance* (M = 7.69, SD = 1.84), followed by *Present-Focus* (M = 7.29, SD = 2.17), *Awareness* (M = 6.63, SD = 1.88), and *Attention* (M = 6.43, SD = 1.86). Post-hoc analyses revealed that *Acceptance* ratings were significantly higher than all other factors, and *Present-Focus* was significantly higher than both *Awareness* and *Attention* (all ps < .001). *Awareness* and *Attention* did not differ significantly ($p = .345$) (**Fig. 4.1c**).

For the 5D-ASC scale, significant differences were found between dimensions ($F(3, 365.58) = 107.00$, $p < .001$, ges = 0.34). Participants expected meditation training to most strongly enhance OBN (M = 2.98, SD = 1.55) and reduce AED (M = -1.01, SD = 2.55). Minor increases were noted for AA (M = 0.84, SD = 1.51) and VRS (M = 0.73, SD = 1.49), while expectations for VIR remained near neutral (M = -0.13, SD = 1.91). Post-hoc comparisons revealed significant differences between all dimensions (all ps < .001) except between AA and VRS ($p = 1.00$) (**Fig. 4.1d**).

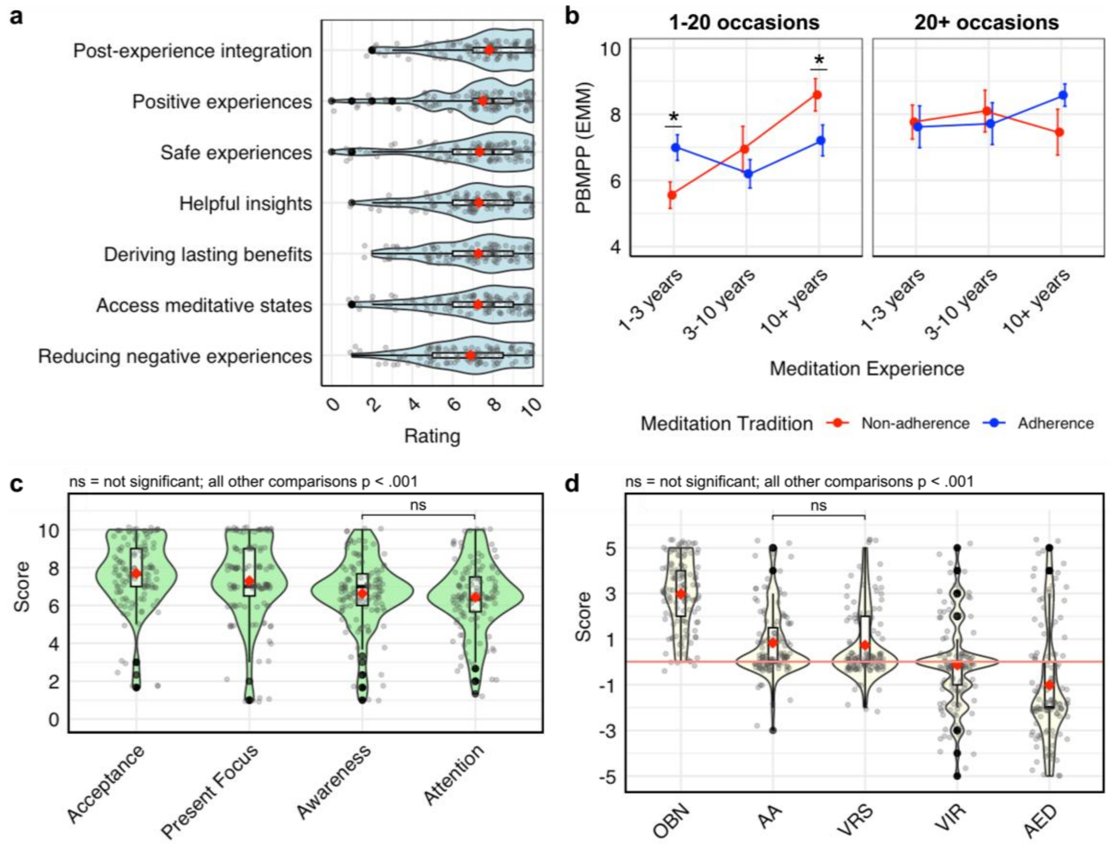


Figure 4.1. Perceived benefits of meditation training on psychedelic experiences

*(a) Violin plots showing score distributions with individual data points (grey dots), means (red diamonds), and medians with interquartile ranges (black boxplots) for Perceived Benefits of Meditation for Psychedelic Preparation (PBMPP) across seven benefit domains; (b) Interaction between meditation experience, tradition adherence, and psychedelic use frequency on PBMPP scores, presented as estimated marginal means ± 95% confidence intervals, stratified by meditation tradition (red: non-adherence, blue: adherence) and psychedelic use frequency (1-20 vs. 20+ occasions). Asterisks indicate significant differences between adherence groups (*p < 0.05); (c) Violin plots as in (a) showing expected effects on Cognitive and Affective Mindfulness Scale-Revised (CAMS-R) factors. All pairwise comparisons were significant (p < .001) except between Awareness and Attention (ns); (d) Violin plots as in (a) showing expected effects on 5D-ASC (Altered States of Consciousness) dimensions. All pairwise comparisons were significant (p < .001) except between AA and VRS (ns). Red horizontal line at 0 indicates neutral expectation; positive/negative scores indicate anticipated enhancement/reduction. OBN: Oceanic Boundlessness; AA: Acoustic Alterations; VRS: Visionary Restructuralisation; VIR: Vigilance Reduction; AED: Anxious Ego-Dissolution.*

4.4.3 Perceived efficacy of meditation approaches for psychedelic preparation

Meditation 'practices'

Participants rated the perceived helpfulness of four meditation practices (LKM, OM, ST and FA) for psychedelic preparation (**Figure 4.2a**). LKM received the highest mean rating ($M = 8.07$, $SD = 2.14$), followed by OM ($M = 7.29$, $SD = 2.11$), ST ($M = 6.96$, $SD = 2.24$), and FA ($M = 5.28$, $SD = 2.02$). A repeated measures ANOVA revealed significant differences in perceived efficacy across meditation categories, $F(3, 363) = 37.19$, $p < .001$, $\eta p^2 = 0.191$. Post-hoc comparisons using Bonferroni-corrected t-tests showed that LKM was rated significantly higher than all other categories (ps < .001, ds ranging from 0.519 to 1.50), while FA was rated significantly lower than all other categories (ps < .001, ds ranging from -0.930 to -1.22). No significant difference was observed between OM and ST ($p = .262$, $d = 0.260$).

Meditative 'elements'

Participants rated 18 meditative elements on their perceived importance for psychedelic preparation (**Fig. 4.2c**; **Appendix A4.7**). Ratings ranged from 'Sense of humour' ($M = 8.01$, $SD = 1.78$) and 'Comfort with discomfort' ($M = 7.86$, $SD = 1.97$) as the highest, to 'Mantra' repetition ($M = 3.67$, $SD = 2.13$) as the lowest.

An EFA of the meditative elements revealed a three-factor structure (**Fig. 4.2d**), explaining 50.16% of the variance. The factors were labelled as: **Positive Emotional States (PES)** (Factor 1; 19.70% variance explained); **Mindful Awareness and Insight (MAI)** (Factor 2; 16.84% variance explained); **Concentration Techniques (CT)** (Factor 3; 13.62% variance explained). Factor loadings, communalities, and reliability analyses are provided in **Appendix A4.8**. Internal consistency was good for all factors: PES ($\alpha = 0.83$), MAI ($\alpha = 0.79$), and CT ($\alpha = 0.72$). Descriptive statistics showed that PES had the highest mean score ($M = 7.72$, $SD = 1.69$), followed by MAI ($M = 6.97$, $SD = 1.64$), and CT ($M = 4.61$, $SD = 1.72$) (**Fig. 4.2e**).

Meditation 'processes'

Participants also rated the perceived relevance of five meditation-related processes for psychedelic preparation (**Fig. 4.2b**). *Emotion Regulation II* received the highest rating ($M = 7.87$, $SD = 2.10$), followed by *Emotion Regulation I* ($M = 7.74$, $SD = 2.19$), *Change in Perspective (of Self)* ($M = 7.37$, $SD = 2.20$), *Body Awareness* ($M = 6.80$, $SD = 2.21$), and *Attention Regulation* ($M = 5.67$, $SD = 2.38$). A repeated measures ANOVA showed significant differences in perceived relevance across meditation-related processes, $F(4, 488) = 21.809$, $p < .001$, $\eta p^2 = 0.116$. Post-hoc tests with Bonferroni correction revealed that *Attention Regulation* was rated significantly lower than all other processes (ps < .001, d values ranging from -0.659 to -1.25). *Body Awareness* was rated significantly higher than *Attention Regulation* ($p < .001$, $d = -0.659$) but significantly lower than both *Emotion Regulation I* ($p < .001$, $d = -0.740$) and *Emotion Regulation II* ($p < .001$, $d = -0.830$). *Change in Perspective (of Self)* was rated significantly higher than *Attention Regulation* ($p < .001$, $d = -0.978$) but did not differ significantly from *Body Awareness* ($p = .098$, $d = -0.335$) or the two emotion regulation processes ($ps > .05$, $ds = -0.297$ to -0.358). Lastly, there was no significant difference between *Emotion Regulation I* and *Emotion Regulation II* ($p = .300$, $d = -0.133$). These findings suggest that participants perceived emotion regulation and perspective-shifting processes as particularly relevant for preparing for psychedelic experiences, while attention regulation was rated as less relevant.

Recommended meditation training parameters

Participants recommended an average of 22.24 days (SD = 11.53) of meditation training for effective psychedelic preparation, with a daily practice duration of 30.81 minutes (SD = 11.90). A significant majority supported online delivery of meditation training (86.2%) and endorsed asynchronous (i.e., completing practices independently rather than through live online sessions) training methods (84.6%).

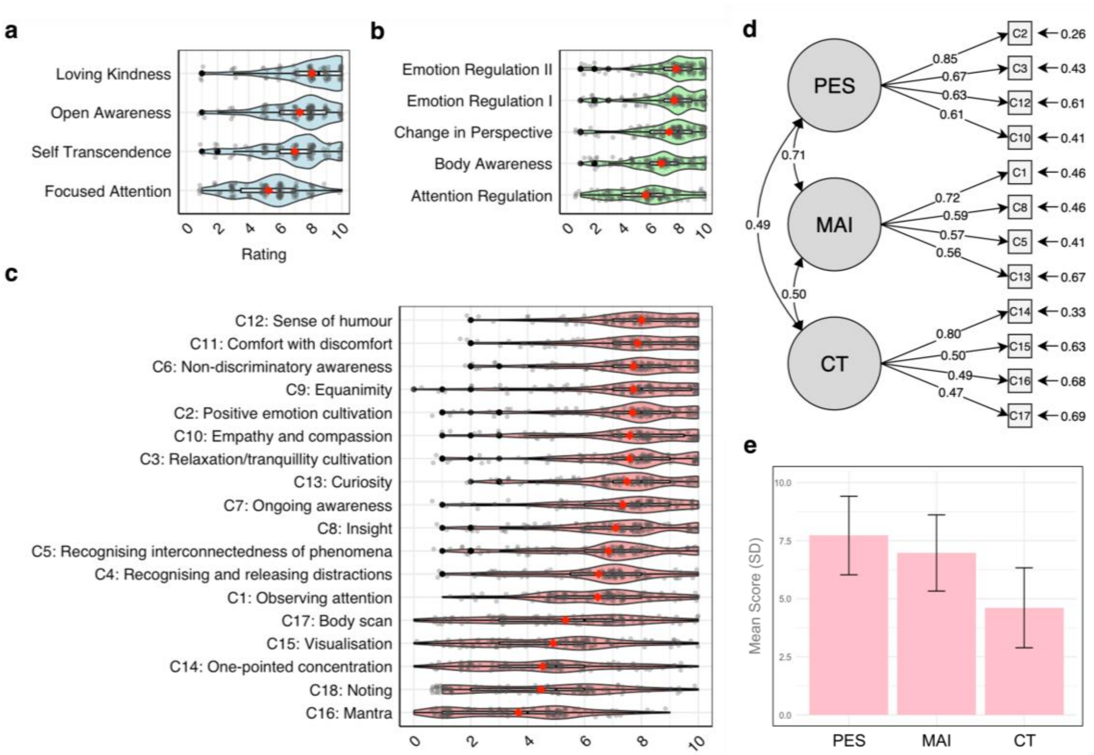


Figure 4.2. Perceived helpfulness of meditation practices, processes, and factor analysis of meditative elements for psychedelic preparation

(a) Violin plots showing rating distributions for meditation practices: Loving Kindness, Open Awareness, Self Transcendence, and Focused Attention. Individual data points (grey dots), means (red diamonds), and medians with interquartile ranges (black boxplots) are displayed. All pairwise comparisons significant (p < .001) except between Open Awareness and Self Transcendence (ns); (b) Violin plots as in (a) showing ratings for meditation-related processes: Emotion Regulation II, Emotion Regulation I, Change in Perspective, Body Awareness, and Attention Regulation. Attention Regulation rated significantly lower than all other processes (p < .001); (c) Violin plots as in (a) showing importance ratings for 18 meditative elements (C1-C18), ordered by mean rating; (d) Exploratory factor analysis showing three factors: Positive Emotional States (PES), Mindful Awareness and Insight (MAI), and Concentration Techniques (CT). Arrows indicate factor loadings and correlations; numbers by boxes show residual variances; (e) Mean scores (±SD) for the three factors identified in (d).

4.5 Discussion

This cross-sectional study of 123 experienced meditator and psychedelic practitioners reveals an important insight into psychedelic preparation: while contemporary meditation research has predominantly examined attentional processes, our findings indicate that the capacity for adaptive affect regulation may be particularly salient for navigating psychedelic states. Through multiple convergent measures - from specific practice evaluations to ratings of anticipated effects - we found that meditation approaches emphasising psychological flexibility and positive emotional states were consistently rated as more beneficial for preparation than concentration-based techniques. These findings, which varied systematically with meditation experience and tradition adherence, suggest meaningful refinements to current theoretical frameworks while offering empirically grounded insights into how meditation might optimally support psychedelic experiences.

Perceived benefits of meditation for psychedelic preparation

Respondents consistently rated meditation as highly beneficial for enhancing positive experiences, deepening insights, supporting integration, mitigating challenges, and fostering lasting positive effects in psychedelic contexts (PBMPP scores). Regarding anticipated acute effects, participants expected meditation training to enhance mystical-type experiences through increased OBN and decreased AED, while also strengthening mindfulness capabilities during sessions (CAMS-R) - particularly *Acceptance*, which was rated significantly higher than other mindfulness dimensions. These findings broadly support previous proposals about the synergistic relationship between meditation and psychedelics [289, 290, 442, 491]. While participants on average endorsed the potential value of pre-psychedelic meditation training, individual PBMPP ratings showed considerable variation and varied systematically based on their own experience levels with psychedelics and meditation, as well as their connection to a meditation tradition. For example, the results suggested that individuals with less personal experience (with both psychedelics and meditation), but who were adherent to a tradition of practice, gave higher ratings for the potential benefits of meditation as a preparation strategy. These findings suggest that endorsement of meditation for psychedelic preparedness is not simply related to accumulated personal experience but is shaped by how that experience is framed within a meditation tradition, particularly among those with less direct experience with either practice.

There are several possible explanations for this interaction pattern. Traditional contemplative frameworks ('traditions') provide systematic methodologies and detailed phenomenological maps for navigating states of consciousness [555–557]. For practitioners with more limited meditation and psychedelic experience, a theoretical grounding in consciousness exploration, distinct from secular approaches which may emphasise practical wellness benefits, could explain their higher perceived value of meditation for psychedelic preparation. Conversely, for more experienced meditators (10+ years), the higher PBMPP scores among non-adherents to (a) meditation tradition(s) might reflect the benefits of a flexible approach across different meditation traditions - particularly valuable given that psychedelic experiences can manifest in varied and unexpected ways that may benefit from diverse frames of reference and practices. Experienced practitioners can draw from multiple approaches while maintaining proficiency in their application. Additionally, strict adherence to specific contemplative traditions often involves accepting doctrinal positions that can conflict with psychedelic use, both explicitly through rules prohibiting consciousness-altering substances and implicitly through incompatibilities between traditional practices and psychedelic effects. These findings suggest that beliefs about the benefits of meditation for psychedelic preparation are shaped not only by the quantity of experience but also by how that experience is contextualised within or outside of traditional frameworks. Further research is needed to disentangle these influences and explore their implications for designing meditation-based psychedelic preparation programs.

Loving-kindness meditation: a foundational practice for psychedelic preparation

In terms of specific meditation approaches, participants rated LKM as the most helpful practice for psychedelic preparation, surpassing approaches such as OM, FA and ST. Derivations of LKM have been informed by *mettā bhavana* in Pali (the liturgical language of Theravada Buddhism), though they have evolved as distinct approaches within modern contexts. LKM systematically cultivates compassion, kindness, and friendliness, beginning with the target of oneself and expanding outward to include all beings without exception[558–560]. Unlike OM and FA, which primarily develop attentional stability and present-moment awareness, LKM actively fosters a proactive, prosocial orientation that may equip individuals to encounter and process challenging or distressing emotions with acceptance and compassion. This practice not only cultivates self-compassion [561, 562] - a mechanism increasingly recognised as central to psychedelics' therapeutic effects [563–566] - but also builds emotional resilience by increasing one's capacity to sustain compassion and kindness in the face of difficulties [567–571]. LKM reframes emotional disturbances as opportunities for growth, providing a structured framework for cultivating compassion and transforming challenges both within and beyond formal meditation practice. Such emotional resilience, coupled with strategies for integrating challenges, is likely to be especially valuable during psychedelic experiences, where intense, and sometimes challenging, emotions are common [15, 68, 100]. Notably, LKM's unique capacity to elevate and sustain positive affect has also been shown to counteract the 'hedonic treadmill' effect [572] - the well-documented tendency for people to adapt to both positive and negative life events, with happiness levels typically returning to a personal baseline or 'set point' [572–574]. While this adaptive mechanism is generally robust, LKM appears to help sustain elevated positive emotional states beyond this typical return to baseline [568, 569]. This sustained uplift in emotional tone may help foster an optimal pre-state, potentially enhancing the depth and positivity of psychedelic experiences [119–122, 155].

Further insights into the potential of LKM for psychedelic preparation draw from both classical Buddhist teachings and contemporary research. The *Karaṇīya mettā Sutta* advocates cultivating a boundless or 'unlimited' mind (*appamāṇa citta*) that radiates compassion universally, free from self-centred attachment [575, 576]. Early Buddhist texts, such as the *Bojjhaṅgasaṃyutta* and the *Visuddhimagga*, elaborate on how LKM can foster these boundless states, which include possible progress toward an advanced concentrative absorption meditation known as *jhāna*, that includes states of transcendence of bodily awareness and self-referential thought (*papañca*) [577–579]. Neuroscientific studies have linked this meditative boundlessness to decreased self-referential processing in the DMN [477, 580–583] - a neural shift often associated with OBN during psychedelics [1, 480]. While LKM may facilitate entry into psychedelic OBN states by reducing fear or resistance, its unique value lies in what the practitioner dissolves into: a mental state infused with warmth, connection, and compassion. This reorients the dissolution experience from one of fear or fragmentation to trust and belonging [584, 585]. Unlike practices emphasising detachment or neutrality, LKM actively cultivates care and acceptance, reframing dissolution as integration into a universal field of goodwill [559, 586]. By training the mind to release rigid self-boundaries while aligning this dissolution with positive emotions, LKM primes individuals for expansive psychedelic states, offering a practical and secular framework that smooths the experience and equips participants to integrate its transformative insights.

LKM also provides a powerful framework for navigating the complexities of psychedelic experiences, which, while often profoundly illuminating, can also pose significant challenges. These include cognitive distortions such as false memories [312, 587] and increased susceptibility to conspiracy theories [588], as well as psychological difficulties including 'spiritual bypassing' - where spiritual beliefs are used to sidestep difficult psychological work [589, 590] - and experiences of emotional overwhelm or depersonalisation [101, 113, 527, 591]. These challenges often stem from the profound intensity of psychedelic-induced insights, such as fearful realisations of interconnectedness and impermanence [70, 592, 593], alongside individual psychological factors, underscoring the need for practices that balance insight with emotional grounding. Drawing on elements of contemplative traditions, LKM practices emphasise both clear awareness and emotional warmth [594, 595], which may help support the processing of insights while fostering emotional stability [596, 597]. This approach may help create conditions conducive to processing both the profound insights and potential challenges of psychedelic experiences[42]. This perspective aligns with the 'apprenticeship' model of psychedelic preparation [599], which emphasises grounding experiences within cultural and emotional frameworks that foster both discernment and connection. By integrating contemplative elements with contemporary approaches, LKM therefore potentially offers a suitable framework for navigating psychedelic experiences and integrating their insights into meaningful, lasting change [461].

Meditation elements and processes: the value of psychological flexibility

Our exploratory factor analysis revealed a three-factor structure underlying the perceived usefulness of meditative elements for psychedelic preparation. These factors: PES, MAI, and CT, offer a novel framework for understanding how meditation can enhance readiness for psychedelic experiences. PES emerged as the most influential factor, encompassing elements like 'sense of humour' and the cultivation of 'empathy and compassion'. By contrast, CT received notably lower ratings, reflecting a preference for meditative elements that prioritise emotional and cognitive flexibility over concentration-heavy techniques. This pattern aligns with our findings regarding LKM's perceived value, suggesting that practices fostering adaptability and openness may be particularly critical for navigating the unique challenges of altered states. While the factors are distinct, their moderate to strong correlations suggest a shared contribution to the intricate process of preparing the mind for the transformative dynamics of psychedelics.

The relatively low rating of the CT factor, including FA practices such as 'one-pointed concentration', reveals an interesting tension in psychedelic preparation. While FA meditation serves as both a foundational practice in classical contemplative traditions and a primary focus of contemporary neuroscientific research [540, 600–603], its application in psychedelic contexts warrants careful consideration. FA traditionally operates by training practitioners to maintain stable attention, often through focused awareness on specific objects or experiences [1, 604–607]. While this focused attention can take many forms and be applied in various ways, including to expansive states of consciousness, there may be some tension between certain applications of FA and the characteristic features of psychedelic experiences, which often involve significant shifts in ordinary mental boundaries. Although FA can be valuable for developing beneficial traits such as mental discipline and attention regulation, its role in psychedelic contexts may be most beneficial when adapted to work with, rather than against, the mind's natural tendencies toward expansion. FA may therefore be particularly useful during integration, rather than preparation, where its stabilising

[42] Sharon Salzberg, a prominent teacher of Loving-Kindness Meditation (LKM), highlights that "*Buddha first taught metta meditation as an antidote: as a way of surmounting terrible fear when it arises.*" [598] This insight aligns with the potential role of LKM in psychedelic preparation, where fostering emotional resilience and grounding can help individuals navigate the intensity and potential challenges of psychedelic experiences.

qualities can help process insights and ground awareness, while also potentially serving during psychedelic experiences themselves as a tool for deep exploration of specific aspects of consciousness.

While the CT factor’s low rating highlights the limitations of control-oriented practices, examining individual elements reveals a nuanced understanding of psychological flexibility in psychedelic preparation. Most notably within the PES factor, ‘sense of humour’ emerged as the highest-rated element. Various contemplative traditions provide frameworks for understanding humour's transformative potential [608–610]: with some emphasising how insights into impermanence and non-attachment can foster a profound lightness of being [611], while others employ paradoxical exchanges to disrupt fixed patterns of thinking[612]. This understanding extends beyond mere levity to a systematic approach for reframing experience. This understanding extends beyond mere levity to a systematic approach for reframing experience [613], with humour facilitating what Loy [614] terms a “healing deconstruction” - revealing incongruities between expectation and reality in ways that foster openness [609]. These traditional insights resonate with contemporary psychological frameworks, including predictive processing, which explains how humour reduces the precision weighting of prior beliefs, enabling practitioners to reinterpret prediction errors as opportunities rather than threats [518, 615]. This capacity is particularly valuable in altered states that challenge predictive models of reality [483, 522, 616]. The high ratings of both humour and ‘comfort with discomfort’ suggest that practitioners recognise humour’s role in transforming encounters with the unexpected into opportunities for growth [617–619]. By reframing challenging experiences as growth opportunities, humour complements the ability to remain at ease with discomfort, a critical skill for navigating the perceptual and conceptual upheavals characteristic of psychedelic states.

This emphasis on adaptive engagement was further reflected in participants’ equal prioritisation of emotion regulation and change in perspective on self as key meditation-related processes, while attention regulation received significantly lower ratings. The high value placed on emotion regulation suggests practitioners recognise a crucial paradox: while psychedelic experiences often overwhelm ordinary regulatory capacities, developing the ability to remain emotionally responsive rather than reactive becomes essential for navigating their intense and unpredictable landscapes [541, 620]. This capacity appears inextricably linked with maintaining a malleable sense of self, as psychedelic experiences frequently induce profound alterations in self-experience [1, 300, 463] that can be either illuminating or destabilising depending on one’s preparedness. While some forms of meditation may cultivate meta-awareness and decreased identification with rigid self-concepts [433, 525, 548], our findings suggest these capacities take on particular significance in psychedelic contexts. The parallel emphasis on emotion regulation and self-perspective flexibility, coupled with our earlier findings about PES and LKM, points to a sophisticated understanding among experienced practitioners: optimal psychological preparation may depend less on maintaining rigid control than on developing the capacity to hold self-experience lightly while maintaining emotional equilibrium [621]. This provides further evidence that adaptability - both emotional and perspectival - may be more valuable than sustained attentional focus in preparing for psychedelic experiences.

Meditation training parameters

Participants recommended a meditation training duration of approximately 22 days with 30-minute daily sessions for psychedelic preparation, strongly favouring online delivery (86.2%) and asynchronous training (84.6%). These preferences align with our previous findings from psychedelic-assisted psychotherapy participants [156], who reported similar preferences for program duration (M = 21 days) and online delivery (89%). While these consistent recommendations offer a practical foundation for accessible preparatory programs, traditional approaches emphasise the value of in-person facilitation for establishing proper meditation technique. A hybrid model might be optimal, combining initial in-person training for proper foundation with subsequent online support for daily practice maintenance. Future research should empirically evaluate outcomes across online, in-person, and hybrid approaches to establish evidence-based guidelines for meditation-based psychedelic preparation.

Limitations and future directions

Our study's primary methodological limitations stem from categorisation simplifications. While our sample included practitioners from diverse meditation backgrounds, limited representation required broad secular/non-secular categorisation, potentially obscuring theoretically significant distinctions between traditions. Similarly, our discrete categorisation of meditation experience and psychedelic use may have masked complex relationships that continuous measures could better capture in future research. The undifferentiated treatment of psychedelic substances and dosages also warrants more nuanced investigation, as different compounds may interact uniquely with specific meditation practices. Future studies should stratify analyses by tradition, substance type, and dosage while developing more precise phenomenological classifications of meditation [471] to better understand how specific meditative qualities interact with psychedelic states.

A fundamental limitation of the current study concerns our participant selection criteria, which required experience with both practices. This likely introduced sampling bias toward individuals predisposed to viewing meditation and psychedelics as complementary, excluding perspectives from practitioners who maintain their separation or oppose their integration. This bias is particularly significant given the diversity of traditional views: while some shamanic and indigenous traditions integrate psychedelics into contemplative practice, many orthodox Buddhist and Hindu schools explicitly discourage the use of psychedelics, viewing them as obstacles to spiritual progress. This tension between tradition and innovation presents a crucial challenge for developing psychedelic preparation protocols. Traditional meditation systems, like indigenous psychedelic practices, are deeply rooted in cultural and spiritual frameworks that resist simple secular translation [622, 623]. While meditation has demonstrated adaptability to Western therapeutic paradigms, developing preparation protocols requires a rigorous approach that preserves contemplative depth while ensuring cultural sensitivity and therapeutic accessibility.

The high rating of LKM points to a specific limitation in our approach to measuring meditation practices. While our study focused on LKM individually, which in its contemporary form draws some inspiration from Theravada Buddhist *mettā* practice, compassion-based practices more broadly exist within integrated systems across many contemplative traditions [624–626]. These traditions often emphasise how different aspects of contemplative practice can complement and balance each other - for instance, how qualities of kindness might be balanced with equanimity, or how compassion might be supported by cultivating joy to prevent emotional fatigue. Future research should examine these practices as interconnected systems rather than in isolation, while also investigating their neurobiological correlates in psychedelic contexts - particularly how specific meditative states might interact with psychedelic-induced brain states. This more comprehensive approach could illuminate how diverse contemplative wisdom traditions might optimally support the emerging field of PAT while respecting both empirical rigour and cultural authenticity.

Conclusion

This cross-sectional investigation of practitioners with both meditation and psychedelic experience reveals a convergent pattern across multiple measures that points to adaptive affect navigation as a central mechanism for both harm reduction and benefit enhancement in psychedelic contexts. This finding emerges consistently through several lines of evidence: the high endorsement of LKM over concentration-based practices, the primacy of the PES factor in our analysis of meditative elements, and the elevated ratings for emotion regulation processes over attention control. The emphasis on psychological flexibility and emotional resilience is further supported by practitioners' high valuation of elements like 'sense of humour' and 'comfort with discomfort', suggesting that successful psychedelic experiences may depend more on the capacity to navigate emotional states fluidly than on maintaining rigid attentional focus. These insights, derived from the complex interplay of meditation experience, tradition adherence, and psychedelic use, provide empirically grounded parameters for developing preparatory protocols, including specific recommendations for scalable online delivery formats. As both meditation and psychedelic research advance into their third wave of scientific investigation [463], this mechanistic understanding of affect navigation as a key preparatory element offers valuable guidance for optimising psychedelic-assisted therapies while enhancing our broader understanding of consciousness modification for therapeutic benefit.

CHAPTER 5

Digital Intervention for Psychedelic Preparation (DIPP): Protocol for a randomised controlled feasibility trial comparing meditation and non-meditation versions

"The true method of knowledge is experiment."

— Blake, W. (1788). All Religions Are One.

5.1 Abstract

Psychedelic therapy shows promise for treating various mental health conditions; however, its reliance on intensive psychological preparation limits its broader application. As discussed in earlier chapters, **Digital Health Interventions (DHIs)** have the potential to address this limitation by providing structured, accessible, and scalable preparation solutions. **Chapter 5** presents the protocol for an upcoming randomised controlled feasibility trial aims to evaluate the feasibility and preliminary efficacy of the Digital Intervention for Psychedelic Preparation (DIPP), a 21-day mobile app-based programme that incorporates guided meditation to prepare individuals for psychedelic experiences. The study will recruit 40 non-treatment-seeking adults without a specific clinical diagnosis, randomly assigning them to one of two conditions: (1) DIPP, featuring guided meditation with background music, or (2) DIPP-NM (No Meditation), providing the same background music without guided meditation. Both groups will complete the 21-day digital intervention remotely. Following the intervention, participants will attend an in-person supervised psilocybin session at UCL, receiving a standardised 25 mg dose. Primary outcomes focus on feasibility metrics including recruitment efficiency, participant retention, and adherence to the intervention protocol. Secondary outcomes assess subjective feasibility, acceptability, and preliminary efficacy, specifically evaluating psychedelic preparedness, the quality of the psychedelic experience, and changes in well-being, with follow-up assessments at 2 weeks, and at 3-, 6-, and 9-months post-session. Exploratory measures include physiological, cognitive, and psychological assessments, as well as real-time voice note experience sampling through a chatbot to monitor inner speech and emotional states during the intervention and follow-up periods. The trial is registered with ClinicalTrials.gov (identifier: NCT06815653).

5.2 Introduction

Effective psychological preparation is foundational for enhancing both the safety and therapeutic potential of psychedelic therapy (see **Chapter 1**). However, existing preparation approaches predominantly rely on intensive therapist-led interactions, significantly restricting scalability and integration into broader healthcare settings. To overcome these limitations, **Chapter 3** introduced the Digital Intervention for Psychedelic Preparation (DIPP) (see **Fig. 3.4** in **Chapter 3** for visualisation of the DIPP structure and mobile interface). The current chapter outlines the protocol for a pilot trial aimed at systematically evaluating DIPP's feasibility, acceptability, and preliminary efficacy (ClinicalTrials.gov identifier: NCT06815653). While this pilot was initially designed to contribute empirical data to the present thesis, administrative and regulatory delays - primarily due to Home Office licensing and import/export procedures - have shifted data collection beyond the thesis submission timeline. Consequently, data acquisition will commence immediately following submission and form part of a subsequent *Wellcome Transition Grant*-funded project.

Section 3.5 provides a detailed account of the general DIPP protocol. Central to DIPP is daily meditation practice, delivered via audio-guided sessions lasting 20-45 minutes, progressively increasing in duration over the 21-day program. **Chapter 4** refined this meditation component by surveying meditation practitioners experienced with psychedelic substances, identifying loving-kindness meditation (LKM; inspired by the Theravada Buddhist practice of *mettā bhavana* [in *Pāli*, the liturgical language]) [627, 628] as the most effective practice for psychedelic preparation. Consequently, LKM is adopted as the primary meditation technique within DIPP. This specific novel meditation framework was collaboratively designed with DK and AL from the *Harvard Meditation Research Programme*, informed by their combined expertise of over 60 years in meditation teaching. The meditation training systematically cultivates loving-kindness (*mettā*) across three stages: initially directed toward oneself (Days 1-7), then extended to another person (Days 8-14), and finally expanded outward to encompass all beings (Days 15-21) [568, 629, 630]. Additionally, participants are introduced to structured methods for managing distractions and refining their meditation practice [32, 33], including the '6Rs' technique (Recognise, Release, Relax, Re-smile, Return, Repeat) - a cyclical approach that gently and effectively disengages attention from distractions [560, 631] - and a framework for recognising different levels of awareness [632, 633] (see **Appendix A5.1** and **A5.2** for details). These elements support the development of attentional stability, clarity of awareness, and insight into mental processes [540, 634, 635] thereby equipping participants with essential skills for navigating shifts in consciousness during psychedelic experiences. **Figure 5.1** provides an overview of the

DIPP meditation training framework. A separate publication will detail the meditation framework underpinning DIPP.

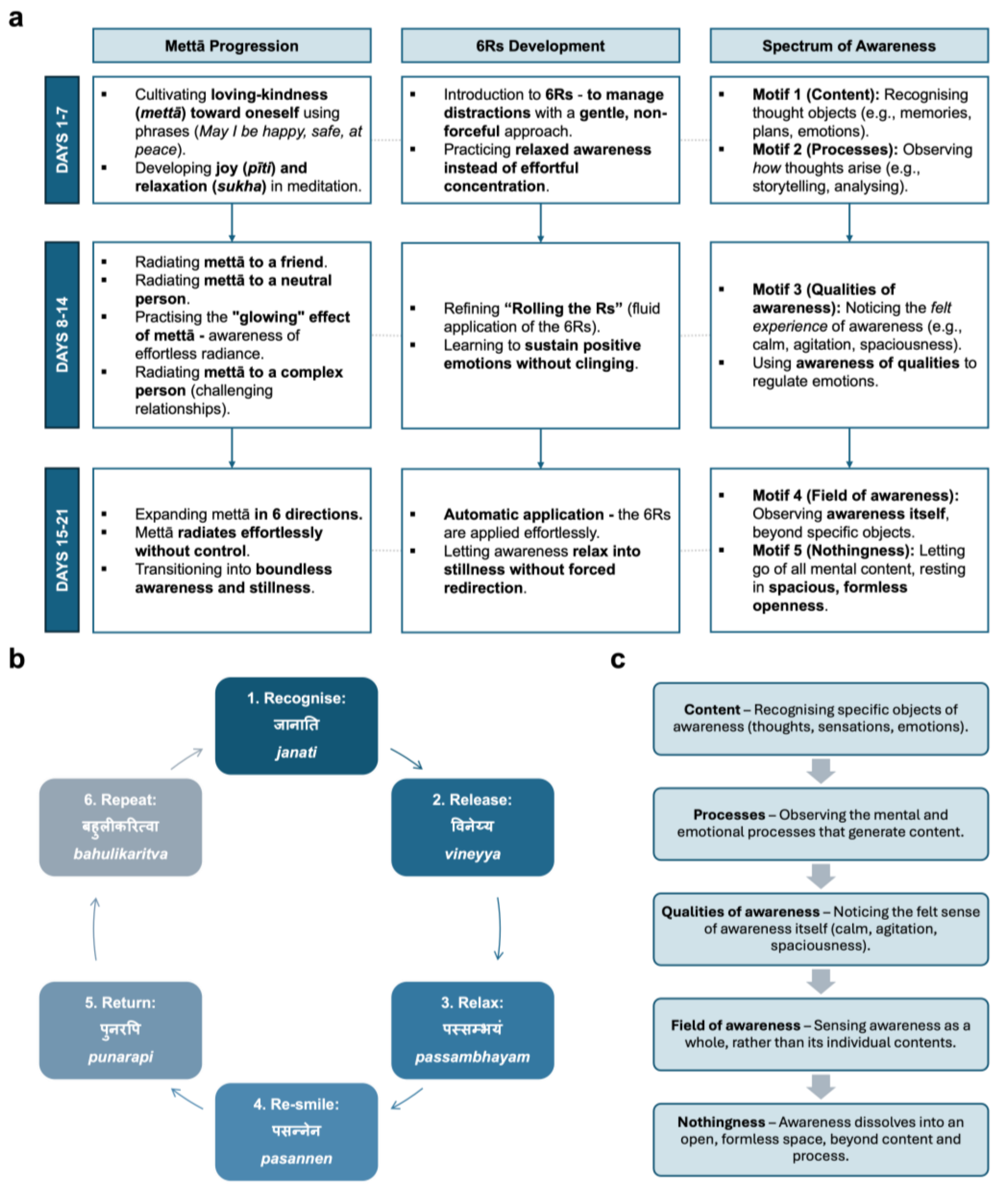


Figure 5.1 Overview of the DIPP meditation training framework

(a) Progression of meditation training over 21 days, integrating Mettā cultivation, 6Rs development, and the Spectrum of Awareness. (b) The 6Rs process, a structured method for working with distractions in meditation. (c) The Spectrum of Awareness, illustrating the deepening levels of awareness from content to formless openness.

As an additional component of this study, the *DIPP-Bot*, a Telegram-based chatbot, is used to facilitate **inner speech sampling (ISS).** It prompts participants to submit brief voice notes and follow-up responses adapted from the **Multidimensional Experience Sampling (MDES)** approach [636], with modifications for remote administration [637]. These responses undergo linguistic and acoustic analysis to explore psychological shifts surrounding the psilocybin experience, capturing dynamic changes that traditional questionnaires may overlook [638]. ISS continues post-dosing at three, six, and nine months, allowing for longitudinal tracking of cognitive and emotional changes.

5.3 Trial objectives

As outlined above, a core component of DIPP is the daily meditation exercises, which are audio recorded guided instructions presented against a background of calming music. To evaluate whether this component has a substantial contribution to acceptability, retention and efficacy, we designed a randomised controlled feasibility trial following **Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT 2013)** guidelines. Forty healthy volunteers will be randomised to one of two conditions. For clarity, the trial timeline is divided into multiple timepoints: t_1 (baseline), t_2 (pre-dosing), t_3 (dosing session), t_4 (post-dosing follow-up), and t_5-t_7 (remote follow-ups at 3, 6, and 9 months, respectively) (see **Fig. 5.2**):

1. **DIPP** ($t_{1\text{-}2}$): The full DIPP intervention, including daily guided meditation exercises.
2. **DIPP-NM** (No Meditation) ($t_{1\text{-}2}$): An otherwise identical intervention, except the meditation elements are removed, leaving only the background music used in the meditation sessions.

The DIPP-NM control was designed to control for attentional aspects, intervention duration, digital engagement, and sensory input, and to isolate the effects of meditation itself. As such, participants in both groups will engage with the same digital platform, follow the same schedule, and receive the same preparatory educational materials, ensuring that any observed differences are specifically attributable to the guided meditation component rather than general exposure to a structured preparation program. By using the same background audio in both conditions, we control for potential effects of music while removing explicit meditation guidance. Crucially, study information simply refers to “preparation activities” without specifying these in detail or mentioning the presence of multiple groups. This was done to ensure expectancy effects could not differ prior to starting the DIPP (±meditation) interventions.

Following the 21-day preparation period, participants will undergo a supervised 25 mg psilocybin session at UCL (t_3). Follow-up assessments will be conducted in person at 2 weeks (t_4) and online at 3-, 6-, and 9-months post-intervention ($t_{5\text{-}7}$). The trial will primarily assess operational feasibility and intervention adherence, while secondary outcomes will evaluate implementation metrics and preliminary efficacy measures.

5.4 Stakeholder Involvement (SI)

Stakeholder Involvement (SI) was central to the intervention's development, following co-creation principles that prioritise working *with* rather than *for* individuals with lived experience [639–641]. This systematic approach, aligned with best practices in digital mental health [405, 443, 444] and psychedelic research [642–644], ensured stakeholder input at multiple stages. Guided by MRC recommendations [411], the process was dynamic and iterative, integrating PPI to shape both core components and delivery methods. The iterative process is outlined in **Chapter 3.**

A SI advisory group comprising four individuals with prior experience with PAT has been established to guide trial implementation. This group has reviewed recruitment materials and strategies to ensure they resonate with potential participants. They have also assessed the burden of participation, including the time commitments for both the digital intervention and follow-up assessments. We will continue stakeholder engagement throughout this feasibility trial. For results dissemination, the group will help develop accessible summaries of the findings for participants and the wider psychedelic research community, determining the most effective formats for communicating various outcomes.

5.5 Methods and analysis

Recruitment

Forty non-treatment-seeking healthy adults residing in the United Kingdom will be recruited through institutional mailing lists, social media platforms, and word-of-mouth referrals. Written informed consent will be obtained from all participants prior to enrolment (**Supplementary S3**). Since this is a feasibility trial, no formal power calculation was conducted. A sample of 40 participants (20 per group) was selected based on published guidance for early-phase trials and similar feasibility studies within clinical psychopharmacology, ensuring sufficient data to assess recruitment, retention, and adherence [43, 645–650].

Eligibility criteria

Participants must be aged between 21 and 65 years and have limited prior psychedelic use, defined as five or fewer full-dose experiences and none within the past six months. Microdosing is not included, defined as the repeated use of sub-perceptual doses that do not produce noticeable alterations in consciousness [651]. Participants must also have minimal meditation experience, defined as no more than ten sessions exceeding 30 minutes and no prior retreats or regular ongoing practice. This criterion is intended to reduce variability in baseline meditation ability and ensure that any observed effects on psychedelic preparedness can be more confidently attributed to the intervention itself. Additional eligibility requirements include being a native English speaker, having normal or corrected-to-normal colour vision, and being able and willing to provide informed consent. Participants must be UK residents registered with a primary care provider, have access to a smartphone, and be able to comply with all study requirements, including both in-person and remote sessions. They must also agree to allow the research team to contact their primary or secondary care providers, if necessary, identify a support person for post-session accompaniment, provide emergency contact details, and maintain access to an electronic device for data entry.

Individuals will be excluded if they have a current or past diagnosis of a mood disorder (e.g., depression, anxiety) unless in clear remission for at least five years and assessed by the clinical team as low risk. Those with a current or past diagnosis of psychotic or bipolar disorder, or an immediate family history of these conditions, are not eligible. Additional exclusion criteria include a history of serious suicidal ideation (e.g., intent or planning) or any past suicide attempts. Participants must not have medically significant physical health conditions that could pose a risk with psilocybin or magnetic resonance imaging (MRI), such as cardiovascular disease, uncontrolled hypertension, epilepsy, migraines, or focal scalp sensitivity. Use of medications that interact with psilocybin, including antipsychotics, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and mood stabilisers, is also a disqualifier. Furthermore, individuals who are pregnant, planning a pregnancy, or breastfeeding will not be eligible. Those who have participated in a drug trial within the past six months or have MRI contraindications (e.g., metal implants, pacemakers, or severe claustrophobia) are also excluded from the study.

Screening

All prospective participants will be directed to complete an online pre-screening questionnaire which contains a list of questions on demographics, physical and mental health, substance use, and other factors essential for assessing initial eligibility. Those who meet the initial criteria will be invited to a remote screening call with a member of the research team, where they will receive detailed information about the study, and can ask questions before electronically providing informed consent. The remote screening call will also include a psychiatric evaluation using the **Mini-International Neuropsychiatric Interview (MINI)** [652], the **Standardised Assessment of Personality (SAPAS)** [653] to screen for personality disorders, and the **Stressful Life Events Screening Questionnaire (SLESQ)** [654] to evaluate exposure to traumatic events. Participants who pass this stage will be invited to a more comprehensive online clinical interview with a licensed clinical psychologist to confirm their eligibility and provide further clarification about study procedures. Physical screening measures, including resting blood pressure and a 3-lead resting **electrocardiogram (ECG),** will be conducted in person during the baseline visit (t_1) to assess cardiovascular suitability for psilocybin administration. Participants with medically significant abnormalities on either measure may be excluded from the study at the discretion of the clinical team.

Allocation methods and blinding

After providing informed consent, participants will be randomly assigned to one of two conditions (DIPP or DIPP-NM) in a 1:1 ratio using a computer-generated sequence. To ensure allocation concealment, the sequence will be generated by a researcher not involved in recruitment, assessment, or intervention delivery and stored securely in an electronic document accessible only to the enrolment researcher. Upon enrolment, the researcher will retrieve the next assignment from the list and register the participant's unique user ID into the DIPP web app, which will automatically deliver the 21-day digital preparation program with or without meditation, according to the assigned condition. Participants will remain blinded to their assignment and informed only that they are participating in a 21-day digital preparation program before their psilocybin session. Intervention materials and instructions will be standardised across conditions to minimise expectation differences. Any instances of unblinding will be documented and reported in the final analysis.

Design

Participants will complete a structured five-week protocol involving four in-person study visits: baseline (t_1), pre-dosing (t_2), dosing (t_3), and post-dosing follow-up (t_4) (see **Fig. 5.2**). At t_1, participants will complete self-report measures and cognitive tasks assessing psychological and cognitive domains of wellbeing and inner experience. ECG will also be recorded for 5 minutes. Between t_1 and t_3, they will engage in the 21-day DIPP. During the 10 days before and after dosing, participants will provide daily voice note samples via the DIPP-Bot mobile app for linguistic and acoustic analysis of inner speech patterns. At t_2, participants will repeat the self-report measures, cognitive tasks and ECG from t_1 and undergo an fMRI-movie scan [655]. One day later at t_3, participants will receive a 25 mg dose of psilocybin, with EEG and ECG recorded at baseline, 90 minutes, and 150 minutes post-administration. At t_4, they will complete another fMRI-movie scan along with repeated self-report measures, cognitive tasks and resting state ECG. Remote follow-ups will continue for nine months, with online assessments at three (t_5), six (t_6), and nine (t_7) months post-dosing. Participants will also resume inner speech sampling via DIPP-Bot for 7 days at these key follow-up time points.

Outcome measures

The study employs a comprehensive, multimodal data collection approach, incorporating self-report measures, neurophysiological assessments, behavioural indices, and qualitative data. The primary outcomes focus on key indicators of feasibility and adherence, including recruitment efficiency, study retention, and engagement (intervention adherence) with DIPP. Recruitment efficiency is measured as the weekly rate of participant enrolment, calculated as the total number of participants successfully completing online screening, researcher screening, and clinical screening, divided by the total number of recruitment weeks. Acceptable recruitment efficacy is defined as maintaining an average recruitment rate of at least one participant per week until the target sample of 40 participants is reached. This measure is tracked from study initiation to the completion of recruitment. Study retention is evaluated as the percentage of participants who complete the two-week post-dose follow-up assessment (t_4). Acceptable study retention is defined as at least 70% of participants completing the (t_4) assessment. Intervention adherence is determined based on completion rates across three daily tasks (daily practice (±meditation), mood ratings, and journal entries) and two weekly (module-specific) tasks. Given the total of 69 tasks across the 21-day program (63 daily + 6 weekly), successful individual adherence is defined as completing at least 48 tasks (≥70% completion rate) [656]. A complete overview of all outcome measures is presented in a SPIRIT table in **Supplementary S4**, with primary, secondary, and other pre-specified outcomes detailed in Supplementary **S5.**

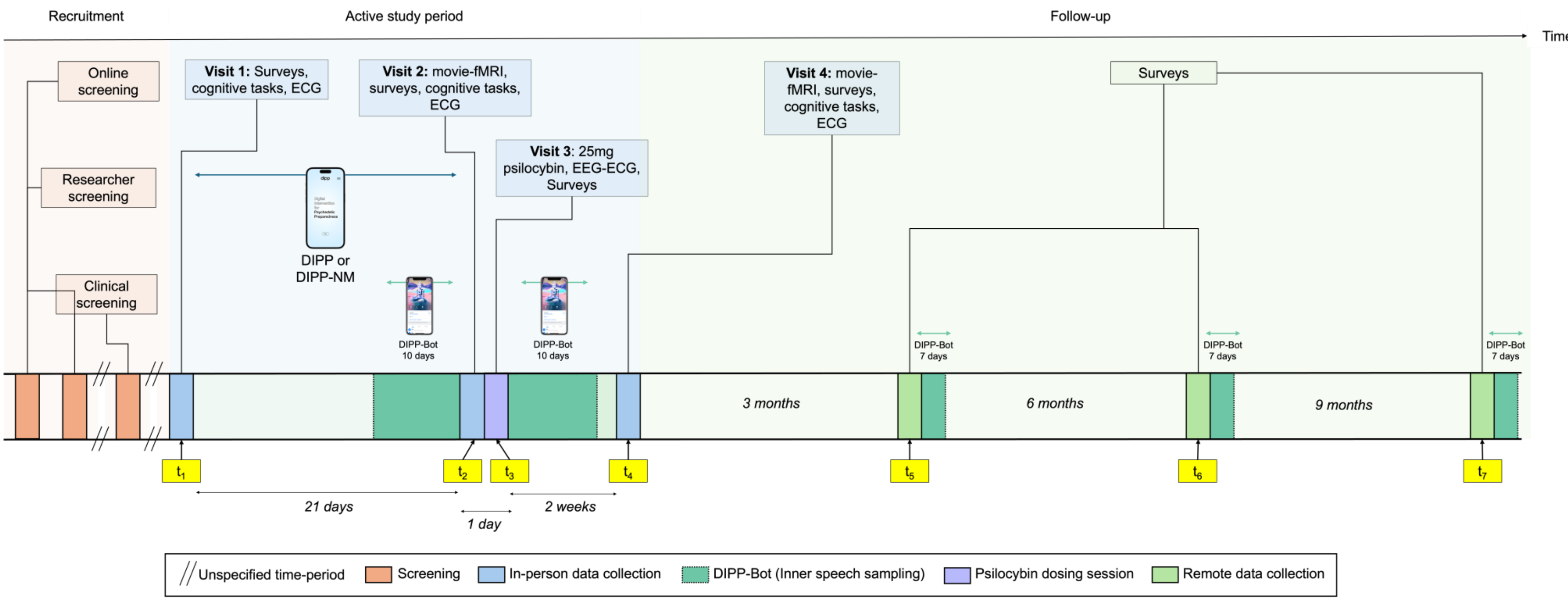


Figure 5.2. DIPP pilot study timeline

Screening activities are shown in orange, in-person data collection (including key study visits) in blue, and remote data collection in green. The purple rectangle represents the psilocybin dosing session. Exploratory components, such as the DIPP-Bot inner speech sampling, are indicated with a dotted outline. ECG: Electrocardiogram; EEG: Electroencephalogram; fMRI: Functional Magnetic Resonance Imaging.

Analysis strategy and missing data

This section outlines the analysis plan for primary and secondary outcomes. Other pre-specified exploratory outcomes, including behavioural, neurophysiological, and additional self-report measures, will be detailed in forthcoming pre-registrations and separate publications.

Primary feasibility outcomes (recruitment efficiency, study retention, and intervention adherence) will be summarised descriptively as frequencies and proportions. For secondary outcomes (SFIS, TFA, SUS, MARS, PPS, 11D-ASC, CEQ, SWEMWBS), between-group comparisons will be conducted using independent t-tests if normality assumptions are met, or Mann-Whitney U tests if violated. Within-group changes (PPS, SWEMWBS) will be assessed using paired t-tests or Wilcoxon signed-rank tests where appropriate. For repeated-measures data (e.g., changes in SWEMWBS over time), repeated-measures ANOVA will be used when assumptions are met, with mixed models applied if substantial missing data is present. All tests will be two-tailed ($\alpha = .05$), and effect sizes will be reported where appropriate.

Missing data will be handled based on outcome type and extent of missingness. For primary feasibility outcomes, all available data will be included, with no imputation, and results will be reported descriptively as proportions. For secondary outcomes, missing data will be handled using complete case analysis. If substantial missingness is detected, exploratory mixed models may be used to assess robustness. All missing data will be reported descriptively, and patterns of missingness will be assessed to determine whether it is systematic or random.

Investigational Medicinal Product (IMP) management

Psilocybin (PEX0101, Psilo Scientific Ltd) The study uses **Good Manufacturing Practice (GMP)**-grade psilocybin manufactured and encapsulated by Filament Health. All handling and storage procedures comply with Schedule I controlled substance regulations under a UK Home Office license. GMP standards are maintained throughout the manufacturing and storage process. The **Investigational Medicinal Product (IMP)** is stored in a secure controlled-drug facility at the **Clinical Psychopharmacology Unit (CPU),** UCL, Bloomsbury, with strict access controls and documentation procedures in place.

Data management

Data management procedures follow UCL's **Standard Operating Procedures (SOP)** and a study-specific data management plan. All voice notes, follow-up responses, and engagement logs collected via the DIPP-Bot are securely stored on **Amazon Web Services (AWS)** servers, managed through OneReach.AI. All data collection and storage systems comply with **General Data Protection Regulation (GDPR)** requirements and have received approval from UCL's Information Security team.

Data monitoring

An independent **Data Monitoring Committee (DMC)** is not required for this study, as it is not a clinical trial evaluating an investigational drug or high-risk intervention. Instead, data monitoring is conducted internally by the study team to ensure protocol adherence, data integrity, and participant safety. All study data are securely stored and periodically reviewed to ensure compliance with ethical and regulatory guidelines.

Safety monitoring

Adverse Events (AEs) will be monitored and documented throughout the study. The clinical team will categorise AEs based on severity (mild: no impact on daily activities; moderate: some interference with daily activities; severe: prevents daily activities), whether they are anticipated or unanticipated, and their causal relationship to the IMP (classified as related, possibly related, or unrelated as determine by a supervising medical doctor). AE summary tables will present the total number of participants reporting an AE, the percentage of participants affected, and the total number of events recorded. **Serious Adverse Events (SAEs)** and **Serious Adverse Reactions (SARs)** will be defined as any significant medical occurrence that (i) leads to death, (ii) poses a life-threatening risk, (iii) necessitates hospitalisation, or (iv) results in long-term disability or impairment. All SAEs and SARs will be promptly reported to the principal investigator (PI) immediately upon the study team becoming aware of the incident. The research ethics committee will also be alerted as soon as any such reaction is detected.

Psychological support

Preparation

This study employs researchers with prior psychedelic trial experience who serve as 'guides' during dosing sessions (t_3). All guides will receive an induction led by the study's clinical psychologist, covering key elements of psychedelic support, safety protocols, and participant care. Guides will also meet regularly with the clinical psychologist for supervision throughout the study. Guides will prepare participants for the experience during their first in-person visit (t_1), covering standardised objectives including psychoeducation, trust building, and intention setting. Additionally, all participants will complete the 21-day DIPP ($t_{1\text{-}2}$) [156]. The day before their dosing session (t_2), participants will return to the research facility for a final preparation session with their guides. Two guides accompany each participant throughout the trial, ensuring physical and psychological safety while remaining neutral to the content of the participant's experience. This approach aligns with standardised practices in psychedelic research [657] while distinguishing the support model from therapeutic intervention.

Dosing session

Following established research protocols [658], the guides maintain a non-directive, person-centred approach that allows participants to process their experiences autonomously. Participants will spend approximately 8 hours at the research facility on their dosing day (t_3). The acute drug effects typically last 4-6 hours. Sessions will be conducted in a comfortable room with adjustable, low lighting. Participants will be provided with an eye mask and headphones, which they can use according to their comfort level, and will be encouraged to maintain a semi-reclined position when possible. The session will include a carefully curated music playlist, developed in collaboration with music therapists. A qualified medical professional will be present on-site throughout the session to monitor participants' safety and wellbeing. Before discharge, the research team will conduct a sobriety assessment (including the **Drug Effects Questionnaire (DEQ)** [659] and the simplified 6-item **Clinician Administered Dissociative Symptom Scale (CADSS-6)** [660]) to ensure participants are fit to leave. All participants must be accompanied home by a trusted companion after the session.

Integration

During the SP module of DIPP, completed in the week prior to dosing, participants create a personalised 'integration plan' to support processing of their upcoming psychedelic experience. They are guided through a structured framework to reflect on potential insights, identify areas for personal growth, and select strategies for integration, including emotional processing, reflection, and behavioural change. The instructions and format are implemented consistently across both conditions; however, the content of each plan is participant-generated, introducing some variability in post-dosing behaviours that may influence longer-term outcomes. Nonetheless, integration planning is considered an essential part of the intervention, included for ethical and safety reasons.

The day after dosing (t_{3+1}), participants receive an integration call with their guides (~1 hour) to check in, discuss their experience, and address any immediate reflections or concerns. This call is not part of data collection but serves as a supportive touchpoint. Two weeks post-dose (t_4), participants attend an in-person integration session, where they reflect on their experience, discuss emerging insights, and explore how to apply them in daily life. This session also includes standardised self-report assessments as part of study data collection.

Data availability statement

De-identified questionnaire, behavioural, and EEC-ECG data will be available upon reasonable request to the corresponding author. Access requires a formal data-sharing agreement to protect participant privacy and will be evaluated based on the scientific merit of the proposed analyses. Additionally, de-identified fMRI data will be made publicly available whenever possible, in compliance with institutional requirements and relevant data protection regulations.

5.6 Conclusion

This protocol publication contributes to methodological transparency and scientific rigour in psychedelic research. By detailing our methods and decision-making processes, we aim to enhance accountability and reproducibility in the field. The study's emphasis on patient involvement in protocol design exemplifies our commitment to conducting relevant and equitable research. This trial will assess both the feasibility and preliminary efficacy of a meditation-based digital intervention for psychedelic preparation, potentially offering a scalable approach to enhancing PAT outcomes.

CHAPTER 6

Mindfulness language modulates the relationship between psychedelic preparedness and 5-MeO-DMT experiences

"I became Consciousness facing the Absolute. It had the brightness of myriad suns, yet it was not on the same continuum with any light I knew from everyday life. It seemed to be pure consciousness, intelligence, and creative energy transcending all polarities. It was infinite and finite, divine and demonic, terrifying and ecstatic, creative and destructive [...] My ordinary identity was shattered and dissolved; I became one with Source."

— *Oroc, J. (2009). Tryptamine Palace: 5-MeO-DMT and the Sonoran Desert Toad.*

6.1 Abstract

5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT) is a fast-acting psychedelic known for inducing profound non-dual experiences, yet its phenomenology and neural effects remain poorly understood. This study investigates how psychedelic preparedness and mindfulness-related language predict subjective 5-MeO-DMT experiences, and how these experiences relate to neural activity. Twenty-nine participants attended a 3-day 5-MeO-DMT retreat, completing pre- and post-session self-report assessments and voice recordings. EEG was recorded during a single 12 mg 5-MeO-DMT session. Hierarchical regression revealed a significant interaction: at low baseline mindfulness language, greater psychedelic preparedness predicted stronger **oceanic boundlessness** (**OBN**, 5D-ASC) and **Everything/Nothing** (**EN**, 5PS) experiences, whereas at high levels, preparedness was not significantly associated with OBN and was negatively associated with EN. EEG analyses revealed widespread increases in slow-wave power (0.5-1.5 Hz) following 5-MeO-DMT, with reductions in occipital alpha power (8-12 Hz) correlating with EN scores. No direct associations between spectral power and subjective experiences were found. These findings suggest that mindfulness-related language moderates the effect of psychedelic preparedness on subjective experience and highlights a dissociation between neural and experiential effects. By integrating linguistic, subjective, and neurophysiological measures, this study offers novel insights into how psychological readiness shapes the phenomenology of 5-MeO-DMT.

6.2 Introduction

5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT) is one of the most potent psychedelics known, yet remains among the least studied [661, 662]. While often grouped with classic serotonergic psychedelics, its pharmacology and phenomenology suggest a distinct profile. Unlike psilocybin, **lysergic acid diethylamide (LSD)**, or **N,N-dimethyltryptamine (N,N-DMT)**, which primarily act via 5-HT$_2$A receptor agonism and reliably induce vivid visual phenomena such as geometric imagery and entity encounters [663, 664], 5-MeO-DMT has significantly greater affinity for 5-HT$_1$A receptors than for 5-HT$_2$A, which *may* contribute to its unique effects. Rather than structured perceptual distortions, its peak experience is often characterised by a rapid and profound disruption of self-referential processing, sensory perception, and conceptual thought [665–668]. This frequently culminates in a nondual state described as *"pure awarenes*s", in which experience becomes minimally differentiated or entirely formless [669–672]. These qualitative differences have led some to describe 5-MeO-DMT as an 'atypical' psychedelic, prompting ongoing discussions about its classification [666]. Despite growing clinical interest [673], research remains sparse. **Appendix Table A6.12** summarises 16 registered clinical trials, which primarily focus on safety, pharmacokinetics, and therapeutic potential. However, no published studies have systematically documented its phenomenology, and only a single preprint has examined its neural effects in humans [674]. Moreover, how preparation practices shape its subjective effects remains entirely unexplored, despite the intensity and disorienting nature of the experience.

Understanding the neural basis of these unique subjective effects has been primarily informed by preclinical research. Studies in awake rodents have shown that 5-MeO-DMT's most pronounced neurophysiological effects involve the augmentation of low-frequency rhythms (<4Hz) [675–677]. In these studies, local field potentials showed increased low-frequency power while multi-unit recordings revealed neural activity alternating between periods of high-firing and widespread silence during normal waking behaviour - a state termed "paradoxical wakefulness" [677]. While dominance of low-frequency oscillations are typically associated with reduced consciousness, as seen in slow-wave sleep [678, 679], general anaesthesia [680], and unresponsive wakefulness syndrome [681, 682], recent human neuroimaging work challenges this interpretation. Blackburne et al. (2024) demonstrated that 5-MeO-DMT induces widespread slow rhythmic activity that, unlike in unconscious states, manifests as spatiotemporally disorganised wave patterns unable to propagate efficiently through cortical hierarchies. Rather than exhibiting the coherent, fluid, and recurrent global waves characteristic of anaesthesia, 5-MeO-DMT produces complex, incoherent, and fleeting local flow patterns. This spatiotemporal fragmentation appears to push broadband neural activity toward a more stable low-dimensional state, potentially reflecting the subjective experience of environmental disconnection and phenomenological dissolution while maintaining awareness. Given the profoundly anomalous nature of 5-MeO-DMT experiences - and the underlying neural disorganisation - preparatory practices may be crucial in helping individuals navigate these effects. In this study, we examine how spectral power changes relate to subjective experiences and whether response to specific preparation practices predicts individual differences in these experiential dynamics.

While these neural findings begin to characterise the brain states induced by 5-MeO-DMT, capturing the associated subjective experience presents unique methodological challenges. Scales such as the **Five-Dimensional Altered States of Consciousness Scale (5D-ASC)** [683], which are widely used in psychedelic research, may have less utility when investigating 5-MeO-DMT. These traditional scales of altered states effectively characterise the altered states induced by classical psychedelics, which profoundly modify phenomenal content - often introducing vivid sensory distortions, enriched perceptual imagery, and novel cognitive-affective states - while often preserving some degree of phenomenal structure. Even at high doses, classical psychedelics typically allow for retrospective reporting, suggesting that some organisational scaffolding of experience remains intact. In contrast, 5-MeO-DMT appears to more reliably disrupt the fundamental structures that organise experience itself [668, 684], often suspending self-world differentiation, temporal continuity, and sensory representation, while paradoxically preserving awareness [665, 667]. Although the 5D-ASC includes dimensions such as **oceanic boundlessness (OBN)**, which captures unity and transcendence, it presupposes the persistence of a subject capable of reporting these states - a condition that may be altered during peak 5-MeO-DMT experiences, where the self as an object of experience can dissolve entirely, even if some form of subjectivity remains. Moreover, while the 5D-ASC effectively assesses alterations in perceptual and cognitive content, it lacks measures that directly capture *contentless* awareness or the disintegration of phenomenal structure. These states are typically highly unfamiliar and quintessentially 'ineffable', creating substantial challenges in quantifying such experiences. This misalignment underscores the need for methodological approaches better suited to capturing the unique boundary-dissolving effects of 5-MeO-DMT with greater precision than can be achieved using typical psychometric approaches.

Recent efforts have sought to sidestep these measurement challenges by employing methods specifically tailored to the unique phenomenology of 5-MeO-DMT. Sanders et al. (*in review*) used micro-phenomenological interviews [75, 685] with individuals immediately following their 5-MeO-DMT sessions to construct a theoretical framework identifying six phenomenological stages of the experience (Fig. 6.1). The *Onset* phase, reported by most participants, is characterised by rapid and dynamic shifts in sensory, cognitive, and self-referential domains, often described in terms of; 'acceleration', 'dissolution', ‘fractalisation’, or ‘collapse’. Following this, participants could enter one of three distinct experiential states. The **Immersion & Merging (IM)** state involves a partial loss of awareness of the external world, accompanied by intense somatic or affective experiences, often described as a merging with emotions or energetic sensations, sometimes without a clear connection to personal identity or narrative. The **Abstract (AB)** state is a disembodied experience characterised by non-ordinary sensory phenomena. In this state, phenomena or concepts such as shapes, colours, or movement, which are characterised by visuospatial parameters often *lack* spatial, temporal, and conceptual structures and may be *felt* rather than seen. The **Everything/Nothing (EN)** state, emerging as the most radically altered, is marked by an extreme dissolution of all phenomenological distinctions, including the loss of spatial, temporal, sensory, and cognitive boundaries, often described in paradoxical terms as both a void and an all-encompassing fullness. As the experience subsides, participants transition into *Reconstitution*, where perceptual and cognitive structures sequentially reintegrate, often in an irregular or fragmented manner. This is followed by the *Afterglow* phase, a return to a more familiar conscious state, which nonetheless retains elements of clarity, emotional openness, or cognitive quietude. Bidirectional transitions were observed between certain states, suggesting fluidity within these phenomenological domains, particularly between EN and AB.

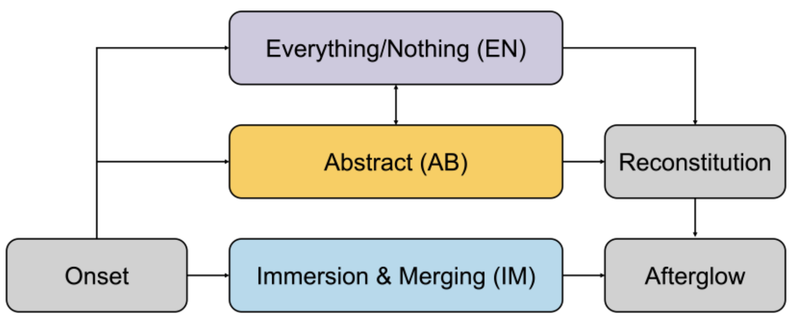


Figure 6.1. Phenomenological stages of the 5-MeO-DMT experience

A temporal progression model of the 5-MeO-DMT experience, adapted from Sanders et al. (in review). The diagram illustrates six distinct phases: Onset, characterised by rapid and intense shifts in perception; three core experiential states - Immersion & Merging (IM), Abstract (AB), and Everything/Nothing (EN) - which capture varying degrees of self-dissolution and altered sensory or cognitive features; and two later phases - Reconstitution, reflecting the gradual return of perceptual and cognitive structures, and Afterglow, a lingering state of clarity and calm. The bidirectional arrow between EN and AB indicates fluidity or potential transitions between these states.

To capture the unique subjective effects of 5-MeO-DMT, we rapidly developed and piloted the **5-MeO-DMT Phenomenology Scale (5PS)**, designed to assess the IM, AB and EN dimensions identified in Sanders et al.’s (*in review*) framework. To assess convergent validity with established constructs, we also administered the 5D-ASC, the **Altered Self-Consciousness Questionnaire (ASCQ)** (*Millière et al., in prep*), and the Emotional Breakthrough Inventory (EBI) [68] (see *Methods*).

While these tools enable a characterisation of 5-MeO-DMT experiences, it remains unclear what factors shape their emergence. One key question is whether *preparation* - widely regarded as essential in psychedelic settings [16] - modulates the subjective effects of 5-MeO-DMT. Unlike classical psychedelics, where preparation often involves setting intentions, cultivating interpretive frameworks, or familiarising oneself with altered states, 5-MeO-DMT presents a unique challenge. Its effects may transiently dissolve the very cognitive and perceptual structures through which preparation, expectation, and meaning making typically operate. Experienced facilitators emphasise the importance of preparation, yet also acknowledge this paradox: how does one prepare for an experience that may render conventional preparatory strategies irrelevant? Our prior research has shown that psychedelic preparedness, as measured by the PPS, predicts mystical-type experiences with classical psychedelics (see **Chapter 2**). However, whether similar predictive relationships hold for 5-MeO-DMT remains an open question. If the experience entails a temporary 'annihilation of selfhood', does psychedelic preparedness as defined in **Chapter 2** retain its meaning, or does the nature of the experience render conventional descriptions and definitions ineffective? More broadly, does preparation for such an encounter require an entirely different conceptualisation of what it means to be prepared?

If conventional preparation strategies are of limited relevance for 5-MeO-DMT, stable psychological traits may better predict individual responses and might inform decision-making regarding its use. One such trait is mindfulness - the tendency to sustain nonjudgmental awareness of present-moment experience without excessive cognitive elaboration or fixation on past or future thoughts [686–688]. Unlike state mindfulness, which can be cultivated through mindfulness practice [516, 689], trait mindfulness refers to an enduring capability associated with the habitual employment of an open and receptive experiential mode [690, 691]. Higher trait mindfulness has been associated with positive mental health outcomes, including life satisfaction, self-esteem, and optimism [506] and several health behaviours (i.e. physical activity, healthy eating, sleep, alcohol use) [692]. It has also demonstrated negative correlations with symptoms of depression, anxiety, and stress-related symptoms [693], neuroticism [694], difficulties in emotion regulation [505, 695], cognitive reactivity [696], and experiential avoidance [697]. In psychedelic contexts, it predicts a greater likelihood of self-transcendent states, reduced anxiety during acute effects, and enhanced long-term psychological benefits [118, 295]. Individuals with higher trait mindfulness - who are more skilled at maintaining open, non-reactive awareness - may therefore be better equipped to surrender to the peak dissolution induced by 5-MeO-DMT, enhancing the likelihood of experiencing, for example, deeper EN states.

While self-report measures like the PPS provide insight into explicit preparation, research suggests that linguistic patterns offer a complementary perspective by revealing underlying psychological states that may not be accessible through direct introspection. Given the limited availability of behavioural measures for assessing mindfulness, linguistic analysis presents a valuable tool for identifying implicit markers of psychological readiness beyond self-report. Previous studies have explored linguistic markers of mindfulness in contexts such as substance addiction treatment [698], trauma recollections [699], and cognitive processing [700], highlighting the potential for language to reflect internal cognitive and affective states. More broadly, language is not merely a vehicle for communication but a reflection of distributed neural processes across emotional and cognitive networks [701], closely tied to psychological wellbeing and inner states [702, 703]. Prior research has successfully leveraged linguistic analysis to detect markers of emotional expression and cognitive processing [704] and to predict treatment outcomes in psychedelic therapy, achieving up to 85% accuracy in forecasting psilocybin response from baseline interviews [705, 706]. Since language fundamentally structures experience - particularly in constructing the narrative self [707], which psychedelics profoundly disrupt [300, 708] - linguistic markers may provide a novel means of assessing psychological readiness for 5-MeO-DMT. To investigate this, we examined both explicit preparedness via PPS scores and implicit readiness through natural language processing of participants' baseline verbal expressions, with a particular focus on mindfulness-related linguistic patterns. This dual approach allowed us to capture both conscious and unconscious aspects of readiness, recognising that preparation for an experience as radical as 5-MeO-DMT may require frameworks that extend beyond conventional cognitive models.

In the present study, we sought to address these fundamental questions about preparation, measurement, and neural correlates of 5-MeO-DMT experiences through a multi-modal investigation combining quantitative self-report measures, natural language analysis, and EEG recordings. We examined how both explicit preparedness (measured through the PPS) and implicit psychological readiness (assessed through mindfulness-related language patterns) might predict the intensity and quality of subjective experiences. Additionally, we investigated the relationship between specific neural signatures - particularly changes in oscillatory power across frequency bands - and various dimensions of subjective experience captured through both standard psychedelic measures and novel instruments designed specifically for 5-MeO-DMT phenomenology. Through this comprehensive approach, we aimed to characterise not only the neural and experiential dynamics of 5-MeO-DMT states, but also to better understand how preparation might influence these profound alterations of consciousness, while remaining mindful of the inherent limitations in measuring experiences that may transcend ordinary frameworks of measurement and description.

6.3 Methods

The study adhered to the principles outlined in the Helsinki Declaration and received approval from UCL REC (ID:19437/004). It was carried out in collaboration with the **Tandava Retreat Centre (TRC),** which provided facilitators and facilities. Participants provided informed consent online after reviewing the study information. Participation was voluntary and without compensation. Participants were free to withdraw at any time without repercussions and were given information on support resources in case of any study-related distress.

6.3.1 Participants and recruitment

Study recruitment occurred globally via multiple channels, including the **F.I.V.E (5-MeO-DMT Information & Vital Education)** platform, social media platforms, news media, and word-of-mouth referrals. The clinical screening process at TRC consisted of an online screening followed by an interview with a TRC facilitator. After completing the TRC screening process, participants were informed about the research study and provided with an information sheet. Those interested in participating followed a link provided in the information sheet to complete the research screening process, which included a UCL online assessment and an interview with UCL researchers to determine study eligibility.

Participants were eligible if they were able to provide informed consent and were willing to complete all research procedures, including wearing an EEG cap during their 5-MeO-DMT experience. Of 36 participants screened by UCL, 32 were enrolled in the study. Three participants withdrew before the retreats began, resulting in 29 participants completing the in-person data collection. Exclusion criteria included: being under 18 years old, having no previous 5-MeO-DMT exposure, having significant self-declared physical conditions (including epilepsy or heart disease), having psychiatric diagnoses, taking psychiatric medications, reporting family history of psychosis, having previous adverse reactions to psychedelics, or having a history of significant physical movement during previous 5-MeO-DMT experiences (as EEG data collection required participants to remain relatively still). Participants were required to adhere to a two-week abstinence period from psychoactive substances (including alcohol) prior to the retreat, with nicotine being the only permitted exception.

6.3.2 Procedures

Each participant followed the same study timeline, consisting of pre-retreat remote data collection (self-report surveys, cognitive tasks, and voice recordings (experience sampling)), a three-day retreat (self-report surveys, micro-phenomenological interviews, and EEG recordings during 5-MeO-DMT administration), and post-retreat remote data collection (self-report surveys, cognitive tasks, and voice recordings (experience sampling)). See **Fig. 6.2** for a detailed study timeline. This protocol was repeated across six retreats, each with a maximum of six participants, conducted between January and February 2024. For this current analysis, we focus specifically on self-report questionnaires administered at t_1 and t_4, qualitative voice recordings gathered in the week preceding the retreat (t_2), and EEG recordings collected during 5-MeO-DMT administration (t_3).

Qualitative data collection via *Retreat-Bot*

For seven days preceding the 5-MeO-DMT session (t_2), qualitative data were collected using *Retreat-Bot,* a custom-built **ecological momentary assessment (EMA)** tool deployed via the Telegram messaging platform and implemented through OneReach.AI services. Designed as a structured, rule-based chatbot rather than a dynamic conversational AI, *Retreat-Bot* followed a predefined decision-tree model. The familiar chat-based interface was selected to facilitate engagement for participants (**Fig. 6.3**). *Retreat-Bot* delivered automated prompts at a participant-selected evening notification time (after 18:00), instructing: "*Take a moment to reflect on your day and share your thoughts, feelings, and experiences. Record a voice note for about one minute*". While structured prompts guided daily submissions, participants could also contribute spontaneous recordings at any time, including beyond the core study period. All voice data were securely stored on a dedicated server, ensuring confidentiality and data integrity.

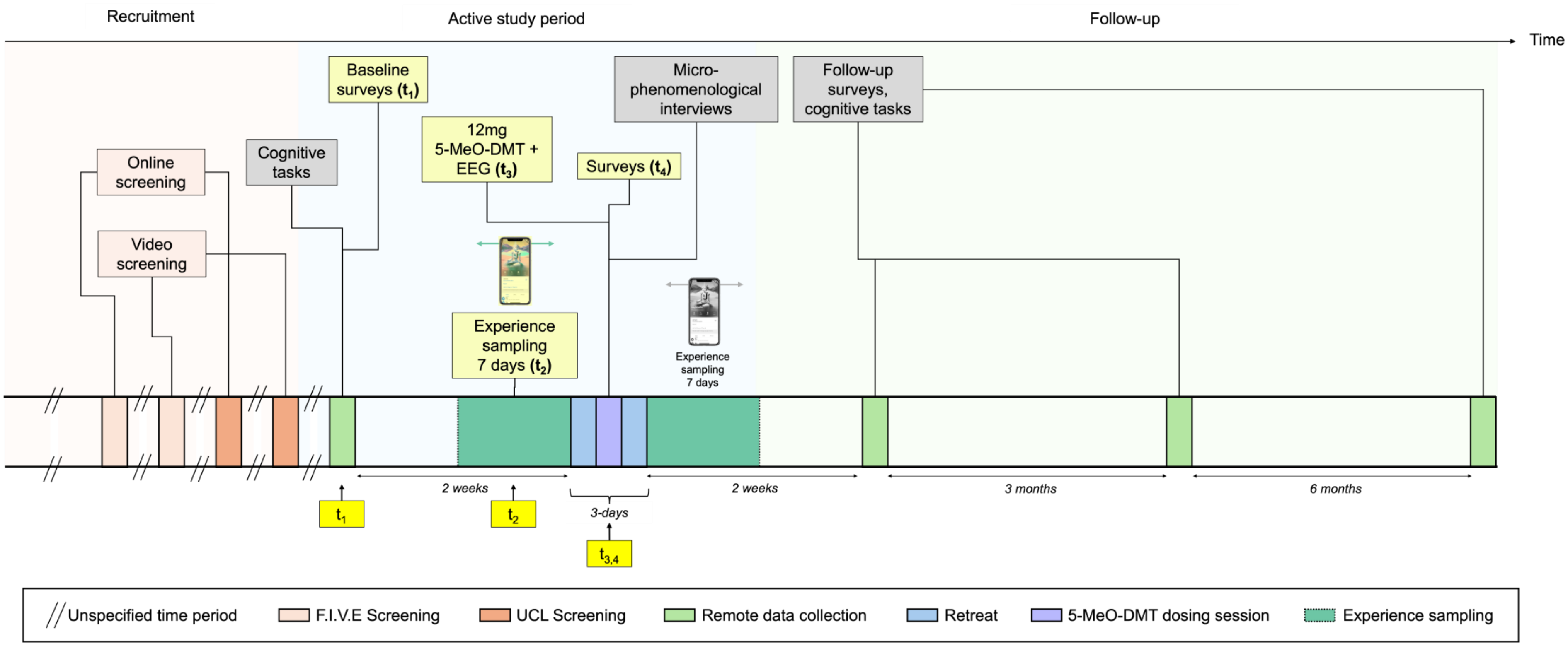


Figure 6.2. 5-MeO-DMT retreat study timeline and data collection phases

Schematic representation of the study timeline, showing the sequence of participant assessments across pre-retreat, retreat, and post-retreat phases. For this current analysis, we focus on self-report questionnaires administered at t_2 and t_4, qualitative voice recordings gathered in the week preceding the retreat (t_2), and EEG recordings collected during 5-MeO-DMT administration (t_3).

Figure 6.3. Images of the Retreat-Bot interface

Illustrating the home screen and step-by-step instructions for journal entry submission during registration.

3-day retreat protocol

The first day of each retreat focused on preparation. Given participants' prior experience with 5-MeO-DMT, much of the typical content usually included in TRC's preparation protocol - such as information on the substance's effects - was condensed. Instead, there was a greater emphasis on the research setup, safety protocols, and what participants could expect during the dosing session. Participants were introduced to the study procedures, including the roles of the researchers and facilitators, as well as the timing of the 5-MeO-DMT dosing session. Additionally, researchers familiarised participants with the EEG equipment, providing clear instructions to remain still until the 20-minute Koshi bell signalled the end of EEG data collection. This careful preparation ensured participants were well-informed and comfortable with the study logistics and the upcoming experience.

On the second day (t_3) participants were administered 5-MeO-DMT individually. Prior to administration, a 7-minute baseline eye-closed resting-state EEG recording was conducted. During this time, participants were seated in a self-selected comfortable position and instructed to remain relaxed yet alert. After the baseline recording, participants transitioned to a centrally located padded recliner, assuming a semi-supine position with a standardised neck pillow and opaque eye mask. A brief 2–3-minute relaxation exercise was then performed to prepare participants for the substance administration. During this period, the synthetic 5-MeO-DMT (12 mg) was vaporised using an argon gas piston vaporiser at 203-210°C over approximately

120 seconds. At the end of the relaxation exercise, participants inhaled the fully vaporised compound in a single breath, following a standardised protocol. Images of the EEG setup, administration setting, and vaporisation equipment can be seen in **Appendix A6.11**.

The EEG data sampling period began immediately after inhalation and continued for 20 minutes post-inhalation to capture the full duration of the acute drug effects. During this time, EEG data were collected using a saline-based 64-channel ANT Neuro Waveguard Net, connected to an NA-261 EEG amplifier, and recorded at 500 Hz. Electrodes were positioned according to the 10-20 system (reference: CPz, ground: AFz), with impedance maintained below 20 kΩ. Ambient non-percussive music played continuously throughout both the baseline and drug administration periods, contributing to a consistent sensory environment. A Koshi bell rang at the end of the 20-minute EEG recording, after which participants remained in a resting state for a self-determined period under continuous supervision. One hour after dosing, once acute drug effects had fully subsided, participants provided retrospective ratings of peak subjective effects.

On the final day, TRC facilitators led group integration sessions, beginning with guided breathing exercises and a short meditation. Each participant was then invited to share for about five minutes on their experience and current feelings. Facilitators provided recommendations for maintaining well-being post-retreat and offered participants unlimited access to TRC's biweekly online integration groups for continued support.

6.3.3 Measures

Self-report questionnaires

Demographic characteristics (t_1)

Demographic data were collected from all participants, including age, gender, ethnicity, education, religious affiliation, and languages spoken. Additionally, participants reported on their lifetime experience with 5-MeO-DMT.

Psychedelic preparedness (t_1)

The Psychedelic Preparedness Scale (PPS) is a 20-item instrument (developed and validated in **Chapter 2**) designed to assess an individual's readiness for a psychedelic experience across four subscales: Knowledge-Expectation (KE), Intention-Preparation (IP), Psychophysical-Readiness (PR), and Support-Planning (SP). Participants rate their agreement with each item on a 7-point Likert scale, ranging from "Not at all" to

"Completely". Subscale scores were calculated by averaging responses for the relevant items, with a maximum score of 7, while the total score was the sum of all items, with a maximum of 140.

Altered state of consciousness (t_4)

The Five-Dimensional Altered States of Consciousness (5D-ASC) scale (94 items) evaluates the intensity and characteristics of the acute psychedelic experience across five primary dimensions: oceanic boundlessness (OBN) (27 items), dread of ego dissolution (DED) (21 items), visionary restructuralisation (VRS) (18 items), auditory alterations (AA) (16 items), and vigilance reduction (VIR) (12 items) [683]. Participants rate the degree to which each statement deviated from their normal waking consciousness using a visual analogue scale (0-100), where 0 represents "No, not at all" and 100 signifies "Yes, much more than usual". Scores for each dimension were normalised to a 0-1 scale to enable direct comparison.

5-MeO-DMT phenomenology (t_4)

The 5-MeO-DMT Phenomenology Scale (5PS) was developed to assess the three distinct phenomenological domains identified in Sanders et al.'s (*in review*) theoretical model (see **Fig. 6.1**): Everything/Nothing (EN) (21 items reflecting experiences of ego dissolution, non-duality, and transcendent states), Abstract (AB) (6 items covering spatial sensations and geometric patterns), and Immersion & Merging (IM) (3 items addressing bodily awareness and environmental connectedness). Two additional subscales, Visionary (VI) (3 items capturing memory recall and sensing presences) and Affective (AF) (4 items measuring emotional and sexual experiences, and resistance), were included to capture additional phenomenological features identified in the initial micro-phenomenological interviews. Participants were instructed to identify a single moment when the effects of 5-MeO-DMT were most intense (the 'peak') and rate all items based solely on this part of their experience. Using a slider, participants rated each item from 0 ("Not at all") to 100 ("Very strongly so"), indicating how strongly each statement described their peak experience. They were encouraged to use the full range of the scale, reserving scores of 0 or 100 for when truly appropriate. All items can be found in **Appendix S6.1**.

Altered self-consciousness (t_4)

The Altered Self-Consciousness Questionnaire (ASCQ) is a 25-item instrument developed by Millière (*in prep*) to assess alterations in self-experience during psychedelic states. The questionnaire captures a range of phenomena including changes in thought ownership, spatial orientation, bodily awareness, personal identity, loss of consciousness, and self-world boundaries. Participants rated each item on a visual analogue scale from 0 ("No, not at all") to 100 ("Yes, completely"), indicating the degree to which they experienced each phenomenon during their 5-MeO-DMT session. All items can be found in **Appendix S6.2**. The regression models use mean ASCQ scores.

Emotional breakthrough (t_4)

The Emotional Breakthrough Inventory (EBI) [68] assesses, retrospectively, episodes of catharsis or emotional release following a psychedelic experience. It is a 6-item scale scored on 0 to 100 visual analogue scale (VAS). The regression models use total EBI scores, ranging from zero to 600.

6.3.4 Data analysis

All data analysis was performed using Python 3.12.2.

Preprocessing

Natural Language Processing (NLP)

Linguistic analysis included 25 participants who provided pre-retreat voice recordings (t_2) and completed all questionnaires ($t_{1,4}$) (four participants were excluded due to incomplete data). Upon submission, voice recordings were automatically transcribed using AssemblyAI's automated speech recognition system (AssemblyAI, 2023) and underwent two rounds of manual qualitative checks to correct transcription errors. Transcripts were segmented into sentences using the NLTK sentence tokeniser [709], and empty entries (i.e., those containing no spoken text) were removed from the dataset. As this study focused only on pre-retreat voice notes, all included entries were recorded within the 14-day period before the retreat up to the dosing event (full pre-post analysis is reported in Kuc et al., *in prep*).

To quantify **baseline mindfulness language (BML),** transcripts were analysed using **Linguistic Inquiry and Word Count (LIWC)** software [703] with a validated mindfulness dictionary [698]. The mindfulness dictionary comprises two primary categories: *Mindfulness: State* (capturing present-moment awareness and acceptance) and *Mindfulness: Journey* (reflecting the ongoing process of cultivating mindfulness). For our analysis, we aggregated these categories to create a comprehensive mindfulness language score that encompassed both experiential states and developmental aspects of mindfulness practice. The dictionary includes terms such as 'awareness', 'present', 'accept*', 'gratitude', 'mindful*', and 'allow*', with asterisks denoting word-stem variations. LIWC scores reflect the proportion of words in each text that belong to predefined categories. For example, in the sentence *"I feel calm"*, one of the three words ("calm") appears in the mindfulness dictionary, yielding a sentence-level score of 1/3 ≈ 0.33.

For each participant, we computed weighted mean BML scores to ensure that longer, more substantive reflections had proportionally greater influence. This was calculated as:

$$Weighted\ Mean = \frac{\sum(WordCounti \times LIWCScorei)}{\sum WordCounti}$$

where $WordCount_i$ is the number of words in sentence i, and $LIWCScore_i$ is the proportion of mindfulness-related words in that sentence. This method ensured that each sentence's contribution to the overall mean was proportional to its length, providing a more accurate representation of participants' linguistic profiles in the pre-retreat period.

EEG

As detailed in Blackburne et al. (2024), EEG data underwent preprocessing using MNE-Python. Key preprocessing steps included: application of a **finite impulse response (FIR)** bandpass filter (0.1-50 Hz), segmentation into non-overlapping 3-second epochs (140 epochs for baseline (7 minutes), 400 for drug condition (20 minutes)), electrolyte bridging assessment using the intrinsic Hjorth algorithm ($16\mu V^2$ cut-off), bad channel interpolation (Rest: 7.579 ± 1.049, 5-MeO-DMT: 7.368 ± 1.06 channels), and extended infomax **independent component analysis (ICA)** for artifact removal. Following quality control procedures, which excluded participants with excessive artifacts (>50% contaminated data) in the first 10 minutes post-administration, 19 participants' data were available for analysis (after exclusions for physiological artifacts (n=10) and electrolyte bridging (n=1)). For complete preprocessing specifications and validation methodology, see [674].

Statistical analyses

Descriptive statistics

Descriptive statistics, including means, standard deviations, ranges, and 95% confidence intervals (CIs), were calculated for the 5D-ASC and 5PS subscales, as well as the EBI, ASCQ, PPS, and BML scores. For the BML measure, participants provided voice recordings during the analysis window (days -14 to 0 relative to 5-MeO-DMT administration). Descriptive analyses were conducted on the number of recordings contributed per participant, the number of sentences per recording, and the pre-retreat weighted BML scores.

Analysis of variance

To compare the relative intensities of different experiential dimensions, we conducted two separate one-way within-subjects ANOVAs: one comparing the five 5D-ASC subscales (OBN, DED, VRS, AUA, VIR), and another comparing the three core 5PS dimensions (EN, AB, IM). Mauchly's test was used to evaluate sphericity, with Greenhouse-Geisser corrections applied when necessary (indicated by non-integer degrees of freedom; see **Appendix A6.3**). Post-hoc pairwise comparisons were conducted using paired t-tests with p-values adjusted according to the Benjamini-Hochberg **False Discovery Rate (FDR)** procedure to control for multiple comparisons ($\alpha = .05$).

Regression models

Associations between the 5D-ASC subscales and 5PS dimensions were examined using Pearson correlations with FDR correction.

Multiple regression analyses examined whether PPS and BML scores predicted acute psychedelic experiences across four domains: OBN (5D-ASC), EN (5PS), and total scores on the ASCQ and EBI. To facilitate direct comparison across measures with different scales, all outcome variables were standardised (z-scored) prior to analysis. Initial bivariate relationships between predictors (PPS, BML) and outcome measures were assessed using Pearson correlations, with FDR correction applied to control for multiple comparisons. Regression models tested main effects and interactions using mean-centered predictors. To formally quantify the unique contribution of the interaction between PPS and BML, we conducted hierarchical regression analyses. For each outcome variable, we first estimated a model with only main effects (PPS and BML), followed by a second model that included the interaction term (PPS × BML). The change in R^2 (ΔR^2) was calculated to determine the amount of additional variance explained by the interaction effect, and its significance was tested using an F-test comparing the two nested models. Significant interactions were decomposed using simple slopes analyses at ±1 SD of BML. All tests were two-tailed ($\alpha = .05$). Effect sizes are reported as Pearson's r for correlations, adjusted R^2 for regression models, and ΔR^2 for the unique contribution of interaction terms. Model assumptions were verified through examination of residual plots and variance inflation factors (all VIFs < 1.5; see **Appendix A6.4**).

Multiple regression analyses examined whether PPS and BML scores predicted acute psychedelic experiences across four domains: OBN (5D-ASC), EN (5PS), ASCQ and EBI scores. To facilitate direct comparison across measures with different scales, all outcome variables were standardised (z-scored) prior to analysis. Initial bivariate relationships between predictors (PPS, BML) and outcome measures were assessed using Pearson correlations, with FDR correction applied to control for multiple comparisons. Regression models tested main effects and interactions using mean-centered predictors. Significant interactions involving baseline mindfulness (BML) were decomposed using simple slopes analyses at ±1 SD of BML. All tests were two-tailed ($\alpha = .05$). Effect sizes are reported as Pearson's r for correlations and adjusted R^2 for regression models. Model assumptions were verified through examination of residual plots and variance inflation factors (all VIFs < 1.5; see **Appendix A6.4**).

We conducted correlation analyses between EEG spectral power changes and self-report measures of subjective experiences. First, we correlated region-level power changes (frontal, central, temporal, parietal, occipital) with OBN, EN and ASCQ scores. Second, we performed electrode-level correlations between power changes and these scores. At each analysis level, we computed Pearson correlations with FDR correction.

EEG analyses

EEG data were analysed using **Empirical Mode Decomposition (EMD),** selected for its suitability with non-linear and non-stationary signals characteristic of rapidly changing altered states under 5-MeO-DMT. For each participant (N = 19), EMD-derived power spectra were computed for resting baseline and peak drug effect periods (1.5–2.5 minutes post-administration). Analyses examined six frequency bands: slow oscillations (0.5–1.5 Hz), delta (1.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz), and gamma (30–50 Hz). Power values were log-transformed, and time-frequency dynamics were visualised using participant-averaged EMD spectrograms across the 20-minute recording period. Electrode-level topographical analyses compared baseline and drug conditions for each electrode using paired t-tests with FDR correction ($\alpha = .05$) across all 64 electrodes and 6 frequency bands. Regional analyses grouped electrodes into five cortical regions (frontal, central, parietal, temporal, occipital; electrode assignments in Appendix A6.6). For each region, power values were averaged across all electrodes within that region to calculate a single mean power value per region. These regional mean power values were then compared between baseline and drug conditions using paired t-tests with FDR correction across all 5 regions and 6 frequency bands. All paired comparisons report Cohen's d effect sizes.

6.4 Results

Sample characteristics

The sample consisted of 29 participants (16 male, 13 females; mean age = 48.52 years, SD = 10.44, range = 34–75). Participants were predominantly White/Caucasian (86.21%) and American (79.31%), with most holding a bachelor's degree (58.62%) and identifying as non-religious (93.10%). Mean lifetime 5-MeO-DMT use was 39.03 occasions (SD = 72.91, range = 1-300). Detailed demographic characteristics are provided in **Appendix A6.7**.

6.4.1 Self-report analyses

Descriptive statistics for all measures are provided in **Appendix A6.8**. Individual item-level responses from the 5PS, ASCQ, and EBI are visualised in **Fig. 6.4c-e**.

Analysis of 5D-ASC subscales showed that different aspects of altered states were differentially affected by 5-MeO-DMT ($F(1.52, 36.58) = 13.46$, $p < .001$, $\eta p^2 = 0.359$). Post-hoc analyses with FDR correction showed that OBN scores were significantly higher than all other subscales: DED ($t(24) = 6.31$, $p < .001$, $d = 1.84$)) VRS ($t(24) = 7.83$, $p < .001$, $d = 1.41$)), AUA ($(24) = 5.24$, $p < .001$, $d = 1.20$)), and vigilance reduction VIR ($t(24) = 4.36$, $p < .001$, $d = 1.18$)). No significant differences were found between the remaining subscales (**Fig. 6.4a**). Similarly, analysis of 5PS subscales revealed differential effects across the three dimensions ($F(2, 48) = 13.04$, $p < .001$, $\eta p^2 = 0.352$). Post-hoc analyses with FDR correction showed a hierarchical pattern: EN ratings were significantly higher than both AB ($t(24) = 2.86$, $p = 0.009$, $d = 0.55$)) and IM ($t(24) = 4.29$, $p < .001$, $d = 1.14$)), and AB scores were significantly higher than IM ($t(24) = 2.89$, $p = 0.009$, $d = 0.57$; **Fig. 6.4b**).

Correlation analyses only revealed significant relationships if non-adjusted p values were used between VRS and IM ($r = .54$, $p_{non\text{-}adjusted} = .006$, $p_{FDR} = .086$) and between OBN and EN ($r = .42$, $p_{non\text{-}adjusted} = .038$, $p_{FDR} = .218$; **Fig. 6.4f**). All other non-adjusted relationships were non-significant.

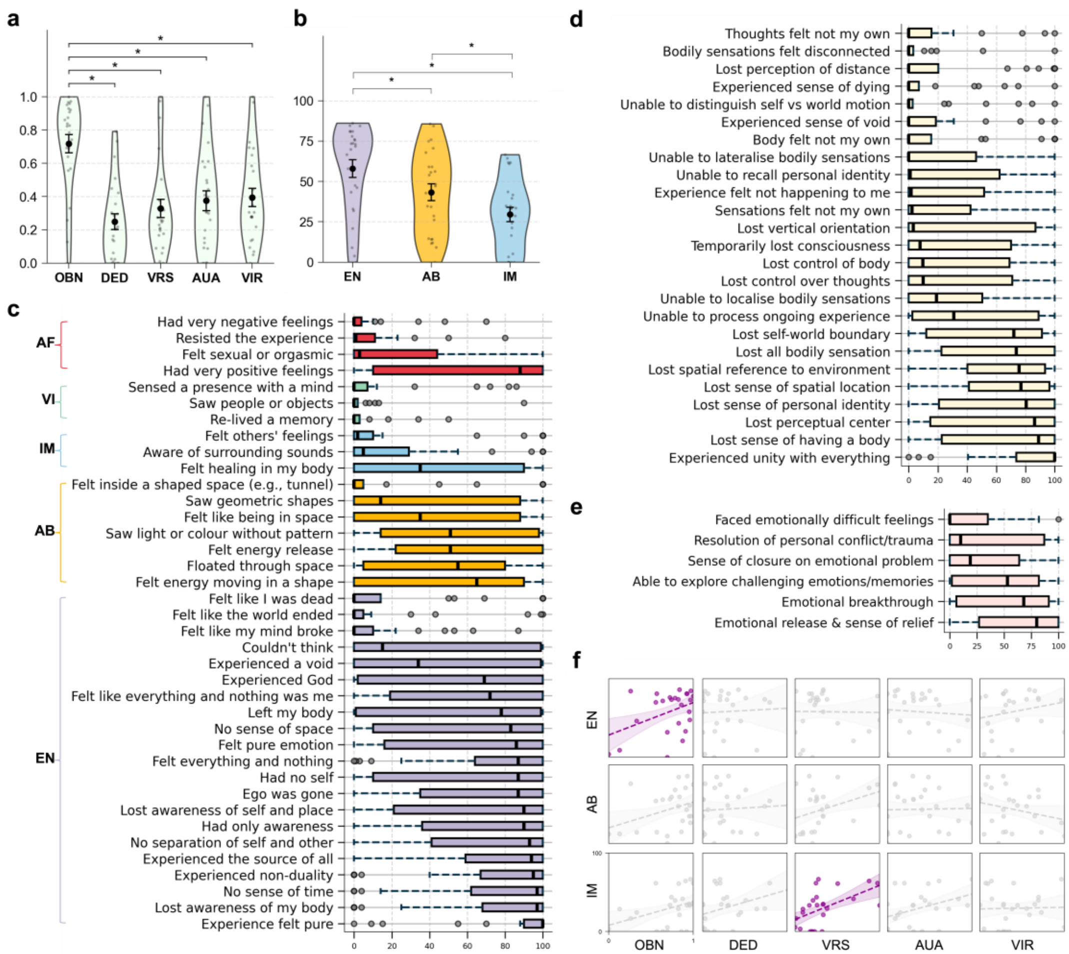


Figure 6.4. 5-MeO-DMT subjective effects

(a) 5D-ASC subscale scores showing significantly higher Oceanic Boundlessness (OBN) compared to Visionary Restructuralisation (VRS), Dread of Ego Dissolution (DED), Auditory Alterations (AUA), and Vigilance Reduction (VIR); (b) 5PS dimension scores showing Everything & Nothing (EN) significantly higher than both Abstract and Immersion & Merging, with AB also exceeding IM; (c) Individual 5PS item responses by dimension (EN: purple, AB: yellow, IM: blue, VI (Visionary): green, AF (Affective): red); (d) Altered Self-Consciousness Questionnaire (ASCQ) item responses; (e) Emotional Breakthrough Inventory (EBI) item responses; (f) Correlations between 5D-ASC subscales and 5PS dimensions, with significant relationships (non-adjusted) in dark magenta. Box plots (c-e) show median, IQR, and whiskers (1.5×IQR). Shaded regions in f represent 95% confidence intervals.

6.4.2 Predictors of subjective experience

The two main predictors of interest were PPS scores and BML scores. PPS scores ranged from 103 to 140, with a mean of 124.52 (SD = 10.60), 95% CI [120.14, 128.90]. Further details on PPS subscales are provided in **Appendix A6.8**.

BML scores, derived from participants' voice recordings before the retreat, had a mean of 4.40 (SD = 1.19, range: 2.60-7.74; **Fig. 6.5d**).

Participants contributed a total of 157 voice recordings during the analysis window (days -14 to 0 relative to 5-MeO-DMT administration; **Fig. 6.5a**). Each participant provided an average of 6.3 recordings (SD = 3.4, range: 1-16; **Fig. 6.5b**). Within each recording, participants produced an average of 13.2 sentences (SD = 8.0, range: 1-47; **Fig. 6.5c**). These voice samples were used to compute BML scores, which served as a linguistic proxy for mindfulness in subsequent analyses.

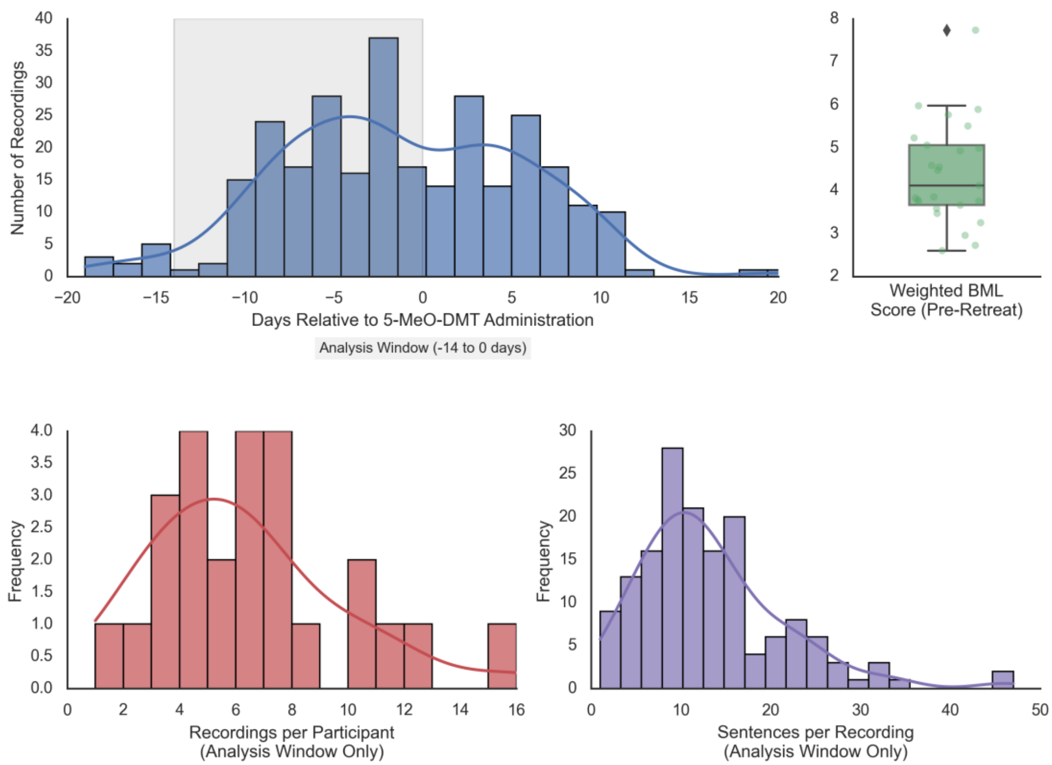


Figure 6.5. Voice recording characteristics and baseline mindfulness distribution

(a) Distribution of number of voice recordings relative to 5-MeO-DMT administration, with grey shading indicating the analysis window (-14 to 0 days). (b) Frequency of recordings per participant within the analysis window. (c) Distribution of sentences per recording within the analysis window. (d) Pre-retreat Baseline Mindfulness Language (BML) scores shown as a boxplot with individual participant data points (N = 25).

Bivariate correlations between preparation, mindfulness, and subjective psychedelic effects were examined. Before correction for multiple comparisons, PPS was positively correlated with BML ($r = 0.475$, $p_{non\text{-}adjusted} = .016$) and OBN ($r = 0.419$, $p_{non\text{-}adjusted} = .037$). BML was also positively correlated with OBN ($r = 0.433$, $p_{non\text{-}adjusted} = .030$). However, after applying FDR correction, none of these correlations remained statistically significant (all ps > .10). Neither PPS nor BML showed significant correlations with EN, ASCQ, or EBI measures before or after correction.

To examine the interactive effects of PPS and BML on the acute subjective effects, we conducted hierarchical regression analyses for each outcome measure. **Table 6.1** presents the full regression models with interaction terms, and **Appendix A6.5** summarises the hierarchical regression results and variance explained by the interaction effects.

Table 6.1. Multiple regression results for 5-MeO-DMT subjective effects

Model	R^2	Adj. R^2	F	p (F-stat)	Predictor	β	SE	t	p	95% CI Lower	95% CI Upper
OBN	0.38	0.30	4.35	**.016***	Intercept	0.21	0.19	1.08	.294	-0.19	0.61
					PPS	0.01	0.02	0.35	.734	-0.04	0.05
					BML	0.42	0.18	2.33	**.030***	0.04	0.80
					PPS × BML	-0.04	0.02	-2.16	**.043***	-0.07	-0.00
EN	0.39	0.30	4.39	**.015***	Intercept	0.33	0.19	1.68	.108	-0.08	0.73
					PPS	-0.01	0.02	-0.57	.572	-0.05	0.03
					BML	0.32	0.18	1.79	.088	-0.05	0.70
					PPS × BML	-0.06	0.02	-3.36	**.003***	-0.09	-0.02
ASCQ	0.19	0.07	1.61	.218	Intercept	0.23	0.22	1.03	.313	-0.23	0.69
					PPS	-0.01	0.02	-0.52	.607	-0.06	0.04
					BML	0.25	0.21	1.20	.245	-0.18	0.68
					PPS × BML	-0.04	0.02	-2.07	.051	-0.08	0.00
EBI	0.10	-0.03	0.78	.521	Intercept	0.08	0.23	0.34	.739	-0.41	0.57
					PPS	-0.00	0.03	-0.07	.944	-0.05	0.05
					BML	0.27	0.22	1.25	.224	-0.18	0.73
					PPS × BML	-0.01	0.02	-0.68	.506	-0.06	0.03

Note. OBN (5D-ASC) = Oceanic Boundlessness; EN (5PS) = Everything/Nothing; ASCQ = Altered Self Consciousness Scale; EBI = Emotional Breakthrough Index. PPS = Psychedelic Preparation Score; BML = Baseline Mindfulness Score. R^2 = proportion of variance explained by the full model; Adj. R^2 = adjusted R^2; F = F-statistic for the overall model with associated p-value (p (F-stat)). All predictors are mean-centered. β = standardised regression coefficient. 95% CI = 95% confidence interval for β. Asterisks indicate statistical significance at $p < .05$.

For OBN (full model $R^2 = .38$, $p = .016$), we found a significant main effect of baseline mindfulness (BML, $p = .030$), indicating that higher BML was associated with stronger OBN experiences. This was qualified by a significant PPS × BML interaction ($p = .043$; see **Figure 6.6a**). The addition of the interaction term explained an additional 13.6% of variance beyond the main effects model ($\Delta R^2 = .136$, $p = .043$). Simple slopes analysis revealed that at low BML (-1 SD), preparation was positively associated with OBN (B =

0.043, SE = 0.020, $p = .043$), whereas at high BML (+1 SD), preparation was not significantly associated with OBN (B = -0.029, SE = 0.032, $p = .365$). These results suggest that preparation particularly benefits individuals with lower baseline mindfulness.

For EN (full model $R^2 = .39$, $p = .015$), we found a marginally significant main effect of baseline mindfulness (BML, $p = .088$) and a significant PPS × BML interaction ($p = .003$; see **Figure 6.6b**). Notably, the interaction term accounted for a substantial 33.0% of additional variance beyond the main effects ($\Delta R^2 = .330$, $p = .003$), representing the strongest interaction effect observed across all outcome measures. Simple slopes analysis revealed differential effects: at low BML (-1 SD), preparation was positively associated with EN (B = 0.045, SE = 0.020, $p = .037$), whereas at high BML (+1 SD), preparation was negatively associated with EN (B = -0.068, SE = 0.031, $p = .042$). This suggests that preparation enhances EN experiences for individuals with lower baseline mindfulness but may dampen them for those with higher baseline mindfulness.

For ASCQ, the hierarchical analysis revealed that the interaction term explained an additional 16.6% of variance ($\Delta R^2 = .166$), though this effect was marginally significant ($p = .051$; see **Figure 6.6c**). For EBI, the interaction explained only 2.0% additional variance and was not statistically significant ($\Delta R^2 = .020$, $p = .506$; see **Figure 6.6d**).

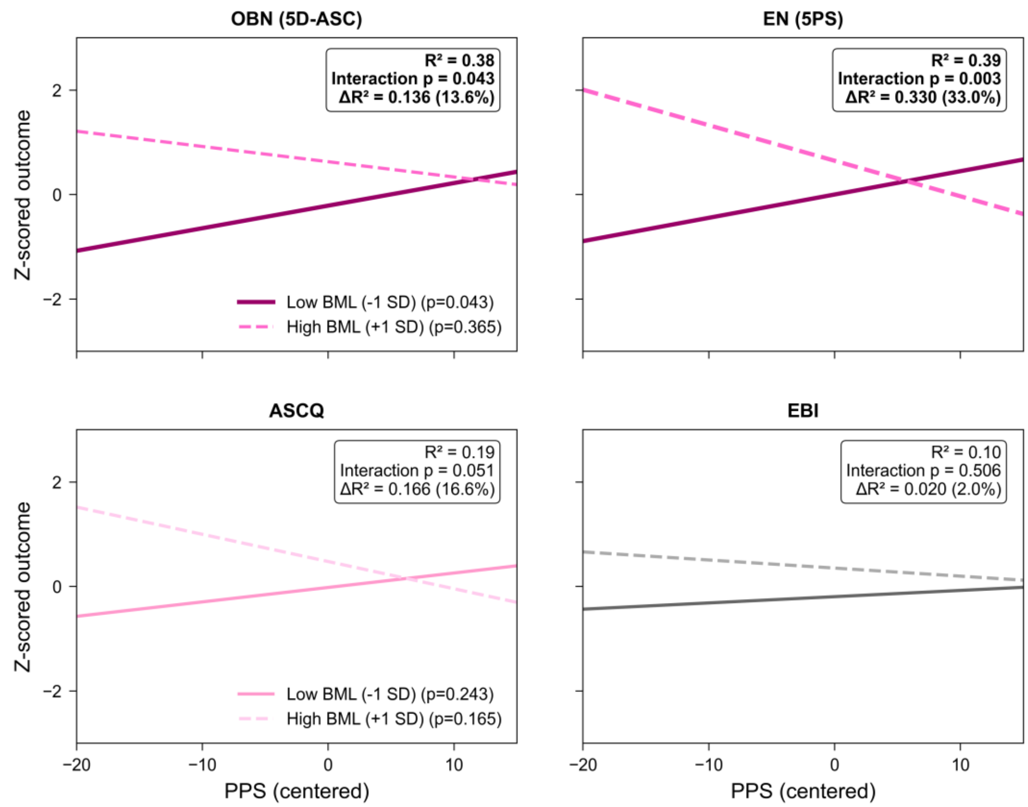


Figure 6.6. Baseline mindfulness moderates the effect of psychedelic preparedness on 5-MeO-DMT subjective experience

Simple slopes analysis showing the interaction between Psychedelic Preparation Scale (PPS) scores and baseline mindfulness levels (BML) on (a) oceanic boundlessness (OBN; 5D-ASC), (b) Everything/Nothing (EN; 5PS), (c) altered self-consciousness (ASCQ), and (d) emotional breakthrough (EBI). Solid and dashed lines represent the relationship between PPS (centered) and each outcome at low (-1 SD) and high (+1 SD) BML, respectively. Significant interactions were observed for OBN and EN, with a marginally significant interaction for ASCQ, while the interaction for EBI was not significant.

6.4.3 EEG analyses

Group-level spectral analysis revealed distinct frequency-dependent changes following 5-MeO-DMT administration (**Fig. 6.7a**). Time-frequency analysis demonstrated changes in spectral power throughout the recording period (**Fig. 6.7b**), with particularly pronounced effects in lower frequencies. We conducted two complementary analyses: a topographical analysis across all electrodes (FDR-corrected across 64 electrodes × 6 frequency bands) and a regional analysis (FDR-corrected across 5 regions × 6 frequency bands). The most prominent effects were observed in slow oscillations (0.5-1.5 Hz), where we found significant increases in power across all cortical regions (all $p_{FDR} < 0.004$; **Fig. 6.7c**). The largest effect was observed in the parietal region ($t(18) = 5.72$, $p_{FDR} = 0.001$, $d = 1.68$), followed by comparably strong effects in frontal ($t(18) = 4.56$, $p_{FDR} = 0.004$, $d = 1.38$) and temporal regions ($t(18) = 4.08$, $p_{FDR} = 0.004$, $d = 1.33$). In the delta band (1.5-4 Hz), significant increases were observed in central ($t(18) = 2.80$, $p_{FDR} = 0.044$, $d = 0.88$) and frontal regions ($t(18) = 2.66$, $p_{FDR} = 0.044$, $d = 0.91$; **Fig. 6.7d**). Higher frequency bands (≥8 Hz) showed a more complex pattern of increases and decreases. Alpha power (8-12 Hz) significantly decreased in occipital regions ($t(18) = 2.96$, $p_{FDR} = 0.042$, $d = -0.59$) while increasing in temporal areas ($t(18) = 2.60$, $p_{FDR} = 0.044$, $d = 0.56$) (Fig. 6.7f). In the gamma band (30-50 Hz), we observed significant power increases in frontal ($t(18) = 2.70$, $p_{FDR} = 0.044$, $d = 0.89$), parietal ($t(18) = 2.57$, $p_{FDR} = 0.044$, $d = 0.84$), and temporal regions ($t(18) = 2.86$, $p_{FDR} = 0.044$, $d = 0.93$) (Fig. 6.7i). No significant changes were detected in the theta band (4-8 Hz) across any region (all $p_{FDR} > 0.230$; **Fig. 6.7e**)). For detailed statistical results across all frequency bands and brain regions, see **Appendix A6.9**.

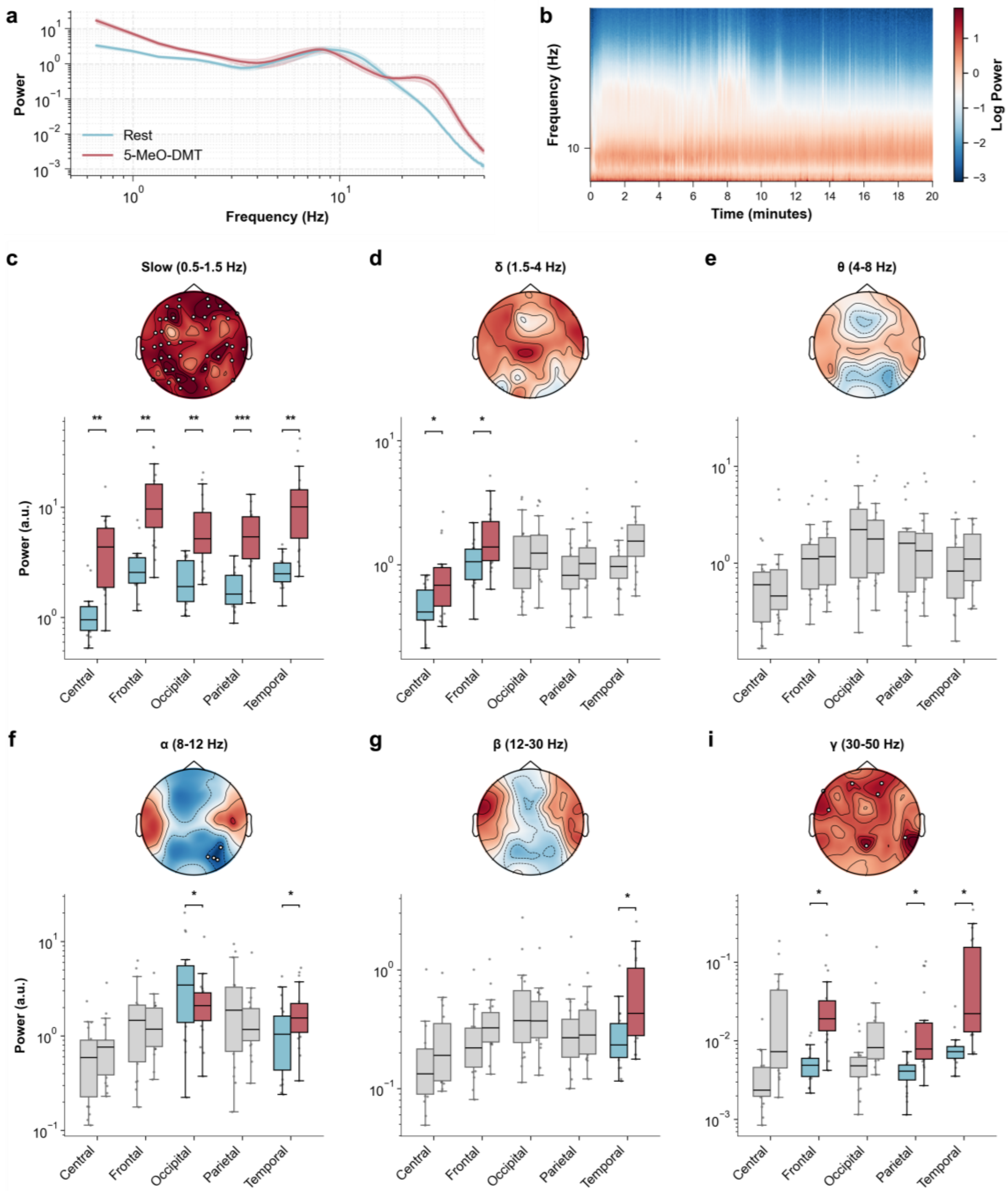


Figure 6.7. Spectral analysis of EEG activity comparing rest and 5-MeO-DMT conditions

*(a) Group-level power spectrum comparing rest (blue) and 5-MeO-DMT (red) conditions across frequencies. (b) Time-frequency representation of spectral power changes across the recording period. (c-i) Topographical maps (top) and regional boxplots (bottom) showing spectral power differences between rest (blue) and 5-MeO-DMT (red) conditions across six frequency bands: (c) slow (0.5-1.5 Hz), (d) delta (1.5-4 Hz), (e) theta (4-8 Hz), (f) alpha (8-12 Hz), (g) beta (12-30 Hz), and (i) gamma (30-50 Hz). Significant differences are indicated by asterisks (*p < .05, **p < .01, ***p < .001, FDR-corrected). White circles on topoplots indicate electrodes with significant differences between conditions. Boxplots display power distribution across five brain regions (central, frontal, occipital, parietal, and temporal), with individual data points shown.*

6.4.4 Brain-behaviour correlations

Analysis of cortical oscillatory power changes revealed specific relationships with subjective experience measures. As shown in **Fig. 6.8a**, reductions in occipital alpha power were significantly correlated with higher EN scores (r = -0.65, $p_{\text{non-adjusted}}$ = 0.005), and, as seen in **Fig. 6.8c**, with higher OBN scores (r = -0.51, $p_{\text{non-adjusted}}$ = 0.035). The correlation between ASCQ scores and occipital alpha power (**Fig. 6.8e**) approached significance (r = -0.47, $p_{\text{non-adjusted}}$ = 0.058). However, after applying FDR correction, these associations were no longer statistically significant. No other significant correlations were observed across lobe-band combinations. Full correlation results, including uncorrected and FDR-adjusted p-values, are provided in Appendix A6.10. Topographical maps in **Fig. 6.8b, Fig. 6.8d**, and **Fig. 6.8f** illustrate power changes across frequency bands. Electrode-level analyses revealed that reductions in alpha-band power were significantly associated with higher EN scores, particularly at C1, TP8, CP2, P8, PO8, and FC3 electrodes (all $p_{FDR} < 0.05$). The strongest effects were observed at TP8 (r = -0.92, p_{FDR} = 0.0016) and C1 (r = -0.91, p_{FDR} = 0.0016). No significant electrode-level correlations were observed for OBN or ASCQ measures after FDR correction.

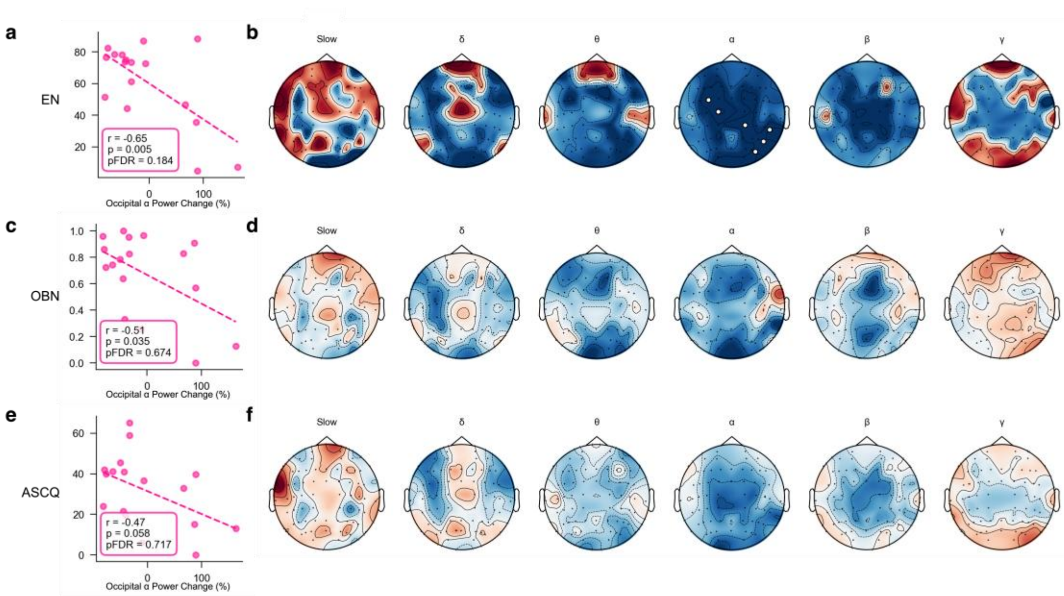


Figure 6.8. Relationships between EEG power changes and subjective effects

Scatter plots depicting correlations between occipital alpha power change (%) and subjective experience measures: (a) EN, (c) OBN, and (e) ASCQ. Each pink data point represents an individual participant, with dashed lines indicating linear fits; (b, d, f): Topographical maps illustrating relative power changes across frequency bands (Slow, δ, θ, α, β, γ) for each measure. Warmer colours indicate power increases, while cooler colours indicate power decreases.

6.5 Discussion

We present the first systematic investigation of 5-MeO-DMT's subjective, and neural effects, and relate these to the extent of psychedelic preparation reported by participants. Participants consistently rated self-transcendence and boundary dissolution as the most intense aspects of their experience. The intensity of these effects was modulated by an interaction between psychedelic preparedness and baseline mindfulness-related language. Spectral analyses revealed widespread increases in slow-wave activity (0.5–1.5 Hz) but no direct relationship with subjective reports. Instead, reductions in occipital alpha power correlated with EN states (5PS). These findings highlight a complex dissociation between neural and subjective effects, emphasising the need for refined measures to capture the full scope of 5-MeO-DMT's impact.

Characterising and measuring 5-MeO-DMT experiences

Unlike the vivid perceptual phenomena typically associated with classical psychedelics, participants on 5-MeO-DMT consistently rated self-transcendence and boundary dissolution as the most intense aspects of their experience, reflected in elevated OBN scores on the 5D-ASC. In addition, ratings were highest on the EN dimension of the 5PS, although the novelty of this measure does not permit a comparison to other psychedelics. While some participants endorsed items describing visual phenomena (such as geometric patterns or light) and spatial sensations (such as feeling inside a shaped space), these were consistently rated as less intense during the peak experience than items capturing non-duality, timelessness, and the dissolution of self-other boundaries. Two moderate correlations emerged between the scales: VRS (5D-ASC) with IM (5PS), and OBN (5D-ASC) with EN (5PS), suggesting partial overlap between these specific aspects of the experience. The ASCQ revealed pronounced alterations in self-experience, particularly the loss of personal identity, bodily awareness, spatial orientation, and self-world boundaries, while the EBI showed high ratings for emotional release and relief, with more variability across other dimensions of emotional processing. This initial mapping provides a characteristic profile of 5-MeO-DMT's effects on consciousness, establishing a foundation for further systematic investigations into its distinctive phenomenological properties.

The 5PS represents a valuable initial framework for capturing the distinct phenomenology of 5-MeO-DMT experiences. However, large-scale psychometric validation is essential to ensure its dimensionality, reliability, and construct validity. Exploratory and confirmatory factor analyses (EFA/CFA) will determine whether the hypothesised factor structure accurately reflects the underlying constructs or whether certain items - such as those assessing self-loss ("My ego was gone", "I had no self") - are redundant or need to be restructured. Validation efforts should also assess the internal consistency of each factor to ensure that items within each dimension are reliably measuring the same construct. Content validity testing, involving expert and participant feedback, will help identify any missing key dimensions of the 5-MeO-DMT experience, such as temporal distortions, memory disruptions, metacognitive shifts, and language breakdowns - all of which may not be fully represented by the current scale. Moreover, criterion and construct validity should be assessed by correlating the scale with existing validated measures, such as the Ego Dissolution Inventory [710] and Mystical Experience Questionnaire [353], to ensure alignment with established theoretical constructs. However, construct validation of an inherently unfamiliar and extreme state presents unique challenges. The uniqueness of 5-MeO-DMT phenomenology may limit the applicability of standard convergent validity approaches, given that existing psychedelic measures may not fully capture its distinctive experiential qualities. Consequently, a broader theoretical lens may be required, incorporating perspectives from transpersonal psychology, contemplative traditions, and Eastern psychological frameworks to ensure that the scale aligns with a more comprehensive understanding of self-loss, non-duality, and ineffability. These validation efforts will ensure the 5PS robustly captures the full range of 5-MeO-DMT phenomenology with precision, parsimony, and psychometric rigour.

Beyond these standard psychometric considerations, the methodology of rating predetermined experiential items presents a fundamental challenge for capturing 5-MeO-DMT experiences. When asked to rate items about their “peak experience”, participants encounter a list of descriptors that all presuppose some form of phenomenal content or experience (e.g., experiencing God, leaving the body, seeing colours, feeling emotions). However, 5-MeO-DMT frequently induces states of complete phenomenal dissolution where there may be no experiential contents to report - periods often described as “white-outs” or even complete cessation of consciousness [300, 711–713]. These contentless states, potentially representing the most profound moments of the experience, may be systematically missed by rating scales that exclusively present items describing positive phenomenal contents. While the current scale encourages full use of the rating range (0-100), participants may default to rating the most memorable phases where some experiential content was present rather than periods where consciousness itself may have been discontinued. Future iterations of the scale would benefit from explicitly addressing this limitation through items that assess temporal sequencing and memory gaps, while phenomenological interviews could help differentiate between genuinely contentless states and those with minimal but present phenomenal contents. Further, direct involvement of users in scale development - particularly those with extensive 5-MeO-DMT experience - could enhance its ecological validity and ensure that it adequately captures the full phenomenological spectrum, including the challenge of reporting on states of complete dissolution. Finally, large-scale psychometric validation will likely depend on data from non-clinical and non-research settings, given the numbers required. Community-based research approaches, including collaborations with retreat centres and experienced 5-MeO-DMT users, may provide the necessary participant diversity while also helping refine the scale to better reflect real-world usage contexts.

Mindfulness modulates the effects of psychedelic preparation on 5-MeO-DMT experiences

BML and PPS interacted to predict specific dimensions of the 5-MeO-DMT experience. For OBN, PPS was associated with stronger experiences only among individuals with lower BML, as indicated by a significant PPS × BML interaction that explained an additional 13.6% of variance beyond main effects. A substantially stronger interaction effect was observed for EN, where the PPS × BML interaction accounted for 33.0% additional variance, showing that PPS predicted more intense experiences at low BML but weaker experiences at high BML. A marginal PPS × BML interaction for altered self-consciousness (ASCQ; $p = .051$) explained 16.6% additional variance and followed a similar pattern. No significant effects were found for EBI, with the interaction explaining only 2.0% additional variance, suggesting that the relationship between psychedelic preparedness and mindfulness is particularly relevant to peak 5-MeO-DMT experiences of self-loss and unity, rather than emotional release.

This study offers a novel approach to psychedelic research by examining how individual differences in BML interact with PPS to shape the peak 5-MeO-DMT experience. The findings suggest that structured preparation enhances peak experiences for individuals with lower mindfulness language use but reduces them for those with higher mindfulness language use. Many PPS items emphasise planning, expectation-setting, and strategies for managing the experience, which may be useful for individuals who struggle with surrender but counterproductive for those already skilled in present-moment awareness. At low BML, structured preparation may act as a necessary support, providing a cognitive framework that reduces resistance and allows for deeper immersion. In contrast, at high BML, additional structured preparation may introduce cognitive expectations that subtly reinforce self-monitoring, limiting full surrender and reducing peak-state intensity. These findings suggest that the effects of preparation depend on an individual’s existing cognitive tendencies - helping those less accustomed to mindfulness but constraining those who already have a strong capacity for letting go. Future research should examine how different types of preparation interact with dispositional traits, optimising readiness while preserving the spontaneity central to 5-MeO-DMT.

Our use of linguistic markers as an implicit measure of a correlate of psychological readiness provided a novel perspective on the role of trait mindfulness in shaping 5-MeO-DMT experiences. Unlike explicit self-report measures, which rely on introspective access and subjective interpretation, language use reflects underlying cognitive and emotional processes that may not be consciously available to participants. This approach aligns with emerging research demonstrating that linguistic patterns can serve as reliable indicators of psychological traits, emotional states, and even psychedelic outcomes. However, despite its promise, our linguistic analysis was limited by its reliance on a word-frequency-based approach using LIWC. While this method allows for systematic quantification of mindfulness-related language, it does not capture context, syntax, or deeper semantic structures that may provide a richer understanding of psychological readiness. More advanced NLP techniques - such as topic modelling, sentiment analysis, or transformer-based embeddings - could offer greater sensitivity in detecting meaningful patterns in speech. Additionally, validating linguistic markers against self-report measures of trait mindfulness would provide a clearer picture of their relationship and ensure that they accurately reflect dispositional mindfulness rather than other psychological constructs [714]. Future studies could benefit from a multimodal approach, combining implicit linguistic markers with explicit trait mindfulness scales to more comprehensively assess psychological readiness for profound psychedelic experiences.

Neural-subjective dissociation in 5-MeO-DMT experiences

Spectral analyses revealed pronounced changes in neural oscillations following 5-MeO-DMT, with the most substantial effects in slow-wave activity (0.5–1.5 Hz), which increased across all cortical regions. Despite the magnitude of this effect, slow-wave power showed no significant correlation with subjective experience measures. In contrast, alpha power (8–12 Hz) exhibited regionally specific changes, decreasing in occipital regions while increasing in temporal areas. Occipital alpha suppression correlated with experiences of unity (EN), with electrode-level analyses identifying significant associations at right-lateralised posterior and midline-central electrodes. Alpha suppression is a well-established marker of serotonergic psychedelics, consistently linked to the intensity of psychedelic effects [664, 715, 716], and typically interpreted as reflecting reduced top-down inhibitory control [717–719]. However, the significance of these effects in the context of 5-MeO-DMT remains unclear and requires further unpacking.

The widespread increase in slow-wave activity following 5-MeO-DMT suggests a state distinct from the structured, content-rich phenomenology associated with classical psychedelics. Unlike the dynamic and high-entropy cortical activity typically linked to peak psychedelic experiences, slow-wave oscillations are more commonly associated with cortical downregulation, deep sleep, anaesthesia, and unconscious states. This raises the possibility that key aspects of the 5-MeO-DMT experience - particularly the so-called *white-out* or complete dissolution states - are not being adequately captured by retrospective self-report measures, not simply because they are ineffable, but because they may involve a temporary cognitive unavailability of conscious content itself.

A useful parallel can be drawn from research on *white dreams*, in which individuals report a sense of having dreamed but cannot recall specific content. Rather than being mere failures of memory, white dreams correlate with reduced high-frequency activity in posterior cortical areas responsible for perceptual and memory processing, suggesting a state of degraded or inaccessible experience [720–722]. Similarly, the *white-out* state induced by 5-MeO-DMT may not simply resist verbalisation but may involve a transient disruption in the neural mechanisms that structure and encode experience itself. This interpretation aligns with findings from deep **Non-Rapid Eye Movement (NREM)** sleep, where individuals frequently report experiencing *nothing* despite ongoing neural activity in sensory-processing regions [723]. It also contrasts sharply with classical psychedelics, which increase cortical entropy and associative richness, often producing hyper-associative, immersive, and highly recallable experiences [227]. By contrast, 5-MeO-DMT's slow-wave dominance may push conscious content below the threshold of access, disrupting the processes necessary for retrospective recall and introspective reconstruction.

If this is the case, then the most profound effects of 5-MeO-DMT may elude conventional phenomenological assessment, requiring alternative methods that account for disruptions in temporal continuity, memory formation, and state-dependent accessibility of experience. Similar challenges arise in the study of minimally conscious states, where introspective self-report is unavailable, and characterisation relies entirely on neurophysiological assessment [724, 725]. It is possible that the *experience* of 5-MeO-DMT's white-out state can only be meaningfully described through objective neurophysiological markers, rather than retrospective self-report. Future research should move beyond static retrospective ratings, incorporating moment-to-moment neurophenomenological probing and post-experience micro-phenomenological interviews to assess qualitative shifts in awareness and recall. These approaches could help determine whether the slow-wave state represents a distinct form of consciousness alteration - one in which experience is not merely difficult to describe but may be *fundamentally absent from cognition* in a way current self-report measures do not accommodate.

Another possibility is that spectral power alone may be too simplistic a metric to capture meaningful relationships between neural activity and subjective experience. Our analysis focused on regional and electrode-level power changes, but this approach does not account for dynamic neural interactions, network-level coordination, or temporal complexity - all of which may be critical in linking 5-MeO-DMT's effects to reported phenomenology. Spectral power measures aggregate activity within predefined frequency bands, but they do not reveal how different brain regions communicate or how signal properties evolve over time. Other techniques, such as connectivity analyses could help assess whether slow-wave increases reflect altered information integration rather than simple cortical downregulation. Additionally, entropy-based measures could determine whether 5-MeO-DMT induces a reorganisation of neural activity that is not captured by power-based metrics alone. Finally, topological approaches (e.g., persistent homology) could provide insight into whether the brain transitions through distinct states, mapping onto different phases of the subjective experience. These methods could help disentangle whether the observed dissociation reflects an actual lack of neural-subjective correspondence or whether the relevant neural signatures are simply not detectable through conventional spectral power analysis.

Conclusion

Our findings provide the first systematic investigation of 5-MeO-DMT's subjective, preparatory, and neural effects, revealing a complex interplay between experiential and physiological dynamics. Self-report data confirmed that 5-MeO-DMT elicits profound self-transcendence and boundary dissolution, with the EN dimension emerging as the most intense aspect of the experience. These effects were modulated by an interaction between psychedelic preparedness and baseline mindfulness-related language, suggesting that psychological readiness influences how individuals navigate these extreme alterations of consciousness. However, the extent to which conventional preparation strategies remain relevant for an experience that may temporarily suspend self-referential processing remains an open question.

Neural analyses demonstrated widespread slow-wave increases, yet these changes showed no direct correspondence with subjective reports. Instead, occipital alpha suppression correlated with EN states, reflecting a possible marker of self-boundary dissolution. This dissociation between slow-wave activity and reported phenomenology suggests that aspects of the 5-MeO-DMT state - particularly transient periods of "white-out" or contentless awareness - may be inaccessible to retrospective self-report, requiring new methodological approaches to assess experiences beyond conventional frameworks. Additionally, our use of spectral power analysis, while informative, may provide only a limited window into the neural mechanisms underlying 5-MeO-DMT's effects. Future research should leverage network-based, entropy, and topological analyses to better capture the dynamic and nonlinear features of these altered states.

Together, these findings highlight both the unique phenomenological profile of 5-MeO-DMT and the challenges inherent in measuring and interpreting its effects. Addressing these challenges will require a multimodal approach, integrating fine-grained neurophenomenological methods, linguistically informed assessments of psychological readiness, and more advanced neurophysiological techniques. By refining both measurement tools and analytical frameworks, future research can better characterise how 5-MeO-DMT shapes consciousness and how preparation, individual differences, and neural mechanisms interact to modulate these profound altered states.

CHAPTER 7

"If you fail to prepare, you are preparing to fail!"

— Commonly attributed to Benjamin Franklin (1706–1790).

General Discussion

The preceding chapters in this thesis focused on methods for measuring and enhancing psychedelic preparation. Despite its widely acknowledged importance, psychedelic preparation has remained conceptually underdeveloped, with limited tools and empirical frameworks guiding its assessment and optimisation. This thesis advances the field by developing a psychometrically validated assessment tool, the Psychedelic Preparedness Scale (PPS), and a scalable, meditation-based digital intervention, the Digital Intervention for Psychedelic Preparation (DIPP). Together, these contributions provide a structured approach to evaluating individual readiness and enhancing preparation practices for safe and meaningful psychedelic experiences. The following sections synthesise key findings (**Section 7.1**), explore theoretical contributions and implications (**Section 7.2**), discuss limitations and future directions for psychedelic preparedness research (**Section 7.3**).

7.1 Summary of key findings

Chapter 1 established the conceptual foundation for this research by critically assessing the current state of psychedelic preparation protocols. A systematic review of clinical trials revealed substantial methodological heterogeneity, with preparation varying widely in duration (1-8 hours), structure (1-4 sessions), theoretical frameworks, and facilitator qualifications. Analysis using a modified TIDieR framework identified significant reporting gaps, particularly regarding cultural adaptations, standardised preparedness assessments, and implementation fidelity. Complementing these findings, this chapter also briefly outlines a preliminary feasibility study of a six-day digital preparation protocol for a N,N-Dimethyltryptamine (DMT) trial, which demonstrated strong adherence and identified participant preferences for experiential components (meditation, breathwork, visualisation). However, this pilot highlighted two critical limitations that shaped subsequent research: the absence of validated instruments to measure psychedelic preparedness and the need for systematic intervention development following established frameworks. These insights directly informed the development of the PPS (**Chapter 2**) and the structured DIPP (**Chapters 3-5**).

The development and validation of the PPS in **Chapter 2** mark a significant advancement in operationalising and measuring readiness for psychedelic experiences. Factor analysis identified four core dimensions of preparedness: Knowledge-Expectation (KE), Intention-Preparation (IP), Psychophysical-Readiness (PR), and Support-Planning (SP), providing a theoretically grounded and empirically supported conceptual framework. The scale demonstrated excellent reliability and strong convergent, discriminant, construct and predictive validity, confirming its robustness as a measurement tool. Critically, the PPS was further tested in a psilocybin retreat setting, where higher preparedness scores correlated with more positive acute and long-term psychological outcomes. Individuals scoring higher on the PPS reported greater well-being, reduced psychological distress, and more meaningful psychedelic experiences post-retreat, providing evidence for the scale's real-world applicability. These findings establish the PPS as a validated empirical tool for assessing and optimising psychedelic preparation, with implications for both research and clinical practice. They also implied that deliberate and structured methods for improving preparation could have a beneficial role in shaping the psychedelic experience and improving sustained wellbeing following psychedelic treatment.

Building on the PPS framework, **Chapter 3** describes the development of the Digital Intervention for Psychedelic Prep (DIPP) - a structured online/remotely delivered 21-day program designed to systematically enhance psychedelic readiness (**Chapter 3**). Developed using a lived experience-centered, mixed-methods approach and aligned with the Medical Research Council (MRC) framework for complex interventions [416], DIPP was co-designed with psilocybin retreat participants and iteratively refined through qualitative feedback. This participatory approach ensured that DIPP was both theoretically grounded and practically relevant, addressing key user needs and challenges in implementation identified in prior research. A key innovation of DIPP is its use of daily meditation, mood tracking, and structured self-reflection exercises to cultivate psychological states conducive to positive psychedelic experiences. The program progressively introduces psychoeducation, embodiment practices, and intention-setting activities, integrating digital health methodologies to enhance accessibility and scalability.

Chapter 4 examined the role of meditation as a core component of psychedelic preparation, identifying the techniques which were subsequently included and refined in the meditation training module of DIPP. A survey of experienced meditators and psychedelic users assessed the perceived benefits of different meditation techniques for psychedelic readiness. The findings revealed that Loving-Kindness Meditation

(LKM) was rated as the most effective practice for enhancing emotional regulation, reducing anxiety, and fostering acceptance - key psychological factors influencing psychedelic experiences. Compared to focused attention and open monitoring meditation, LKM was associated with greater perceived benefits for psychedelic preparation, particularly in reducing anxious ego-dissolution and increasing oceanic boundlessness. Importantly, the study also found that meditation experience level moderated these effects. While intermediate-level meditators (1-3 years of practice) showed the greatest perceived benefit of meditation-based preparation, highly experienced meditators (>10 years) and novices exhibited more varied responses. These findings suggest that tailoring meditation practices to individual experience levels may optimise psychedelic preparation outcomes. Based on these results, LKM was formally integrated as the primary meditative technique in DIPP.

Chapter 5 outlined the protocol for an upcoming randomised controlled feasibility trial at UCL, designed to evaluate DIPP. This parallel-group trial will compare a meditation-based preparation program to a structurally matched music-only program, assessing whether a programme of meditation enhances psychedelic readiness. The study aims to evaluate key feasibility outcomes, alongside secondary measures such as perceived preparedness, emotional regulation, and the quality of psychedelic experiences. Beyond subjective self-report measures, the study integrates multi-modal neurophysiological assessments to investigate the neural and physiological mechanisms underlying psychedelic preparation and experience. Additionally, a novel, real-time voice note experience sampling method will capture inner speech patterns, emotional states, and engagement levels throughout the 21-day intervention and follow-up periods. Participants will complete the intervention before undergoing a supervised 25 mg psilocybin session, with follow-ups conducted at 2 weeks, 3 months, 6 months, and 9 months post-experience. While the study is yet to be completed, its findings will provide critical insights into the feasibility, acceptability, and preliminary efficacy of digital psychedelic preparation tools. These results will inform future refinements of DIPP, contributing to both clinical applications and research on scalable psychedelic preparation interventions.

Chapter 6 examined the interaction between mindfulness, psychedelic preparedness, and 5-MeO-DMT experiences, integrating Natural Language Processing (NLP)**,** self-report assessments, and EEG recordings. The study found that individuals with lower mindfulness-related language exhibited a stronger relationship between psychedelic preparedness and intensity of psychedelic states such as oceanic boundlessness (OBN) and Everything/Nothing (EN) experiences, while those with higher mindfulness-related language showed weaker associations, suggesting the relationship between psychedelic preparedness and intensity of psychedelic states was conditional on BML. EEG analyses revealed a dissociation between neural and experiential effects, with reductions in occipital alpha power correlating with EN experiences, but no direct relationship between global spectral power changes and subjective intensity ratings. These findings highlight the complex interplay between baseline cognitive traits, preparation, and psychedelic response, underscoring the need for personalised intervention strategies rather than uniform preparation approaches.

7.2 Theoretical contributions and implications

7.2.1 The Psychedelic Preparedness Scale (PPS)

The PPS addresses a common issue in psychological science: concepts that seem self-evident often go unexamined precisely because of their intuitive appeal [726, 727]. As Brown (2011) notes in her discussion of "duh science", research that formalises the apparently 'obvious' serves a critical role by transforming assumptions into testable constructs, allowing for systematic investigation [728]. Psychedelic preparation has long been recognised as essential, yet it has remained conceptually ambiguous and difficult to measure. The PPS resolves this by providing an empirically validated framework that identifies four distinct dimensions, offering the first structured articulation of preparation's multidimensional nature. This structure was refined through input from clinical experts and individuals with lived experience in PAT, enhancing its practical relevance. By demonstrating that preparation is both measurable and predictive of acute psychedelic experiences and therapeutic outcomes, the PPS transforms preparation from a loosely defined prerequisite - often acknowledged as important but inconsistently structured in clinical trials - into a clearly defined, empirically grounded variable.

The development and validation of the PPS provides a robust tool for advancing psychedelic research by offering a standardised method for assessing an individual's psychological readiness for a psychedelic experience. This scale enables researchers to investigate which specific dimensions of preparedness predict acute psychedelic responses, as well as longer-term therapeutic outcomes. These insights can support the identification of mechanisms through which preparation influences outcomes in PAT, including the potential mediating role of particular preparedness factors. Furthermore, the PPS introduces consistency in how preparedness is measured across studies, which, if widely adopted, could improve reproducibility and enable meta-analytic comparisons, helping to resolve current inconsistencies in the literature. The scale also offers a structured framework for empirically comparing different preparation protocols, allowing researchers to evaluate whether certain approaches are more effective than others. Collectively, these applications of the PPS can inform the optimisation of preparation strategies, enhancing both the safety and efficacy of psychedelic interventions.

The PPS also has implications for clinical practice, offering a structured tool for assessing and tracking psychedelic preparedness. It can be used as a baseline measure to evaluate an individual's readiness before treatment, as a framework for personalised preparation by identifying areas where additional support may be needed, and as an outcome measure to assess changes in preparedness following targeted interventions.

While the PPS may also inform screening decisions - helping clinicians consider whether an individual appears sufficiently prepared for a psychedelic session - specific clinical cutoffs have not yet been validated, and its use in this context should be guided by professional judgement. The PPS is already being implemented in diverse settings, with >10 retreat centres across Europe and South America using it to guide preparation discussions and tailor individualised support. It is also being incorporated into upcoming clinical trials, such as *Probing the functional magnetic resonance imaging response to psilocybin in functional neurological disorder (PsiFUND)* at King's College London, where it provides a systematic method for evaluating participant preparedness prior to treatment. However, the PPS is not intended to serve as a standalone diagnostic tool to evaluate whether an individual is prepared or not. Instead, it should be integrated with broader clinical assessments as part of a comprehensive treatment approach, ensuring that preparedness is evaluated within the full clinical context of each individual. Moreover, it provides a basis for individualised clinical decision-making when determining if/which aspects of preparation could be improved prior to acute dosing.

Importantly, the PPS findings from **Chapter 6** demonstrate that the effects of preparedness are not necessarily uniform across individuals or psychedelic substances. Rather, the predictive power of preparedness may vary based on psychological traits and drug-specific factors. In the case of 5-MeO-DMT, baseline mindfulness language moderated the relationship between preparedness and subjective experience, suggesting that readiness interacts dynamically with stable cognitive traits. These results challenge the assumption that preparedness operates as a one-size-fits-all mechanism, highlighting the need for more personalised approaches to psychedelic readiness. However, as the interaction between subjective psychedelic states was only tested with 5-MeO-DMT - a compound known for its rapid onset and intensity - it remains unclear whether similar effects emerge with other classic serotonergic psychedelics like psilocybin, where the acute effects unfold more gradually and are phenomenologically quite different. The upcoming DIPP trial (**Chapter 5**) will directly address this question, leveraging real-time experience sampling via the DIPP-bot to assess how language-based markers of preparedness shape the relationship between PPS scores and acute and longer-term outcomes. This study will refine our understanding of how individual differences modulate the impact of preparation, ultimately informing more tailored and effective approaches to psychedelic-assisted interventions.

7.2.2 The role of meditation in psychedelic preparation

This thesis challenges the growing assumption that attentional absorption is the most relevant meditative competency for psychedelic preparation. In recent discourse, particularly within the emerging "third wave" of meditation research [463], there has been increasing interest in concentration-based practices and advanced absorption states such as *jhāna* [94, 300, 476], due to their perceived phenomenological overlap with psychedelics, including non-dual awareness and alterations in self-boundaries [469, 729, 730]. While intuitively appealing, our expert survey indicates that compassion-based practices, such as LKM, may better support psychedelic preparedness. Unlike concentration-based practices, which stabilise attention through 'one-pointed' focus [731], LKM cultivates an open, emotionally receptive awareness, softening self-other boundaries by fostering warm-hearted intentions toward oneself and others [14]. Classical Pāli texts describe *mettā-cetovimutti* - liberation of mind through universal love - not as a narrowing of perception, but as a boundless, expansive state of connection [732]. Psychologically, this relational openness suggests that the capacity to approach dissolving experiences with warmth and compassion may be more crucial than attentional refinement alone. Whether a psychedelic experience is felt as overwhelming or expansive may depend less on stabilising attention and more on relating to boundary dissolution with openness and care [733]. This perspective aligns with theoretical work suggesting that compassion practices foster hypo-egoic self-processing through reduced self-focus and increased prosocial orientation [734, 735], as well as with emerging evidence linking LKM to self-transcendence [736, 737]. These insights underpin the *mettā*-based meditation framework developed for DIPP, presented in **Chapter 5** and summarised in **Figure 5.3**.

This interpretation is supported by emerging models of self-representation within computational neuroscience [584, 738, 739]. Predictive processing accounts suggest that psychedelics induce ego dissolution by reducing the precision of high-level priors related to selfhood, effectively loosening the brain's top-down constraints on perception and identity [483, 616, 740]. In this state of increased uncertainty, the way an individual responds - whether with fear and resistance or with acceptance and openness - may shape the trajectory of the experience. Concentration-based practices, such as those used in *jhāna* training, strengthen attentional control and reduce distractibility [634, 741], which may help regulate experience during altered states but do not directly train the affective capacities that influence how self-boundary dissolution is interpreted. In contrast, LKM practices cultivate warmth, care, and a sense of connection with others, potentially biasing the system toward interpreting boundary loss as safe and meaningful, rather than threatening. Hence, practices like *mettā* may not only support emotional regulation during psychedelics, but also shape the underlying predictive landscape in ways that facilitate positive, integrated forms of ego dissolution - expanding, rather than fragmenting, one's sense of self [742].

The implications of these findings extend across research and clinical practice. For researchers, this work opens new avenues for investigating how different meditative techniques may shape specific dimensions of the psychedelic experience, particularly the affective tone and self-other dynamics involved in ego dissolution. Clinically, these findings suggest that PAT protocols could benefit from incorporating practices that emphasise relational warmth and prosocial orientation, particularly those that engage the self-other boundary in emotionally resonant ways. Rather than positioning attentional training as the sole or primary meditative preparation strategy, these results invite a broader view, one that also considers emotionally engaged, relationally embedded techniques. While further empirical work is needed to determine the relative benefits of focused attention, open monitoring, and constructive practices such as LKM, the present findings offer initial support for including affective and relational contemplative approaches in psychedelic preparation. Future research could examine whether other prosocial or heart-based practices, such as *karuṇā* (compassion), *muditā* (appreciative joy), or devotional forms of meditation, foster similar benefits. Structured training in such practices may support not only acute adaptation during the psychedelic session, but also post-experience integration, with relevance for clinical populations and individuals with treatment-resistant conditions.

7.2.3 Digital meditation training for psychedelic preparedness

The development of DIPP (**Chapter 3**) represents a significant theoretical contribution by challenging the assumption that high-quality psychedelic preparation necessarily requires therapist-facilitated guidance. DIPP also demonstrates how meditation-based training can be potentially standardised and delivered digitally while preserving psychological depth and engagement. By structuring the intervention around the empirically validated four-factor model of psychedelic preparedness (established in **Chapter 2**), DIPP translates abstract readiness components into a concrete, testable framework that can be systematically evaluated and refined. Unlike traditional approaches that often rely on implicit or loosely structured guidance, DIPP provides a theory-driven intervention. As digital mental health interventions gain increasing adoption [743, 744], DIPP illustrates how PAT can integrate scalable methodologies while preserving the psychological preparation necessary for safe and meaningful psychedelic engagement.

Digital mental health interventions (DMHIs) offer several empirically supported advantages for psychedelic preparation, including improved accessibility, flexibility, anonymity, and cost-effectiveness [391–395]. Research has demonstrated that digital platforms can be non-inferior to in-person delivery in various therapeutic contexts [389, 390] and can empower participants by fostering greater autonomy in managing their own psychological processes [396–398]. Despite the increasing recognition of digital tools in psychedelic research [399], no published or publicly available digital interventions currently provide standardised, scalable psychedelic preparation, highlighting an opportunity to enhance both accessibility and efficiency while reducing burdens on service providers. However, a primary challenge in DMHIs is suboptimal user engagement [395, 404, 405], underscoring the need for person-centric approach to intervention design. In contrast to the general lack of co-production and participatory frameworks in psychedelic research [337, 417], the DIPP project deliberately involved stakeholders throughout the development process, with the aim of improving usability, adherence, and real-world impact [411–416].

Beyond its practical advantages, digital meditation training represents a broader theoretical shift in how readiness for altered states might be conceptualised and cultivated. Traditional models of psychedelic preparation have primarily emphasised psychoeducation and therapist-led psychological support (see systematic review in **Chapter 1**), often assuming that effective preparation requires direct clinical guidance. While the therapeutic alliance likely plays a crucial role in PAT [319], DIPP's structured approach suggests that certain aspects of readiness can be cultivated independently through self-directed reflective practices. This reframes psychedelic preparedness not merely as an informational or therapeutic process, but as a trainable set of cognitive-affective skills. This is reminiscent of recent developments in psychological therapies, in which there is an increasing recognition that largely self-guided interventions are efficacious for a range of disorders [745]. Moreover, the integration of digital tools enables standardised, scalable delivery of meditation-based training, allowing its efficacy to be systematically measured and optimised for diverse populations. As PAT moves toward broader clinical implementation, scalable interventions like DIPP provide a structured framework for incorporating contemplative training into preparation protocols. Rather than replacing traditional therapeutic models, this approach expands the range of available preparation strategies, bridging the gap between therapist-facilitated support and emerging digital health interventions.

7.3.4 Measurement challenges in 5-MeO-DMT

The findings from **Chapter 6** offer an important step toward refining our understanding of how individual differences shape responsiveness to psychedelic preparation, but they should not be taken as definitive. While the observed interaction between psychedelic preparedness and mindfulness-related language points to a more conditional model of readiness, one in which preparatory efforts may benefit those with lower dispositional mindfulness but potentially constrain those with higher baseline mindfulness, this effect must be interpreted with caution. The linguistic measure of mindfulness used in this study was necessarily limited: it drew on a single dictionary, captured only word frequency rather than deeper semantic or contextual information, and did not differentiate between trait and state-level language. Nevertheless, the methodological principle holds considerable promise. This study demonstrates that naturalistic language use can serve as a minimally invasive, scalable window into psychological tendencies that may shape how individuals encounter altered states of consciousness. Crucially, the implications extend far beyond mindfulness alone. Future work could expand this approach by examining how a broader array of linguistic features (e.g., markers of emotional tone, cognitive style, syntactic structure, prosody etc.,) influence psychedelic response. In this sense, the present findings are not a final answer but a generative starting point: they suggest that the integration of natural language processing into psychedelic science may provide a dynamic and unobtrusive means of assessing readiness, offering complementary insights to self-report and behavioural measures.

One of the most striking findings in **Chapter 6** was the apparent dissociation between neural and subjective markers of the 5-MeO-DMT experience. Although participants showed widespread increases in slow-wave activity, a dramatic neural signature rarely seen in classical psychedelics, these changes did not correlate with self-reported measures of altered state intensity or ego dissolution. The only robust relationship was a negative correlation between occipital alpha power and Everything/Nothing (EN) scores. This raises important questions about what is available for retrospective report, and what may be inaccessible - not because the experience lacked intensity, but because it disrupted the very structures that support encoding, memory, or narrative coherence. At the same time, more mundane explanations must be considered: it is possible that some participants simply struggled to engage fully with the questionnaires, particularly in the fragile post-session period following such a profound and disorienting experience. This limitation applies broadly across psychedelic science and underscores the need to balance critical reflection with practical trust in self-report data. Importantly, rather than rejecting these tools, the findings point to the need for their evolution. Existing instruments could be adapted to probe not only the presence of specific phenomenological content, but also the absence of content, the inaccessibility of memory, and the difficulty of narrative reconstruction. In parallel, future work should incorporate complementary methods (e.g., microphenomenological interviews) to help triangulate moments that may resist articulation. Ultimately, building a fuller account of 5-MeO-DMT's effects will require methods that can measure both what is reported and what escapes report.

7.3 Limitations and future directions

7.3.1 Measuring psychedelic preparedness

Beyond the methodological limitations of the PPS outlined in **Chapter 2**, psychedelic preparedness faces potential conceptual challenges related to its temporal framework. A consideration worth exploring is whether capturing the four preparedness factors at a single point in time adequately represents what may be a dynamic preparation process. It remains untested, but plausible, that different factors follow distinct temporal patterns. For example, foundational KE might develop early and because it is based on declarative knowledge, is expected to remain stable throughout the preparation phase, while PR (particularly surrender and psychological preparation) could fluctuate as the psychedelic experience approaches. This possible temporal variability would align with complex systems perspectives where psychological states emerge from evolving component interactions [746–749]. Hypothetically, participant who scores highly across all factors a week before their session might still experience acute anxiety the day prior, potentially altering their PR scores. This scenario illustrates the non-linear dynamics often observed in other psychological processes [750, 751]. Similarly, the relative importance of factors might shift throughout preparation: SP may become increasingly salient as the experience nears, while IP could exert greater influence when established early, possibly reflecting self-organising properties similar to those in therapeutic change [752]. Future research should test these suppositions through longitudinal assessments to determine if and how each factor evolves throughout preparation, which aspects might fluctuate, and which assessment timepoints might best predict positive outcomes.

Another important concern relates to the cultural specificity of the PPS and the assumptions embedded in its four-factor structure. As currently formulated, the scale largely reflects Western scientific and therapeutic paradigms of psychedelic use, with an emphasis on cognitive preparation (e.g., understanding effects and setting expectations), individual psychological readiness, and structured planning processes. These dimensions may not fully capture essential elements of preparation in other cultural contexts. For instance, while the IP factor includes introspective practices such as meditation and journaling, it does not account for key elements commonly emphasised in Indigenous frameworks, such as dietary practices, storytelling, or guidance from spiritual leaders [753]. Similarly, while SP focuses on immediate social support and post-session logistics, it may overlook the deeper sense of community embeddedness that characterises traditional settings [754]. This raises critical questions about the cross-cultural validity of the scale: beyond mere translation, the very construct of "preparedness" may be differently defined and operationalised across cultures. Alternative frameworks may prioritise spiritual, relational, or communal dimensions of readiness that significantly influence outcomes but are currently unassessed. Future work should explore these ideas and consider the development of culturally responsive supplementary modules to enhance the PPS's applicability across varied settings.

A further complexity involves disentangling transient preparation states from stable psychological traits [755, 756]. Some items in the PPS - particularly within the PR dimension (e.g., "I am ready to experience whatever 'comes up' during the experience" or "I trust my own mind and body to safely process the experience") - may capture stable individual differences rather than modifiable preparation outcomes. This creates an interpretative challenge: high PPS scores may reflect a combination of preparation activities and pre-existing psychological traits that independently predict positive psychedelic experiences. For example, individuals with greater baseline psychological flexibility may naturally endorse PR items about readiness for challenging experiences, while those with higher trait openness may more readily engage with intention-setting measured in the IP factor. This makes it difficult to determine the unique contribution of preparation activities beyond pre-existing psychological resources. Such ambiguity might have implications for both research and clinical applications: preparation protocols developed from PPS findings may be calibrated toward individuals already predisposed to positive experiences, potentially overestimating their effectiveness for those with different psychological profiles. Future research should address this question by employing longitudinal designs that evaluate sensitivity of specific items to preparation-oriented interventions and test temporal precedence of specific PPS factors in predicting proximal (e.g. OBN) and distal (e.g. wellbeing) outcomes. Including measures of stable traits (e.g. 'acceptance' or openness to experience) as covariates in statistical models will help to parse the unique contribution of pliable preparatory states to desirable outcomes of psychedelic treatment.

Finally, questions remain about whether the PPS fully captures the scope of preparedness required to counteract the potentially harmful effects of especially intense or "ontologically challenging" psychedelic experiences [527]. While the scale items were developed through rigorous methodology involving lived experience accounts and expert consultation, certain dimensions of preparation may remain underrepresented, particularly for substances associated with profound existential experiences such as DMT or 5-MeO-DMT [666]. These substances often occasion experiences that fundamentally challenge one's sense of reality, identity, and ontological understanding - experiences that may require specific types of philosophical or existential preparation not fully addressed in the current scale [757, 758]. For instance, while the KE factor assesses awareness of potential emotional states and unpredictability, it may not adequately capture preparation for the dissolution of self-boundaries, encounters with perceived entities, or radical shifts in metaphysical understanding commonly reported with certain substances [13, 759].

Similarly, the PR items focus on general psychological and physical preparation but may not sufficiently address readiness for experiences that transcend ordinary conceptual frameworks [760]. This limitation raises questions about whether substance-specific scales that extend the PPS are needed, particularly for compounds associated with atypical phenomenological profiles [1, 666]. Future research could investigate whether preparation needs differ substantially across substance classes and whether additional preparation dimensions - such as philosophical readiness, metaphysical flexibility, or existential openness - might enhance the predictive validity of the PPS for particularly profound psychedelic experiences.

7.3.2 Enhancing psychedelic preparedness

A legitimate concern for DIPP involves balancing accessibility with interpersonal connection [761, 762]. While digital platforms democratise access to preparation resources, they may compromise the human elements that strengthen preparation effectiveness [319, 763]. Meaningful preparation involves more than just delivering information - it also requires building trusting relationships, which digital environments may find challenging to support [764, 765]. This raises a critical question: Can self-guided digital interventions fully address all dimensions of psychedelic preparedness? Although the DIPP comprehensively covers four distinct preparation factors, certain aspects - such as the security fostered through trusted relationships and real-time personalised feedback - may be enhanced through human interaction. These limitations may be particularly significant for individuals experiencing anxiety or ambivalence about their upcoming psychedelic experiences. Future research should investigate hybrid approaches that combine digital convenience with meaningful human connection (e.g. 'telehealth' approaches), potentially including synchronous group preparation sessions via digital platforms, mentor-supported online learning, and community-based digital resources that maintain relational continuity throughout the preparation process.

Another challenge for implementation of DIPP concerns balancing standardisation with adaptability to individual needs [766, 767]. While the structured digital program offers consistency and scalability [768], effective preparation for a psychedelic experience is likely highly individual, shaped by prior experience, psychological profile, cultural background, intention, and substance choice. Although DIPP was developed with diverse stakeholder input, the current iteration offers limited adaptability to these individual differences. Future versions could implement a staged approach to personalisation, beginning with periodic PPS assessments to recalibrate intervention components based on users' evolving preparation needs. This foundation could be incrementally enhanced through targeted, low-complexity technological adaptations, such as branching psychoeducation modules that adjust content based on prior knowledge, customisable meditation sequences that adapt to reported experience levels, and natural language processing for journaling, providing reflective prompts tailored to recurring themes in users' entries. Beyond these immediate refinements, future iterations could explore substance-specific preparation modules that address variations in phenomenology and psychological demands between compounds (e.g., psilocybin vs. 5-MeO-DMT).

Moreover, as noted in our stakeholder demographics, participants were predominantly White and highly educated, raising questions about the intervention's cultural responsiveness across diverse populations. The requirement for self-directed learning further assumes levels of motivation, cognitive resources, and psychological stability that may not be equally distributed across potential users. Future interactions should prioritise expanding stakeholder involvement to ensure broader representation, incorporating multimedia formats to accommodate varying literacy levels [769, 770], offline accessibility for users with limited connectivity [771, 772], and culturally adaptive design principles [773, 774] that align with diverse frameworks for psychedelic preparation. Collaborative design processes that meaningfully involve stakeholders from historically underrepresented communities will be essential to creating truly inclusive digital preparation resources [775, 776].

Monitoring and safety considerations also warrant careful attention for DIPP, particularly if the intervention is implemented more widely [777, 778]. While in-person preparation allows therapists to observe verbal and non-verbal cues in real time and adjust treatment plans accordingly, a digital platform lacks this kind of immediate interpersonal oversight [779, 780]. However, it is envisaged that clinical implementation of DIPP would occur within a broader therapeutic context, where participants undergo comprehensive assessment by trained clinicians prior to enrolment in psychedelic treatment. This allows for serious or immediate concerns, such as complex trauma histories, dissociative tendencies, or unstable mental health conditions, to be identified and addressed before digital preparation begins. Nonetheless, reduced real-time monitoring remains a consideration during the preparation phase itself, particularly as the intervention scales. Future developments should explore ways to enhance in-process safety, such as integrated screening updates, automated flagging tools, and clear guidance about when to seek additional support. Pathways to connect with human facilitators should also be available when concerning patterns emerge. The development of ethical guidelines specifically addressing digital preparation for psychedelic experiences will be essential, particularly in non-research or community contexts. Such frameworks should clarify the division of responsibilities between digital and clinical components, define best practices for monitoring high-risk individuals, and ensure adequate safety oversight while preserving the accessibility and scalability that make digital interventions promising.

The integration of *mettā* meditation within DIPP raises important considerations around individual suitability and emotional safety [585]. Although compassion-based practices, including *mettā* and LKM, have demonstrated potential benefits (e.g., such as enhancing self-compassion [561, 781], improving life satisfaction [782], and supporting mental health more broadly [558, 783]) their acceptability and efficacy remain uncertain for certain populations. Despite a growing body of research suggesting their therapeutic value, reviews highlight mixed findings, often constrained by small samples and limited methodological rigour [784]. Furthermore, in the context of PAT, expert recommendations around meditation integration are still largely shaped by personal experience and consensus, rather than empirical evaluation. As such, the perceived value of LKM in this domain may reflect practitioner enthusiasm more than systematic evidence. This carries the risk of overlooking potential harms, especially for individuals who struggle most with compassion-based practices, such as those with self-critical tendencies, histories of complex trauma, or **borderline personality disorder (BPD)** [785]. For some, these practices can elicit distress, resistance, or shame, confirming deeply held beliefs of unworthiness or emotional deficiency - particularly when forgiveness or kindness feels inaccessible. While such individuals may stand to benefit most from cultivating compassion, they may also find the practice emotionally overwhelming or invalidating.

These concerns are particularly relevant to DIPP, which, although currently piloted in healthy populations, is ultimately intended for broader application, including clinical contexts in which such presentations are likely to arise. DIPP attempts to address these challenges by offering flexible, guided meditations that normalise difficulty and invite participants to adapt the practice to their needs. For instance, in Week 1, participants are encouraged to offer kind wishes to themselves, but if this proves too difficult, they are explicitly invited to begin with someone or another being (e.g. a pet) they care about. While these adaptations help support accessibility, the emotional complexity of compassion-based practices remains a crucial consideration in their wider application. It may also be that psychedelics are better positioned to facilitate access to compassion in individuals who struggle with LKM, rather than the other way around, for example, by lowering emotional defences or enabling the felt experience of forgiveness following MDMA.

A further consideration is the extraction of *mettā* meditation from its traditional Buddhist context, where it forms part of a broader ethical, philosophical, and soteriological framework [786]. In early Buddhist teachings, *mettā* is one of the four *brahmavihāras* (divine abodes), alongside *karuṇā* (compassion), *muditā* (sympathetic joy), and *upekkhā* (equanimity), and is cultivated within a holistic path toward liberation (*nibbāna*) [787]. Its development is supported by ethical conduct (*sīla*) and meditative concentration (*samādhi*), as outlined in classical texts such as the *Visuddhimagga* (*Path of Purification*) [556]. More broadly, *mettā* unfolds within the threefold training - morality, concentration, and wisdom (*sīla, samādhi, paññā*) - with each component reinforcing the others [788]. These foundations can be understood as a kind of preparation for mettā itself, establishing the conditions for the practice to unfold meaningfully.[43] This preparatory structure mirrors the logic of psychedelic preparation, which similarly emphasises the cultivation of psychological, ethical, and attentional readiness. Whether it warrants a "Preparation for Preparedness Scale" (PPS-2) is an open question, but the structural parallel is compelling. In modern settings, however, such practices are often adapted and secularised to enhance accessibility, a move that can strip away the structural and philosophical supports that traditionally sustain their depth and transformative potential [789–791]. In the case of DIPP, *mettā* has been adapted for a secular therapeutic context. While the term is retained here, future iterations may benefit from using more neutral or descriptive language, such as "Loving-Kindness Meditation (LKM)", to reflect its recontextualised form and avoid conflation with its religious origins.

7.3.3 Integration as a critical counterpart to preparation

While this thesis focuses specifically on psychedelic preparation, it is important to acknowledge that *psychedelic integration*, though outside the primary analytic scope, plays a critical role in shaping long-term outcomes [792]. Integration generally refers to the process of understanding and incorporating psychedelic experiences into everyday life in a way that supports lasting psychological and behavioural change [792, 793]. Despite widespread agreement on its importance, integration remains loosely defined, with limited consensus on when it should begin, what it should involve, or how it is best supported [599, 794]. Crucially, preparation and integration are inherently linked, as the quality and effectiveness of preparation may directly influence how an individual makes sense of and applies their psychedelic experiences afterward. Recognising this connection, we propose three theoretical path models to clarify the relationship between preparation, acute experience, and integration, using illustrative constructs (**Fig. 7.2**). These models are not intended as exhaustive or definitive representations of PAT but rather as conceptual tools for articulating different structural assumptions about how change unfolds. In all three models, preparation is represented by the Psychedelic Preparation Scale (PPS), the acute psychedelic experience by oceanic boundlessness (OBN), and integration by the Experienced Integration Scale (EIS) [795].

[43] As Bache (2019) notes, "Purification is one of those 'pay me now or pay me later' things. In Tibetan Buddhism, monks must do Ngöndro before they are allowed to receive the higher initiations that engender realisation. Ngöndro are the foundational practices that prepare the body and mind to receive the advanced teachings." This echoes the broader principle that deep practices often require careful preparatory groundwork.

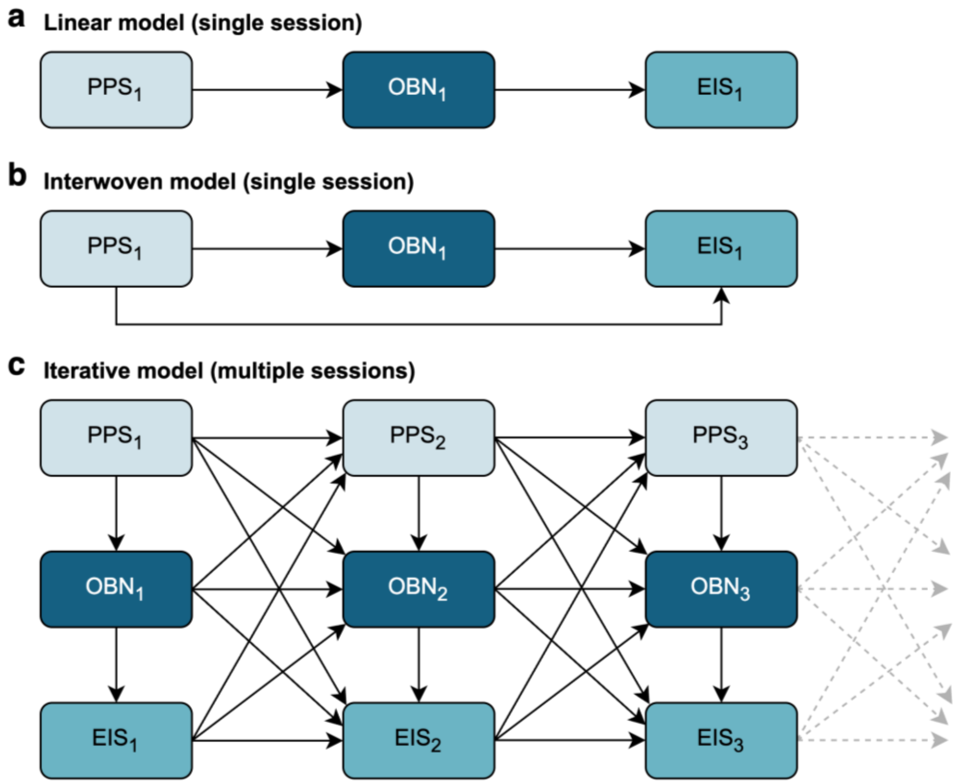


Figure 7.2 Conceptual models of the relationship between preparation and integration

Three models illustrating the relationship between preparation and integration. (a) Linear model: Preparation, the psychedelic experience, and integration occur sequentially with no feedback. (b) Interwoven model: Preparation directly influences integration. (c) Iterative model: Preparation and integration form a self-reinforcing cycle across multiple psychedelic experiences, where integration informs future preparation, shaping long-term engagement. Solid arrows indicate the primary flow of the process, light blue arrows represent feedback loops where integration shapes preparation, and the dotted arrow signifies continued progression beyond the diagram.

As illustrated in **Fig. 7.2a**, the *linear model* reflects a structure implicitly assumed in many contemporary PAT protocols. In this model, preparation (PPS_1) shapes the nature of the acute psychedelic experience (OBN_1), which in turn determines the extent of integration (EIS_1). Preparation and integration are treated as discrete and temporally sequential stages, with integration positioned as a downstream outcome of the session. While intuitive, this framing may obscure the complex and overlapping dynamics that shape longer-term change [792, 796]. The *interwoven model* (**Fig. 7.2b**) offers a more nuanced perspective by introducing a direct path from preparation (PPS_1) to integration (EIS_1), in addition to the indirect path via the acute experience (OBN_1). This structure reflects the hypothesis that psychological capacities developed during preparation (e.g., emotional regulation, intention setting, and self-reflective awareness) may directly support integration, independently of the specific qualities of the psychedelic experience. It also aligns with emerging theoretical perspectives that view integration not as a process that begins only after the session, but as one that is actively scaffolded in advance [797, 798]. In this view, preparation establishes the psychological, relational, and conceptual frameworks that shape how experiences are later interpreted, retained, and applied. Rather than being strictly separate phases, preparation and integration can be understood as interlinked elements within a continuous transformational process.

Although this thesis primarily focuses on preparation, it also takes meaningful steps toward embracing the interwoven model. Both tools developed herein - the PPS and DIPP - are designed with integration in mind, incorporating elements that explicitly anticipate the processes of interpreting. For example, the PPS includes the item, *"I have made a plan for what I will do in the hours and days after the psychedelic experience",* encouraging individuals to consider post-session processes in advance. Likewise, the SP module within the DIPP intervention guides users in developing personalised integration strategies as part of their preparatory work. The DIPP meditation training component also serves a dual purpose: it equips participants with skills to navigate the acute experience and cultivates psychological resources (e.g., such as openness, emotional flexibility, and self-awareness) that may facilitate later integration. **Chapter 4** demonstrated that meditation was rated highly not only for supporting the session itself, but also for enabling smoother post-experience readjustment and promoting lasting psychological benefits. While this thesis does not aim to develop a comprehensive intervention encompassing all phases of psychedelic engagement (i.e., preparation, acute experience, and integration), it takes a focused and strategic approach by investigating preparation as a potentially necessary - and, in some cases, sufficient - component of effective PAT. By developing standardised, evidence-informed tools that target the preparatory phase, this work lays the groundwork for future research exploring both the independent and interactive contributions of preparation and integration. Such research could help determine whether anticipatory attention to integration meaningfully enhances outcomes, and how preparation might be adapted to better support integration from the outset.

The *iterative model* (**Fig. 7.2c**) conceptualises psychedelic engagement as a cyclical, multi-session process. In this structure, each round of preparation (PPS_{2-3}), acute experience (OBN_{2-3}), and integration (EIS_{2-3}) is directly informed by the outcomes of previous sessions. Unlike linear or interwoven models, the iterative model emphasises that each phase within a session not only shapes the subsequent phases but also has a cumulative impact on future sessions. For example, practices and skills developed during one integration phase may directly influence how preparation is approached in the next session, while the nature of a previous psychedelic experience may shape expectations and strategies for future experiences. This model reflects a more realistic account of psychedelic practice, particularly outside clinical contexts, where individuals often participate in multiple sessions over time. It also aligns with ceremonial and Indigenous traditions that view psychedelic engagement as an ongoing process embedded within relational, spiritual, and communal frameworks, rather than as isolated events [792, 799, 800]. Although this work primarily addresses first-time or early-stage psychedelic users, acknowledging the iterative nature of engagement highlights the potential for preparatory interventions, such as DIPP, to explicitly account for continuity across sessions. For instance, incorporating structured reflection modules that link past integration with future preparation could enhance the long-term impact of such interventions. Further research exploring how integration practices shape subsequent preparations may clarify how to best support sustained therapeutic outcomes, particularly in naturalistic or community-based psychedelic use.

7.4 Conclusion

As psychedelic therapies move toward broader clinical application, the question of how best to prepare individuals for these experiences becomes increasingly urgent. This thesis has taken initial steps toward addressing that question through the development of both a validated measure of psychedelic preparedness and a scalable digital intervention designed to enhance it. Together, these tools offer a structured yet adaptable approach to preparation, with potential applications in research, clinical practice, and personal use. At the same time, the thesis points to the idea that preparation is not a fixed or uniform process. It is likely shaped by psychological traits, cultural contexts, and the evolving relationship between experience and integration. Effective approaches must therefore be grounded in evidence while remaining responsive to the complexities and nuances of individual experience.

The epigraph that opened this thesis offers a simple but powerful truth: even the most overwhelming psychedelic experiences can be manageable - and perhaps even beneficial - if one is prepared to meet them. It is telling that the emphasis is on manageability first. This does not downplay the potential for insight or growth, but it reminds us that transformation cannot happen without first being able to withstand the intensity. In a cultural moment where psychedelics are often portrayed as inherently healing or universally transformative, this perspective feels particularly relevant. The reality is more complex. People are curious, motivated, and increasingly drawn to explore these states, but curiosity alone does not ensure readiness. Preparedness is not just about maximising positive outcomes; it is about being equipped to handle whatever arises - the awe, the fear, the unexpected. In this sense, preparation is not a guarantee of insight, but a way of making space for it to emerge when conditions allow.

As the field of psychedelic research continues to grow, we must resist the temptation to oversimplify what these substances can do. Their potential is undeniable, but so is their unpredictability. Rather than asking whether psychedelics will revolutionise mental health care, we should be asking how we can support those who choose to explore these states in ways that are safe, informed, and respectful of their complexity. This thesis has taken early steps toward answering that question by developing tools designed to enhance preparedness. There is still much work to be done, but if we centre preparation as a core part of psychedelic engagement, not as an afterthought or a checkbox but as an ongoing commitment, we can help ensure that exploration is both meaningful and responsible. In doing so, we honour not just the potential of psychedelics but the people who choose to engage with them.

Appendices

Appendix 1

A1.1 Systematic review methodology and search strategy
An advanced search was conducted in November 2024 using the Web of Science and Ovid platforms (MEDLINE, EMBASE, and PsycINFO databases). Search strings combined terms related to three constructs: classical psychedelics, therapy, and mental health disorders. Boolean operators ("AND" / "OR"), as well as title and abstract field restrictions were employed, with database-specific syntax adaptations. Studies were limited to English-language publications from January 2000 onwards, reflecting the contemporary focus of this review and translational resource constraints. Systematic reviews, meta-analyses, and animal studies were excluded at the search level to focus on primary human research. Duplicates were removed prior to screening.

Eligibility Criteria
Inclusion criteria:

- Population: Human adults (≥18 years) diagnosed with a mental health condition, including depression, anxiety, addiction or alcoholism, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), or eating disorders (anorexia, bulimia)
- Intervention: Administration of classic serotonergic psychedelics (psilocybin/psilocin, LSD, DMT/ayahuasca, 5-MeO-DMT, ibogaine) at a full dose in a controlled, therapeutic, or research setting, with psychotherapy components (e.g., preparation, acute, or integration).
- Study Design: Clinical trials including randomised controlled trials (RCTs), non- randomised controlled trials, larger open-label studies, pilot studies or proof-of- concept studies. Studies must be peer-reviewed and published.
- Outcomes: Studies reporting mental health outcomes as the primary outcome (including symptom reduction, functional improvement)
- Timeframe: Studies published from January 1, 2000, onwards.
- Language: Articles published in English (or other languages if translation resources are available).

Exclusion criteria:

- Population: Non-human studies (e.g., animal models), studies including children (<18 years), studies including only healthy participants (non-clinical samples), physical illnesses where mental health symptoms are secondary to the physical condition (e.g., cancer, chronic pain).
- Intervention: Studies involving non-classical psychedelics (MDMA, ketamine, cannabis), microdosing psychedelics, self-administered psychedelics, or psychedelics used in naturalistic or observational settings (e.g., ceremonial retreats, recreational use), or interventions without psychotherapy components.
- Study Design: Case reports, qualitative studies, non-clinical, presentation or workshop or conference articles, review articles, systematic reviews, prospective or follow up studies, online questionnaires, meta-analyses, interview, editorial, surveys, guidelines, perspectives or commentaries, mechanistic or physiological basis studies, studies focusing exclusively on physical health outcomes (e.g., pain), sub study or secondary analyses of data from parent (original) clinical trials.
- Publication Type: Unpublished studies, symposia, poster abstracts, preprints, full text unavailable or grey literature (e.g., trial registry results) unless they meet peer-reviewed criteria.
- Timeframe: Studies published before January 1, 2000.
- Language: Articles not available in English, unless translation resources are available.

- Duplicates: Duplicate studies retrieved across databases.
- Disease Modifying therapies or Dance Movement Therapy (DMT mesh term issue with the search)

Database Search Strategies

Ovid Search

Databases: Embase 1980 to 2024 Week 46, MEDLINE(R) ALL 1946 to November 19, 2024, and APA PsycINFO 1806 to November 2024 Week 3*

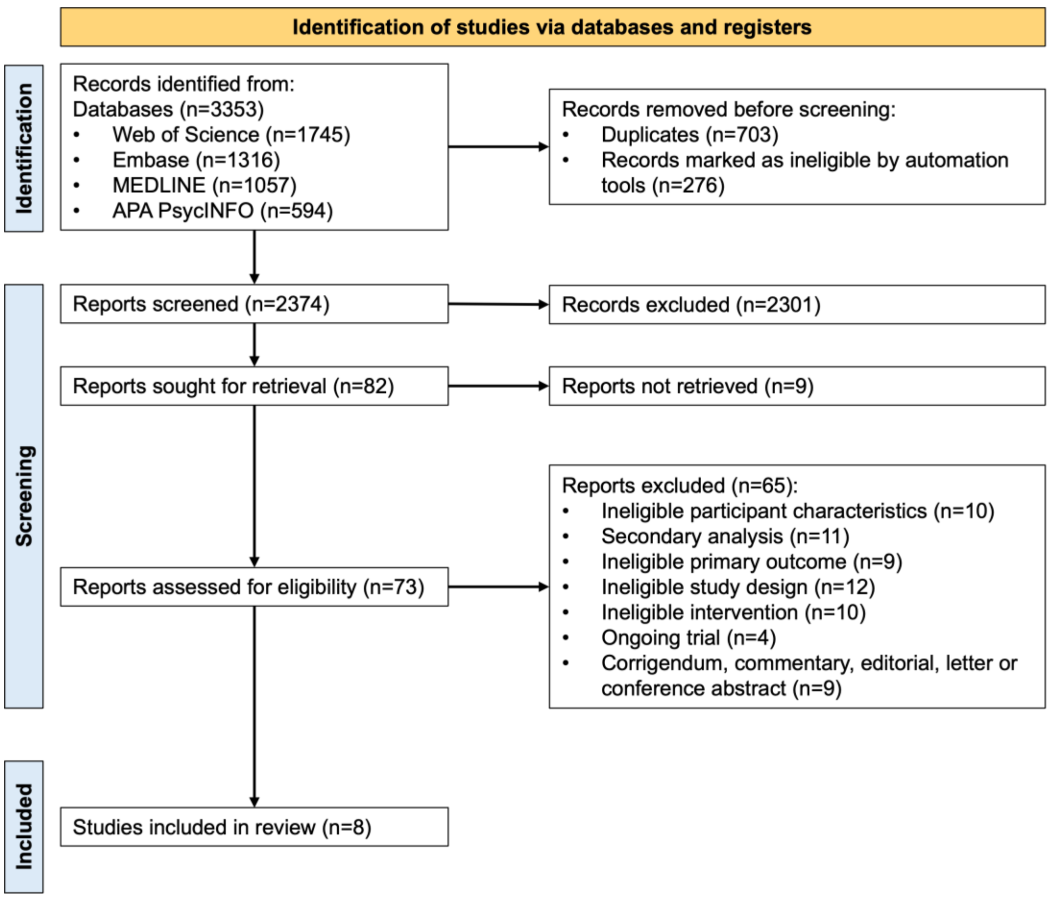
1. (psychedelic* or "classic psychedelic*" or "classical psychedelic*" or hallucinogen* or entheogen* or psilocyb* or psilocin or "magic mushroom*" or LSD or "lysergic acid diethylamide" or DMT or "N,N-DMT" or dimethyltryptamine or "n,n-dimethyltryptamine" or ayahuasca or "5-MeO-DMT" or "5-methoxy-N,N-dimethyltryptamine" or bufotenin* or ibogaine or iboga or "12-hydroxyibogamine" or mescaline or peyote or "san pedro").ti,ab.
2. (psychotherap* or therap* or "cognitive behavio#ral therap*" or CBT or "acceptance commitment therap*" or ACT or "dialectical behavio#r therap*" or DBT or "mindfulness-based therap*" or "psychodynamic therap*" or "interpersonal therap*" or "humanistic therap*" or "gestalt therap*" or "existential therap*" or "psychedelic-assisted therap*" or "psychedelic-assisted psychotherap*" or "psychedelic therap*" or "substance-assisted psychotherap*" or "psychological support*").ti,ab.
3. (depress* or "major depressive disorder" or MDD or "treatment resistant depression" or "unipolar depression" or "mood disorder*OR bipolar" or "anxiety disorder*" or GAD or "social anxiety" or "panic disorder" or OCD or "obsessive compulsive disorder" or "obsessive-compulsive disorder" or PTSD or "post-traumatic stress disorder" or "posttraumatic stress disorder" or "eating disorder*" or anorexi* or bulimi* or "binge eating disorder" or "substance use disorder*" or "substance abuse" or "drug dependence" or addict* or alcoholi* or "alcohol use disorder*" or "alcohol dependence" or "substance dependence" or "drug addiction").ti,ab.
4. 1 and 2 and 3
5. remove duplicates from 4
6. limit 5 to english language
7. limit 6 to human
8. limit 7 to yr="2000-Current"
9. ("systematic review" or "meta analysis" or "meta-analysis").ti.
10. 8 not 9

Web of Science Search

1. (psychedelic* or "classic psychedelic*" or "classical psychedelic*" or hallucinogen* or entheogen* or psilocyb* or psilocin or "magic mushroom*" or LSD or "lysergic acid diethylamide" or DMT or "N,N-DMT" or dimethyltryptamine or "n,n-dimethyltryptamine" or ayahuasca or "5-MeO-DMT" or "5-methoxy-N,N-dimethyltryptamine" or bufotenin* or ibogaine or iboga or "12-hydroxyibogamine" or mescaline or peyote or "san pedro").ti,ab.
2. (psychotherap* or therap* or "cognitive behavio#ral therap*" or CBT or "acceptance commitment therap*" or "acceptance and commitment therap*" or ACT or "dialectical behavio#r therap*" or DBT or "mindfulness-based therap*" or "psychodynamic therap*" or "interpersonal therap*" or "humanistic therap*" or "gestalt therap*" or "existential therap*" or "psychedelic-assisted therap*" or "psychedelic-assisted psychotherap*" or "psychedelic therap*" or "substance-assisted psychotherap*" or "psychological support*").ti,ab.
3. (depress* or "major depressive disorder" or MDD or "treatment resistant depression" or "unipolar depression" or "mood disorder* OR bipolar" or "anxiety disorder*" or GAD or "social anxiety" or "panic disorder" or OCD or "obsessive compulsive disorder" or "obsessive-compulsive disorder" or PTSD or "post-traumatic stress disorder" or "posttraumatic stress disorder" or "eating disorder*" or anorexi* or bulimi* or "binge eating disorder" or "substance

use disorder*" or "substance abuse" or "drug dependence" or addict* or alcoholi* or "alcohol use disorder*" or "alcohol dependence" or "substance dependence" or "drug addiction").ti,ab.
4. 1 and 2 and 3
5. limit 4 to human
6. limit 5 to yr="2000-Current"
7. limit 6 to english language
8. remove duplicates from 7
9. ("systematic review" or "meta analysis" or "meta-analysis").ti.
10. 8 not 9

PRISMA flow diagram of study selection



A1.2 Study design and outcome information table

Authors (Year)	N	Mental Health Condition	Therapeutic Model	Compound	Number of Doses (Dosage)	Study Design	Blinding and Control Methods	Primary Outcome Measure	Follow-up of Primary Outcome	Sig. (Effect Size)	Location; Demographics
Davis et al. (2021)	24	MDD	Non-directive	Psilocybin	2 doses (20 mg/70 kg; 30 mg/70 kg)	RCT with a waiting list–controlled design	Blinded clinician-rated assessments; waitlist control	GRID-HAM-D	4 weeks	p < .001 (Cohen's d = 2.3)	Baltimore, Maryland, USA; 92% White non-Hispanic participants
Schneier et al. (2023)	12	BDD	Non-directive	Psilocybin	1 dose (25 mg)	Open-label pilot study	Unblinded; no control group	BDD-YBOCS	End of the dosing day, 1 day, and 1, 2, 3, 6, 9, and 12 weeks	p < .001 (Partial Eta Squared = 0.54)	New York, USA; 75% White non-Hispanic, 25% Asian/Pacific Islander
Carhart-Harris et al. (2016)	12	TRD	Non-directive	Psilocybin	2 doses (10mg; 25mg)	Open-label feasibility trial	Unblinded; no control group	QIDS	1 week	p = .002 (Hedge's g = 3.1)	London, UK; 78.9% Western white, 68.4% female participants
Sloshower et al. (2023)	15	MDD	ACT	Psilocybin	1 dose (0.3mg/kg)	Exploratory placebo-controlled, within-subject, fixed-order trial	Double blinding; placebo control (microcrystalline cellulose)	GRID-HAM-17	2, 4, 6 and 12 weeks	p = .310 (N/A)	USA; VA Connecticut Healthcare System
Palhano-Fontes et al. (2019)	29	TRD	Non-directive	Ayahuasca	1 dose (1ml/kg containing 0.36 mg/kg)	Parallel-arm, double-blind RCT	Double-blind; placebo control (liquid of similar taste and colour)	MADRS and HAM-D	1, 2 and 7 days	p = .019 (Cohen's d = 0.98)	Brazil: all participants were Brazilian, with low socioeconomic status (41% earning minimum wage)

(A1.2 continued)

Authors (Year)	N	Mental Health Condition	Therapeutic Model	Compound	Number of Doses (Dosage)	Study Design	Blinding and Control Methods	Primary Outcome Measure	Follow-up of Primary Outcome	Sig. (Effect Size)	Location; Demographics
Goodwin et al. (2022)	233	TRD	Non-directive	Psilocybin	1 dose (25 mg, 10 mg, or 1 mg)	Phase 2, double-blind, randomised, dose-finding clinical trial	Double-blind; placebo control (1mg psilocybin)	MADRS	3 weeks	p < .001 (N/A)	Czech Republic, Denmark, Germany, Ireland, the Netherlands, Portugal, Spain, UK, Canada and USA
Raison et al. (2023)	104	MDD	Non-directive	Psilocybin	1 dose (25 mg)	Phase 2 RCT	Double-blind; active placebo control (100mg niacin)	MADRS	43 days	p < .001 (N/A)	USA; conducted at 11 research sites
von Rotz et al. (2023)	52	MDD	Non-directive	Psilocybin	1 dose (0.215mg/kg)	Single-centre, double-blind, placebo-controlled, parallel-group RCT	Double-blind; placebo control (mannitol capsules)	MADRS and BDI	2 weeks	p = .001 (Cohen's d = 0.97)	Zurich, Switzerland; participants fluent in German
Carhart-Harris et al. (2021)	59	MDD	Non-directive	Psilocybin	2 doses (25mg)	Phase 2, double-blind RCT	Double-blind; active placebo control (1 mg psilocybin) or placebo control (10mg escitalopram)	QIDS-SR	6 weeks	p = .170 (N/A)	London, UK

Note. RCT, Randomised-Control Trial; TRD, Treatment-Resistant Depression; MDD, Major Depressive Disorder; BDD, Body Dysmorphic Disorder; MADRS, Montgomery-Åsberg Depression Rating Scale; BDI, Beck's Depression Inventory; HAMD, Hamilton Depression Rating scale; QIDS(SR), 16-item Quick Inventory of Depressive Symptomatology (-Self-Report); BDD-YBOCS, Yale-Brown Obsessive Compulsive Scale Modified for BDD, N,N-Dimethyltryptamine

A1.3 Modified TiDieR checklist for quality assessment

Scoring System (all Items)
0: No criteria met; information is not reported.
1: At least 1 criterion (1% - 33%) met; reporting is vague or minimal.
2: Some criteria (34% - 66%) met; moderate detail and clarity.
3: Most/all criteria (67% -100%) met; highly detailed, comprehensive reporting.

- Calculate % Elements Met
- Score (0-3) based on percentage of elements met

TiDiER-Based Items [T]

Naming and Describing the Protocol [T1]

a) Clear name or phrase identifying preparation methods
b) Consistent naming of preparation methods
c) Facilitates identification of preparation elements
d) Clearly differentiates preparation from other stages

Rationale for Preparation Methods [T2]

a) Describes the overall aim of preparation
b) Explains inclusion of specific components
c) Rationales are informed by theoretical/evidence frameworks
d) Identifies essential vs. optional elements

Materials and Resources [T3]

a) Describes physical/informational materials
b) Specifies material formats (e.g., print, audio)
c) Accessible materials for replication
d) Cites material availability elsewhere
e) If no materials/resources used: explicitly states no materials used, and/or why (0 or 3)

Session and Inter-Session Procedures [T4]

a) Outlines procedures, activities, or processes
b) Details actions by facilitators
c) Includes descriptions of supporting activities if included
d) In-depth descriptions of specific preparation components

Facilitator Details [T5]

a) Categories of facilitators (e.g., psychologist, nurse)
b) Background, expertise, qualifications
c) Details of training provided
d) Other factors influencing facilitator ability (e.g., incentives, recruitment methods, compensation, competence assessments, contextual factors etc)

Delivery Mode and Setting [T6,7]

a) Describes delivery modes (e.g., in-person, online)
b) Specifies synchronous/asynchronous
c) Individual/group sessions and size
d) Setting description (e.g., privacy, comfort)

Timing and Intensity [T8]

a) Number and duration of sessions
b) Scheduling details
c) Time period for delivery
d) Timing relative to key events (e.g., dosing session)

Tailoring and Modifications [T9/10]

a) Describes any personalised or protocol-level modifications
b) Reports whether changes were planned or unplanned
c) Reports decision frameworks or tools used for tailoring
d) If no tailoring or modification implemented: reports and justifies use of no tailoring or modifications (0 or 3)

Implementation Fidelity [T11/12]

a) Protocol adherence assessment
b) Strategies to maintain fidelity
c) Extent of intervention adherence
d) Deviations from the protocol
e) If no implementation fidelity assessments or strategies used: reports and justifies lack of implementation fidelity assessment or strategies

Preparation-Specific Additions [P]

Risk Management Framework [P1]

a) Reports specific psychological or cultural risks identified
b) Describes risk mitigation strategies (e.g., rapport-building, environment familiarisation, guidance for challenging experiences)
c) Outlines emergency response protocols for crises, or facilitator training in risk management (e.g., de-escalation techniques, crisis intervention)
d) Reports documentation and review of adverse events

Preparedness Assessment [P2]

a) Describes methods for evaluating participant readiness whether formal standardised assessments or at facilitator discretion

b) Specifies decision-making frameworks for readiness assessment
c) If no implementation fidelity assessments or strategies used: explicitly acknowledges and justifies lack of preparedness measurements

Preparation-Integration Alignment [P3]
a) Explicitly connects preparation and integration phases
b) Describes shared objectives, content or continuity of methods between the two stages
c) Reports therapeutic framework to align goals and activities in preparation and integration

Clinical Governance Structure [P4]
a) Defines roles and responsibilities of all individuals involved in the trial (e.g., investigators, sponsors)
b) Describes oversight of preparation sessions (e.g., formal supervisory meetings, ad-hoc support, session reviews, or case review processes)
c) Specifies reporting lines, decision-making hierarchy, and escalation pathways
d) Describes quality monitoring methods (e.g., session recordings, facilitator checklists, audits)
e) Reports compliance with ethical guidelines

Cultural and Accessibility Adaptations [P5]
a) Acknowledges cultural considerations in preparation (e.g., cultural backgrounds, beliefs, taboos around help-seeking or altered states)
b) Reports how therapeutic concepts and practices are explained or modified for cultural accessibility (e.g., adapting language, mindfulness practices, therapeutic frameworks)
c) Describes practical accessibility considerations (e.g., language support, scheduling, physical access)
d) Reports any cultural competency requirements or training for preparation facilitators
e) If no cultural or accessibility adaptations used: explicitly acknowledges and justifies lack of cultural adaptations, or use of homogenous sample

Additional notes
1. Due to the addition of 4 new items, some TiDieR-based items with overlapping constructs were condensed into one for simplicity.
2. Risk taking framework added as an item based on guidelines for safety in section about preparation.
3. Preparedness assessment was added as an item due to the need for standardised readiness assessment measures to ensure participant safety and efficacy of protocols.
4. Preparation-integration alignment added as consistency in methodology, goals and activities of both stages might lead to more optimal therapeutic outcomes (which needs empirical testing).
5. Clinical governance structure added as it is essential to ensure responsible, safe, effective, and ethical treatment delivery particularly in the context of hallucinogens.
6. Cultural and accessibility considerations were added as a separate item to highlight which studies implemented them. Reporting of these should not be optional, but imperative, to ensure safety of diverse participants. Historical exploitation of ethnic minorities has created barriers to trust Western medical contexts, making transparency around these issues imperative, particularly during preparation where trust and rapport is built.

A1.4 TiDiER-based quality assessment of protocol reporting

A1.4 T1-T12									
Author (Year)	**Naming and Describing the Protocol [T1] (0-3)**	**Rationale for Preparation Methods [T2] (0-3)**	**Materials and Resources [T3] (0-3)**	**Session and Inter-Session Procedures [T4] (0-3)**	**Facilitator Details [T5] (0-3)**	**Delivery Mode and Setting [T6,7] (0-3)**	**Timing and Intensity [T8] (0-3)**	**Tailoring and Modifications [T9,10] (0-3)**	**Implementation Fidelity [T11,12] (0-3)**
Sloshower et al. (2023)	(a) Clear name or phrase identifying preparation methods: Y (b) Consistent naming of preparation methods: N (c) Facilitates identification of preparation elements: Y (d) Clearly differentiates preparation from other stages: N % Elements Met: 50 Score (0-3): 2	(a) Describes the overall aim of preparation: Y (b) Explains inclusion of specific components: Y (c) Rationales are informed by theoretical/evidence frameworks: Y (d) Identifies essential vs. optional elements: N % Elements Met: 75 Score (0-3): 3	(a) Describes physical/informational materials: N (b) Specifies material formats: N (c) Accessible materials for replication: N (d) Cites material availability elsewhere: N % Elements Met: 0 Score (0-3): 0	(a) Outlines procedures, activities, or processes: Y (b) Details actions by facilitators: Y (c) Includes descriptions of supporting activities if included: N/A (d) In-depth descriptions of specific preparation components: Y % Elements Met: 100 Score (0-3): 3	(a) Categories of facilitators: Y (b) Background, expertise, qualifications: Y (c) Details of training provided: Y (d) Other factors influencing facilitator ability: N % Elements Met: 83 Score (0-3): 3	(a) Describes delivery modes (e.g., in-person, online): Y (b) Specifies synchronous/asynchronous: Y (c) Individual/group sessions and size: Y (d) Setting description (e.g., privacy, comfort): Y % Elements Met: 100 Score (0-3): 3	(a) Number and duration of sessions: Y (b) Scheduling details: Y (c) Time period for delivery: Y (d) Timing relative to key events (e.g., dosing session): Y % Elements Met: 100 Score (0-3): 3	*No tailoring or modification used: (d) Reports and justifies use of no tailoring or modifications: N % Elements Met: 0 Score (0-3): 0	*No implementation fidelity assessments or strategies implemented (0 or 3): (e) Reports and justifies lack of implementation fidelity assessment or strategies: Y % Elements Met: 100 Score (0-3): 3
Raison et al. (2023)	(a) Clear name or phrase identifying preparation methods: Y (b) Consistent naming of preparation methods: Y (c) Facilitates identification of preparation elements: N (d) Clearly differentiates preparation from other stages: Y % Elements Met: 75 Score (0-3): 3	(a) Describes the overall aim of preparation: Y (b) Explains inclusion of specific components: N (c) Rationales are informed by theoretical/evidence frameworks: Y (d) Identifies essential vs. optional elements: N % Elements Met: 50 Score (0-3): 2	(a) Describes physical/informational materials: N (b) Specifies material formats: N (c) Accessible materials for replication: N (d) Cites material availability elsewhere: N (e) Clear if no materials used: N % Elements Met: 0 Score (0-3): 0	(a) Outlines procedures, activities, or processes: Y (b) Details actions by facilitators: Y (c) Includes descriptions of supporting activities if included: N/A (d) In-depth descriptions of specific preparation components: N % Elements Met: 67 Score (0-3): 3	(a) Categories of facilitators: Y (b) Background, expertise, qualifications: Y (c) Details of training provided: Y (d) Other factors influencing facilitator ability: Y % Elements Met: 100 Score (0-3): 3	(a) Describes delivery modes (e.g., in-person, online): Y (b) Specifies synchronous/asynchronous: Y (c) Individual/group sessions and size: N (d) Setting description (e.g., privacy, comfort): N % Elements Met: 50 Score (0-3): 2	(a) Number and duration of sessions: N (b) Scheduling details: N (c) Time period for delivery: Y (d) Timing relative to key events (e.g., dosing session): Y % Elements Met: 50 Score (0-3): 2	(a) Describes any personalised or protocol-level modifications: Y (b) Reports whether changes were planned or unplanned: N (c) Reports decision frameworks or tools used for tailoring: N % Elements Met: 33% Score (0-3): 1	*No implementation fidelity assessments or strategies implemented (0 or 3): (e) Reports and justifies lack of implementation fidelity assessment or strategies: N % Elements Met: 0 Score (0-3): 0

A1.4 T1-T12 (continued)									
von Rotz et al. (2023)	(a) Clear name or phrase identifying preparation methods: Y (b) Consistent naming of preparation methods: Y (c) Facilitates identification of preparation elements: Y (d) Clearly differentiates preparation from other stages: Y % Elements Met: 100 Score (0-3): 3	(a) Describes the overall aim of preparation: Y (b) Explains inclusion of specific components: N (c) Rationales are informed by theoretical/evidence frameworks: N (d) Identifies essential vs. optional elements: N % Elements Met: 25 Score (0-3): 1	*No materials/ resources used (0 or 3): (e) Explicitly states if no materials used, and/or why: N % Elements Met: Score (0-3): 0	(a) Outlines procedures, activities, or processes: Y (b) Details actions by facilitators: N (c) Includes descriptions of supporting activities if included: N/A (d) In-depth descriptions of specific preparation components: Y % Elements Met: 67 Score (0-3): 3	(a) Categories of facilitators: Y (b) Background, expertise, qualifications: Y (c) Details of training provided: N (d) Other factors influencing facilitator ability: N % Elements Met: 50 Score (0-3): 2	(a) Describes delivery modes: Y (b) Specifies synchronous/asynchronous: Y (c) Individual/group sessions and size: N (d) Setting description: Y % Elements Met: 100 Score (0-3): 3	(a) Number and duration of sessions: Y (b) Scheduling details: Y (c) Time period for delivery: Y (d) Timing relative to key events: Y % Elements Met: 100 Score (0-3): 3	(a) Describes any personalised or protocol-level modifications: N (b) Reports whether changes were planned or unplanned: N (c) Reports decision frameworks or tools used for tailoring: N % Elements Met: 0 Score (0-3): 0	*No implementation fidelity assessments or strategies implemented (0 or 3): (e) Reports and justifies lack of implementation fidelity assessment or strategies: N % Elements Met: 0 Score (0-3): 0
Goodwin et al. (2022)	(a) Clear name or phrase identifying preparation methods: Y (b) Consistent naming of preparation methods: N (c) Facilitates identification of preparation elements: Y (d) Clearly differentiates preparation from other stages: N % Elements Met: 50 Score (0-3): 2	(a) Describes the overall aim of preparation: Y (b) Explains inclusion of specific components: N (c) Rationales are informed by theoretical/evidence frameworks: N (d) Identifies essential vs. optional elements: N % Elements Met: 25 Score (0-3): 1	*No materials/ resources used (0 or 3): (e) Explicitly states if no materials used, and/or why: N % Elements Met: 0 Score (0-3): 0	(a) Outlines procedures, activities, or processes: Y (b) Details actions by facilitators: N (c) Includes descriptions of supporting activities if included: N (d) In-depth descriptions of specific preparation components: N % Elements Met: 25 Score (0-3): 1	(a) Categories of facilitators: Y (b) Background, expertise, qualifications: Y (c) Details of training provided: Y (d) Other factors influencing facilitator ability: N % Elements Met: 75 Score (0-3): 3	(a) Describes delivery modes: Y (b) Specifies synchronous/asynchronous: N (c) Individual/group sessions and size: N (d) Setting description (e.g., privacy, comfort): N % Elements Met: 25 Score (0-3): 1	(a) Number and duration of sessions: Y (b) Scheduling details: Y (c) Time period for delivery: Y (d) Timing relative to key events (e.g., dosing session): N % Elements Met: 75 Score (0-3): 3	(a) Describes any personalised or protocol-level modifications: N (b) Reports whether changes were planned or unplanned: N (c) Reports decision frameworks or tools used for tailoring: N % Elements Met: 0 Score (0-3): 0	(a) Protocol adherence assessment: Y (b) Strategies to maintain fidelity: Y (c) Extent of intervention adherence: N (d) Deviations from the protocol: N % Elements Met: 50 Score (0-3): 2

A1.4 T1-T12 (continued)									
Carhart-Harris et al. (2021)	(a) Clear name or phrase identifying preparation methods: Y (b) Consistent naming of preparation methods: Y (c) Facilitates identification of preparation elements: N (d) Clearly differentiates preparation from other stages: Y % Elements Met: 75 Score (0-3): 3	(a) Describes the overall aim of preparation: Y (b) Explains inclusion of specific components: Y (c) Rationales are informed by theoretical/evidence frameworks: Y (d) Identifies essential vs. optional elements: N % Elements Met: 75 Score (0-3): 3	(a) Describes physical/informational materials: Y (b) Specifies material formats: N (c) Accessible materials for replication: Y (d) Cites material availability elsewhere: Y % Elements Met: 75 Score (0-3): 3	(a) Outlines procedures, activities, or processes: Y (b) Details actions by facilitators: Y (c) Includes descriptions of supporting activities if included: Y (d) In-depth descriptions of specific preparation components: N % Elements Met: 75 Score (0-3): 3	(a) Categories of facilitators: Y (b) Background, expertise, qualifications: Y (c) Details of training provided: N (d) Other factors influencing facilitator ability: N % Elements Met: 50 Score (0-3): 2	(a) Describes delivery modes: Y (b) Specifies synchronous/asynchronous: N (c) Individual/group sessions and size: Y (d) Setting description (e.g., privacy, comfort): N % Elements Met: 50 Score (0-3): 2	(a) Number and duration of sessions: Y (b) Scheduling details: Y (c) Time period for delivery: Y (d) Timing relative to key events (e.g., dosing session): Y % Elements Met: 100 Score (0-3): 3	(a) Describes any personalised or protocol-level modifications: Y (b) Reports whether changes were planned or unplanned: N (c) Reports decision frameworks or tools used for tailoring: Y % Elements Met: 67 Score (0-3): 3	(a) Protocol adherence assessment: Y (b) Strategies to maintain fidelity: Y (c) Extent of intervention adherence: N (d) Deviations from the protocol: N % Elements Met: 50 Score (0-3): 2
Davis et al (2021)	(a) Clear name or phrase identifying preparation methods: Y (b) Consistent naming of preparation methods: N (c) Facilitates identification of preparation elements: N (d) Clearly differentiates preparation from other stages: Y % Elements Met: 50 Score (0-3): 2	(a) Describes the overall aim of preparation: Y (b) Explains inclusion of specific components: Y (c) Rationales are informed by theoretical/evidence frameworks: N (d) Identifies essential vs. optional elements: N % Elements Met: 50 Score (0-3): 2	*No materials/ resources used (0 or 3): (e) Explicitly states if no materials used, and/or why: N % Elements Met: 0 Score (0-3): 0	(a) Outlines procedures, activities, or processes: Y (b) Details actions by facilitators: N (c) Includes descriptions of supporting activities if included: N/A (d) In-depth descriptions of specific preparation components: N % Elements Met: 33 Score (0-3): 1	(a) Categories of facilitators: Y (b) Background, expertise, qualifications: Y (c) Details of training provided: N (d) Other factors influencing facilitator ability: N % Elements Met: 50 Score (0-3): 2	(a) Describes delivery modes: Y (b) Specifies synchronous/asynchronous: Y (c) Individual/group sessions and size: N (d) Setting description (e.g., privacy, comfort): N % Elements Met: 50 Score (0-3): 2	(a) Number and duration of sessions: N (b) Scheduling details: Y (c) Time period for delivery: Y (d) Timing relative to key events (e.g., dosing session) Y: % Elements Met: 75 Score (0-3): 3	(a) Describes any personalised or protocol-level modifications: Y (b) Reports whether changes were planned or unplanned: N (c) Reports decision frameworks or tools used for tailoring: Y % Elements Met: 67 Score (0-3): 3	*No implementation fidelity assessments or strategies implemented (0 or 3): (e) Reports and justifies lack of implementation fidelity assessment or strategies: N % Elements Met: 0 Score (0-3) 0

A1.4 T1-T12 (continued)									
Carhart-Harris et al. (2016)	(a) Clear name or phrase identifying preparation methods: N (b) Consistent naming of preparation methods: Y (c) Facilitates identification of preparation elements: Y (d) Clearly differentiates preparation from other stages: Y % Elements Met: 75 Score (0-3): 3	(a) Describes the overall aim of preparation: Y (b) Explains inclusion of specific components: N (c) Rationales are informed by theoretical/evidence frameworks: N (d) Identifies essential vs. optional elements: N % Elements Met: 25 Score (0-3): 1	*No materials/ resources used (0 or 3): (e) Explicitly states if no materials used, and/or why: N % Elements Met: 0 Score (0-3): 0	(a) Outlines procedures, activities, or processes: Y (b) Details actions by facilitators: N (c) Includes descriptions of supporting activities if included: N/A (d) In-depth descriptions of specific preparation components: N % Elements Met: 33 Score (0-3): 1	(a) Categories of facilitators: Y (b) Background, expertise, qualifications: N (c) Details of training provided: N (d) Other factors influencing facilitator ability: N % Elements Met: 25 Score (0-3): 1	(a) Describes delivery modes: Y (b) Specifies synchronous/asynchronous: N (c) Individual/group sessions and size: N (d) Setting description (e.g., privacy, comfort): Y % Elements Met: 50 Score (0-3): 2	(a) Number and duration of sessions: N (b) Scheduling details: Y (c) Time period for delivery: Y (d) Timing relative to key events (e.g., dosing session): Y % Elements Met: 75 Score (0-3): 3	(a) Describes any personalised or protocol-level modifications: Y (b) Reports whether changes were planned or unplanned: Y (c) Reports decision frameworks or tools used for tailoring: N % Elements Met: 67 Score (0-3): 3	(a) Protocol adherence assessment: Y (b) Strategies to maintain fidelity: N (c) Extent of intervention adherence: N % Elements Met: 33 Score (0-3) : 1

A1.4 P1-P5						
Author (Year)	**Risk Management Framework [P1] (0-3)**	**Preparedness Assessment [P2] (0-3)**	**Preparation-Integration Alignment [P3] (0-3)**	**Clinical Governance Structure [P4] (0-3)**	**Cultural and Accessibility Adaptations [P5] (0-3)**	**Total (0-42)**
Sloshower et al. (2023)	(a) Reports identified psychological or cultural risks: Y (b) Describes risk mitigation strategies implemented in preparation: N (c) Outlines emergency response protocols for crises, or facilitator training in risk management: N (d) Reports documentation and review of adverse events: Y % Elements Met: 50 Score (0-3): 2	*No preparedness assessments conducted (0 or 3): (c) Explicitly acknowledges and justifies lack of preparedness measurements: N % Elements Met: Score (0-3): 0	(a) Explicitly connects preparation and integration phases: Y (b) Describes shared objectives, content or continuity of methods between the two stages: Y (c) Reports therapeutic framework to align goals and activities in preparation and integration: Y % Elements Met: 100 Score (0-3): 3	(a) Defines roles and responsibilities of all individuals involved in the trial: Y (b) Describes oversight of preparation sessions: Y (c) Specifies reporting lines, decision-making hierarchy, and escalation pathways: N (e) Describes quality monitoring methods: N (f) Reports compliance with ethical guidelines: Y % Elements Met: 60 Score (0-3): 2	*No cultural adaptations implemented (0 or 3): (e) Explicitly acknowledges and justifies lack of cultural adaptations, or use of homogenous sample: Y % Elements Met: 100 Score (0-3): 3	30
Raison et al. (2023)	(a) Reports specific psychological or cultural risks identified: N (b) Describes risk mitigation strategies: N (c) Outlines emergency response protocols for crises, or facilitator training in risk management: Y (d) Reports documentation and review of adverse events: Y % Elements Met: 50 Score (0-3): 2	(a) Describes methods for evaluating participant readiness: Y (b) Specifies decision-making frameworks for readiness assessment: N % Elements Met: 50 Score (0-3): 2	(a) Explicitly connects preparation and integration phases: N (b) Describes shared objectives, content or continuity of methods between the two stages: N (c) Reports therapeutic framework to align goals and activities in preparation and integration: Y % Elements Met: 33 Score (0-3): 1	(a) Defines roles and responsibilities of all individuals involved in the trial: Y (b) Describes oversight of preparation sessions: N (c) Specifies reporting lines, decision-making hierarchy, and escalation pathways: N (e) Describes quality monitoring methods: Y (f) Reports compliance with ethical guidelines: Y % Elements Met: 60 Score (0-3): 2	(a) Acknowledges cultural considerations in preparation: N (b) Reports how therapeutic concepts and practices are explained or modified for cultural accessibility: N (c) Describes practical accessibility considerations: Y (d) Reports any cultural competency requirements or training for preparation facilitators: N % Elements Met: 25 Score (0-3): 1	24

A1.4 P1-P5 (continued)						
von Rotz et al. (2023)	(a) Reports specific psychological or cultural risks identified: Y (b) Describes risk mitigation strategies: Y (c) Outlines emergency response protocols for crises, or facilitator training in risk management: Y (d) Reports documentation and review of adverse events: Y % Elements Met: 100 Score (0-3): 3	*No preparedness assessments conducted (0 or 3): (c) Explicitly acknowledges and justifies lack of preparedness measurements: N % Elements Met: 0 Score (0-3): 0	(a) Explicitly connects preparation and integration phases: N (b) Describes shared objectives, content or continuity of methods between the two stages: N (c) Reports therapeutic framework to align goals and activities in preparation and integration: N % Elements Met: 0 Score (0-3): 0	(a) Defines roles and responsibilities of all individuals involved in the trial: Y (b) Describes oversight of preparation sessions: N (c) Specifies reporting lines, decision-making hierarchy, and escalation pathways: N (e) Describes quality monitoring methods: Y (f) Reports compliance with ethical guidelines: Y % Elements Met: 60 Score (0-3): 2	*No cultural adaptations implemented (0 or 3): (e) Explicitly acknowledges and justifies lack of cultural adaptations, or use of homogenous sample: N % Elements Met: 0 Score (0-3): 0	20
Goodwin et al. (2022)	(a) Reports specific psychological or cultural risks identified: N (b) Describes risk mitigation strategies: N (c) Outlines emergency response protocols for crises, or facilitator training in risk management: Y (d) Reports documentation and review of adverse events: Y % Elements Met: 50 Score (0-3): 2	(a) Describes methods for evaluating participant readiness: N (b) Specifies decision-making frameworks for readiness assessment: n % Elements Met: 0 Score (0-3): 0	(a) Explicitly connects preparation and integration phases: N (b) Describes shared objectives, content or continuity of methods between the two stages: Y (c) Reports therapeutic framework to align goals and activities in preparation and integration: N % Elements Met: 33 Score (0-3): 1	(a) Defines roles and responsibilities of all individuals involved in the trial: Y (b) Describes oversight of preparation sessions: Y (c) Specifies reporting lines, decision-making hierarchy, and escalation pathways: Y (e) Describes quality monitoring methods: Y (f) Reports compliance with ethical guidelines: Y % Elements Met: 100 Score (0-3): 3	*No cultural adaptations implemented (0 or 3): (e) Explicitly acknowledges and justifies lack of cultural adaptations, or use of homogenous sample: N % Elements Met: 0 Score (0-3): 0	19
Carhart-Harris et al. (2021)	(a) Reports specific psychological or cultural risks identified: Y (b) Describes risk mitigation strategies: Y (c) Outlines emergency response protocols for crises, or facilitator training in risk management: N (d) Reports documentation and review of adverse events: Y % Elements Met: 75 Score (0-3): 3	*No preparedness assessments conducted (0 or 3): (c) Explicitly acknowledges and justifies lack of preparedness measurements: N % Elements Met: 0 Score (0-3): 0	(a) Explicitly connects preparation and integration phases: N (b) Describes shared objectives, content or continuity of methods between the two stages: Y (c) Reports therapeutic framework to align goals and activities in preparation and integration: Y % Elements Met: 67 Score (0-3): 3	(a) Defines roles and responsibilities of all individuals involved in the trial: Y (b) Describes oversight of preparation sessions: Y (c) Specifies reporting lines, decision-making hierarchy, and escalation pathways: Y (e) Describes quality monitoring methods: Y (f) Reports compliance with ethical guidelines: Y % Elements Met: 100 Score (0-3): 3	*No cultural adaptations implemented (0 or 3): (e) Explicitly acknowledges and justifies lack of cultural adaptations, or use of homogenous sample: N % Elements Met: 0 Score (0-3): 0	33

A1.4 P1-P5 (continued)						
Davis et al (2021)	(a) Reports specific psychological or cultural risks identified: Y (b) Describes risk mitigation strategies: Y (c) Outlines emergency response protocols for crises, or facilitator training in risk management: Y (d) Reports documentation and review of adverse events: Y % Elements Met: 100 Score (0-3): 3	*No preparedness assessments conducted (0 or 3): (c) Explicitly acknowledges and justifies lack of preparedness measurements: N % Elements Met: 0 Score (0-3): 0	(a) Explicitly connects preparation and integration phases: N (b) Describes shared objectives, content or continuity of methods between the two stages: Y (c) Reports therapeutic framework to align goals and activities in preparation and integration: N % Elements Met: 33 Score (0-3): 1	(a) Defines roles and responsibilities of all individuals involved in the trial: N (b) Describes oversight of preparation sessions: N (c) Specifies reporting lines, decision-making hierarchy, and escalation pathways: Y (e) Describes quality monitoring methods: N (f) Reports compliance with ethical guidelines: Y % Elements Met: 40 Score (0-3): 2	*No cultural adaptations implemented (0 or 3): (e) Explicitly acknowledges and justifies lack of cultural adaptations, or use of homogenous sample: Y % Elements Met: 3 Score (0-3): 3	24
Carhart-Harris et al. (2016)	(a) Reports specific psychological or cultural risks identified: Y (b) Describes risk mitigation strategies: Y (c) Outlines emergency response protocols for crises, or facilitator training in risk management: Y (d) Reports documentation and review of adverse events: Y % Elements Met: 100 Score (0-3): 3	*No preparedness assessments conducted (0 or 3): (c) Explicitly acknowledges and justifies lack of preparedness measurements: N % Elements Met: 0 Score (0-3): 0	(a) Explicitly connects preparation and integration phases: N (b) Describes shared objectives, content or continuity of methods between the two stages: N (c) Reports therapeutic framework to align goals and activities in preparation and integration: N % Elements Met: 0 Score (0-3): 0	(a) Defines roles and responsibilities of all individuals involved in the trial: Y (b) Describes oversight of preparation sessions: N (c) Specifies reporting lines, decision-making hierarchy, and escalation pathways: Y (e) Describes quality monitoring methods: Y (f) Reports compliance with ethical guidelines: Y % Elements Met: 80 Score (0-3): 3	*No cultural adaptations implemented (0 or 3): (e): Explicitly acknowledges and justifies lack of cultural adaptations, or use of homogenous sample: N % Elements Met: 0 Score (0-3): 0	21

Appendix 2

A2.1 Adapted PGTI-SF

The next set of questions ask about the impact of your most significant psychedelic experience and the extent to which you believe things have changed in your life because of that experience. Please indicate how much you agree or disagree with the following statements (0: Strongly disagree; 7: Strongly agree)

1. The experience has changed who i am
2. The experience has become a reference point for the way I understand myself and the world.
3. The experience has become a central part of my life story.
4. The experience has coloured the way I think and feel about other experiences.
5. The experience permanently changed my life.
6. I often think about the effects the experience will have on my future.
7. The experience was a turning point in my life.

A2.2 Adapted COES

The next set of questions ask about the impact of your most significant psychedelic experience and the extent to which you believe things have changed in your life because of that experience (0: Strongly disagree; 7: Strongly agree).
Since my most significant psychedelic drug experience…

1. I have changed my priorities about what is important in life.
2. I have a greater appreciation for the value of my own life.
3. I have a better understanding of spiritual matters.
4. I have established a new path for my life.
5. I have a greater sense of closeness with others.
6. I am better able to handle difficulties.
7. I am able to do better things with my life.
8. I have a stronger religious faith.
9. I discovered that I'm stronger than I thought I was.
10. I learned a great deal about how wonderful people are.

A2.3 Demographic characteristics of Delphi participants ('expert judges')

		Round 1 (n = 12)	Round 2 (n = 10)	Round 3 and 4 (n = 7)
Gender	Male	7 (58.3%)	6 (60%)	4 (57.1%)
	Female	5 (44.7%)	4 (40%)	3 (42.9%)
Mean age in years (SD)		42.08 (7.34)	42.30 (7.97)	43.71 (7.89)
Country of residence	UK	4 (33.3%)	2 (20%)	2 (28.6%)
	USA	4 (33.3%)	4 (40%)	3 (42.9%)
	Netherlands	2 (16.7%)	2 (20%)	1 (14.3%)
	Australia	1 (8.3%)	1 (10%)	0 (0%)
	Germany	1 (8.3%)	1 (10%)	1 (14.3%)
Current role	Professor	5 (44.7%)	3 (30%)	2 (28.6%)
	Associate Professor	1 (8.3%)	1 (10%)	0 (0%)

	Lecturer	1 (8.3%)	1 (10%)	1 (14.3%)
	Psychiatrist [a]	3 (25%)	3 (30%)	2 (28.6%)
	Clinical Psychologist [a]	2 (16.7%)	2 (20%)	2 (28.6%)
Years working in the field	10+ years	7 (58.3%)	6 (60%)	4 (57.1%)
	6-9 years	3 (25%)	2 (20%)	1 (14.3%)
	4-5 years	1 (8.3%)	1 (10%)	1 (14.3%)
	1-3 years	1 (8.3%)	1 (10%)	1 (14.3%)

[a] *Non-clinical professionals*

A2.4 Demographic characteristics of focus group participants ('participant judges')

Gender (n = 6)	Male	3 (50%)
	Female	3 (50%)
Mean age in years (SD)		44 (7.21)
Ethnicity	White	5 (83.3%
	Latin American	1 (16.7%)
Country of residence	UK	2 (33.3%)
	USA	2 (33.3%)
	Portugal	1 (16.7%)
	Hawaii	1 (16.7%)
Education Level	Undergraduate Degree	1 (16.7%)
	Master's Degree	2 (33.3%)
	Doctorate Degree	3 (50%)
Experience with PAP	Psilocybin for depression trial participant	3 (50%)
	Psilocybin for alcohol use disorder trial participant	1 (16.7%)
	Psilocybin retreat participant	1 (16.7%)
	Underground PAP client	1 (16.7%)

A2.5 Demographic characteristics of qualitative pretest interview participants

Gender (n = 6)	Male	4 (66.7%)
	Female	2 (33.3%)
Mean age in years (SD)		36.5 (9.69)
Ethnicity	White	5 (83.3%
	Mixed	1 (16.7%)
Country of residence	UK	2 (33.3%)
	USA	2 (33.3%)
	Netherlands	1 (16.7%)

	Germany	1 (16.7%)
Education Level	Undergraduate Degree	3 (50%)
	Master's Degree	2 (33.3%)
	Doctorate Degree	1 (16.7%)
Experience with PAP	Attended a 5-day psilocybin retreat in Netherlands with 2 dosing sessions	3 (50%)
	Attended a 5-day psilocybin retreat in Mexico with 2 dosing sessions	1 (16.7%)
	Attended a 7-day psilocybin retreat in Mexico with 2 dosing sessions	2 (33.3%)

A2.6 Examples of QPI informed item modifications. Prospective adaptations are presented in brackets.

Domain	Original Item	QPI Response	Updated Item
Expectation-management	I had (have) realistic expectations for the psychedelic experience	P2: "I'm thinking back to what I expected of the experience, mainly in the weeks leading up to it, and I don't know if [I] really understand what a realistic expectation is. Does this mean my expectations became in line with my actual reality or does it mean they were suitable and not too far-fetched, and they possibly could have become my reality... I also feel like it slightly trips me up because I really have to think back to the, almost, accuracy or good-ness of those expectations and then reality check them. Basically, er, I think this is a bit confusing." P3: "As I'm reading this out loud, the word realistic… it seems sort of jarring. I don't really know what it would mean to be realistic, and I don't feel immediately as if I'm in the position to assess the realistic-ness of these expectations or the experience. It just, well, I feel like something simpler about expectations matching experience would be better. If that's what you're asking."	My expectations for the experience were (are) accurate
Psychological mindedness	I went into (am going into) the psychedelic experience with a willingness to try and understand myself more	P2: "I'm not really sure if the word try works here. It makes me wonder how hard I tried to do this back then, and I get a bit caught up in this. So, [it] becomes kinda meaningless for me. I can't really tell if I was trying, or if I was trying hard enough. I do think I tried this, but if you asked me something, like, if I was willing and open, I'd be able to answer more easily." P4: "I get what this is saying but the phrase willingness to try and understand seems a bit odd. Does this mean I was willing to do something, or a willingness to try and understand, or that I really was able to understand. Just because I'm willing to try and understand something, does this then impact whether or not I then understood it. I feel like I get a bit caught up in working out what this means."	I went into (am going into) the experience willing to learn more about the meaning behind my thoughts
Willingness to surrender	I was (am) willing to accept whatever 'came up' ('comes up') during the psychedelic experience	P1: "It's hard for me to remember whether or not I was capable [of] saying before the experience that I could accept whatever came up during it, but I do get what this question is trying to ask. I just don't know if before the experience I could really make claims like this, because the accepting bit is sometimes pretty hard. I don't think I would want to accept everything during the experience. That kind of takes all of your autonomy away from [it]. I don't think it's just about accepting." P5: "Accept is pretty loaded in this statement. It makes me feel slightly as though I've given up on something - in a weird way. You could try shifting the word 'experience', so 'I was willing to experience' and then whatever came up for me." P5: "Er, well, I feel like if you've decided and consented to taking the drug, you are kind of agreeing and expecting things to come up associated with that drug. You've chosen to take this drug so this kind of implies you're willing to allow the drug to take its effects. Maybe for some people they took the drug and then didn't want anything to come up, like, maybe they wanted a funny nice time with friends. But I just think it's a bit confusing because… surely, you're going to take the drug knowing that these things will come up. It's also really ambiguous like I'm not really sure what 'come up' even means, differentiated from allowing the drug to just do its thing."	I was (am) ready to experience whatever 'came up' ('comes up') during the psychedelic experience

A2.6 (continued)

Prepared for change	I feel as though the psychedelic experience has permanently changed me	P3: "This one is tricky because I can't really tell if I've been permanently changed. I feel different and I can track certain changes. But erm, I feel this is too broad. Especially if we are trying to measure this within one single item."	I correctly anticipated the kinds of changes that occurred
		P6: "The first thing that comes to mind is the question of what is 'me', like, can I really describe 'me' in a single way. I'm thinking about certain qualities I possess and I feel as though I am made up of various parts. I do feel as though my psychedelic experience changed parts of me, but I still feel like, at the core, I am me."	

A2.7 51-items (11 subdomains) selected at the end of the DelFo rounds and QPIs

	Retrospective	Prospective
Psychoeducation	I had done some of my own research into the effects of the substance (e.g., reading articles/books, watching videos, listening to podcasts etc)	I have done some of my own research into the effects of the substance (e.g., reading articles/books, watching videos, listening to podcasts etc)
	I had learned about the effects of the substance through conversations with other people	I have learned about the effects of the substance through conversations with other people
	I understood that the experience could evoke a range of intense emotions, from bliss to horror	I understand that the experience might evoke a range of intense emotions, from bliss to horror
	I was completely unaware of what to expect from the experience	I am completely unaware of what to expect from the experience
	I should have known more about the substance I was going to take	I should know more about the substance I am going to take
	My prior research and knowledge about the psychedelic were crucial to what I experienced (PE)	-
Intention Setting	I had a clear intention for the psychedelic experience	I have a clear intention for the psychedelic experience
	I was sure that keeping my intention in mind would help guide the psychedelic experience	I am sure that keeping my intention in mind will help guide the psychedelic experience
	I had carefully contemplated my reasons for undergoing the psychedelic experience	I have carefully contemplated my reasons for undergoing the psychedelic experience
	My intentions influenced my experience (PE)	-
Expectation Management	I expected the psychedelic experience to completely change my life	I expect the psychedelic experience to completely change my life
	I was expecting the psychedelic experience to be easy and fun	I expect the psychedelic experience to be easy and fun
	I understood that events from my past could surface into the psychedelic experience	I understand that events from my past might surface into the psychedelic experience
	I knew that my experience would be somewhat unpredictable	I know that my experience will be somewhat unpredictable
	My expectations for the experience were accurate (PE)	-
Psychological Mindedness	I spoke with a therapist/counsellor as part of my preparation for the psychedelic experience	I have spoken with a therapist/counsellor as part of my preparation for the psychedelic experience
	I went into the experience willing to learn more about the meaning behind my thoughts	I am going into the experience willing to learn more about the meaning behind my thoughts
	I went into the experience with a curiosity about my own mind	I am going into the experience with a curiosity about my own mind
	Engaging with my thoughts/feelings in the lead up to my experience impacted the experience itself (PE)	-

A2.7 (continued)		
Emotional Readiness	I felt ready for the psychedelic experience	I feel ready for the psychedelic experience
	I had serious doubts before going into the psychedelic experience	I have serious doubts about going into the psychedelic experience
	I felt afraid going into the psychedelic experience	I feel afraid about going into the psychedelic experience
	I felt comfortable going into the psychedelic experience	I feel comfortable about going into the psychedelic experience
	I felt emotionally ready for what I experienced (PE)	-
Willingness to Surrender	I was ready to experience whatever 'came up' during the psychedelic experience	I am ready to experience whatever 'comes up' during the psychedelic experience
	I was prepared to deal with uncomfortable and challenging aspects of the psychedelic experience	I am prepared to deal with uncomfortable and challenging aspects of the psychedelic experience
	I felt ready to surrender to whatever the psychedelic experience would be	I feel ready to surrender to whatever the psychedelic experience will be
	I was able to surrender during the experience (PE)	-
Psychophysical Robustness	I felt psychologically prepared for the psychedelic experience	I feel psychologically prepared for the psychedelic experience
	I was prepared for the physical effects of the psychedelic	I am prepared for the physical effects of the psychedelic
	I felt as though my mind and body would be 'strong enough' for the upcoming experience	I feel as though my mind and body will be 'strong enough' for the upcoming experience
	I was mentally and physically prepared for what I experienced while on the psychedelic substance (PE)	-
Safety/Security	In the lead up to the actual psychedelic experience, I felt a trusting, positive connection with the people around me	I feel a trusting, positive connection with the people who will be around me during the psychedelic experience
	I felt the substance would be safe to take	I feel the substance will be safe to take
	I trusted the quality and purity of the of the substance	I trust the quality and purity of the of the substance
	I trusted my own mind and body to safely process the experience	I trust my own mind and body to safely process the experience
	I felt safe and supported throughout my psychedelic experience (PE)	-

A2.7 (continued)

Prepared for Change	I was aware that the psychedelic experience might change me in some way	I am aware that the psychedelic experience might change me in some way
	I felt ready to accept some big changes that might occur in myself as a result of the psychedelic experience	I feel ready to accept some big changes that might occur in myself as a result of the psychedelic experience
	My family and/or friends were prepared and well-informed about the changes that could occur in me	My family and/or friends are prepared and well-informed about the changes that might occur in me
	My friends and/or family were ready to support me through any changes I experienced	My friends and/or family are ready to support me through any changes I experience
	I was worried about becoming too different after the psychedelic experience	I am worried about becoming too different after the psychedelic experience
	I was afraid that I might change in a negative way after the psychedelic experience	I am afraid that I might change in a negative way after the psychedelic experience
	I correctly anticipated the kinds of changes that occurred (PE)	-
Preparatory Practices	I dedicated time to preparing for the psychedelic experience	I have dedicated time to preparing for the psychedelic experience
	I engaged with specific preparation practices before the psychedelic experience (e.g., meditation, yoga, breathwork, journaling, diet, exercise)	I have engaged with specific preparation practices in the lead up to the psychedelic experience (e.g., meditation, yoga, breathwork, journaling, diet, exercise)
	I planned out what I would do in the hours and days after the psychedelic experience	I have planned out what I will do in the hours and days after the psychedelic experience
	I told close/trusted friends and/or family that I was going to have the psychedelic experience	I have told close/trusted friends and/or family that I am going to have the psychedelic experience
	I didn't do anything to prepare for the psychedelic experience	I haven’t done anything to prepare for the psychedelic experience
	I had prepared some strategies in case things started to get difficult during the psychedelic experience	I have prepared some strategies in case things start to get difficult during the psychedelic experience
	My preparation impacted my experience (PE)	-

Note: Psychedelic Efficacy items (PE) were not included in the PPS

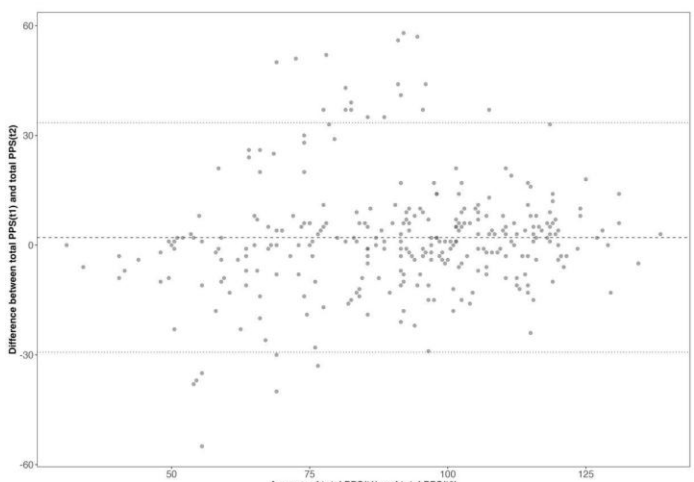
A2.8 Model evaluation methods

We used the likelihood ratio test ($\Delta\chi^2/\Delta df$, also called the χ^2 difference test) as a method of comparing between nested models, meaning those that have the same amount of items and differ in the number of factors i.e. latent variables (Brown, 2015). The hypothesized 4-factor model was the parent model to which all the other nested models were compared. At df=1, the critical value of χ^2 is 3.84 (α=.05), so a χ^2 difference of >3.84 for a change in 1df from parent to the (compared) nested model indicates that the parent model provides a significantly better fit (Brown, 2015). We also calculated changes in RMSEA (ΔRMSEA) relative to the parent model to compare models more easily.

A2.9 Tests of reliability and validity

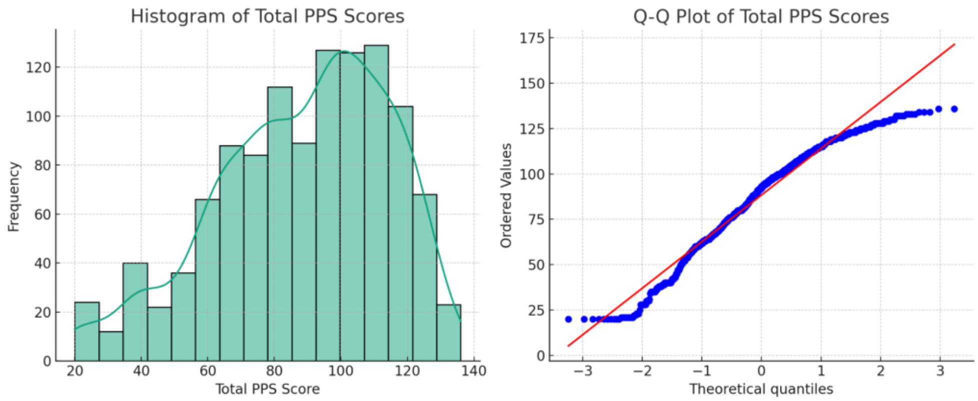
The ICC makes it possible to assess whether and to what extent systematic and random errors affect measurement repeatability; its possible values are in the range of 0.00–1.00 [801]. Reliability is thought to be poor if ICC values are lower than 0.40, fair if the values range from 0.40 to 0.59, good if the values are between 0.60 and 0.74, and excellent if the values are between 0.75 and 1.00 [802].

A plot of each participant's mean PPS score plotted against the patient score difference (PPS score in Survey A minus PPS score on Survey B) was constructed to check for possible systematic bias. The Bland–Altman plots displayed the 95% limits of agreement (95% LOA) which give a range within which it is expected the 95% of future differences in measurements between measurement days to lie. The 95% LOA was calculated as the difference in the mean scores of the test ± the score difference SD × 1.96.



Test-retest reliability Bland-Altman plot. Intraindividual differences (n = 296) between mean PPS scores for test–retest, plotted against the average of the two scores. The central line represents the mean difference, and the top and bottom lines display the 95% confidence interval.

A2.10 Histograms and Q-Q plots illustrating the distribution of the total PPS scores

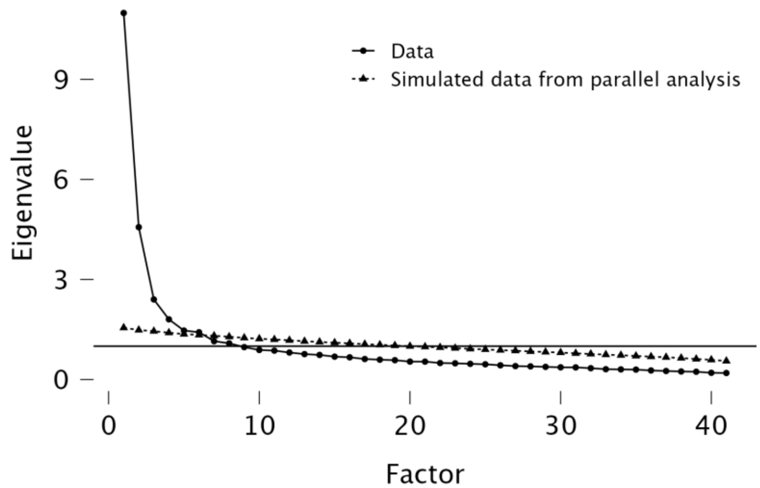


A2.11 Demographic characteristics of Sample A and B

		Survey A (N = 518)	Survey B (N = 718)
Gender	Male	288 (55.6%)	314 (43.7%)
	Female	202 (39.0%)	372 (51.8%)
	Other	28 (5.4%)	32 (4.5%)
Mean age in years (SD)		33.72 (12.81)	37.24 (12.64)
Lifetime psychedelic use	On 1 occasion	33 (6.4%)	35 (4.9%)
	On 2-5 occasions	130 (25.1%)	139 (19.4%)
	On 6-10 occasions	103 (19.9%)	114 (15.9%)
	On 11-20 occasions	69 (13.3%)	127 (17.7%)
	On more than 20 occasions	183 (35.3%)	303 (42.2%)
Religion	Not religious	285 (55.1%)	293 (40.8%)
	Christian	45 (8.7%)	60 (8.4%)
	Islam	10 (1.9%)	9 (1.3%)
	Sikhism	2 (0.4%)	0 (0.0%)
	Secular	2 (0.4%)	n/a
	Judaism	9 (1.7%)	11 (1.5%)
	Hinduism	7 (1.4%)	9 (1.3%)
	Buddhism	21 (4.1%)	26 (3.6%)
	Spiritual	104 (6.2%)	379 (52.8%)
	Other	33 (0.1%)	31 (4.3%)
Education	Secondary/High School	136 (26.3%)	179 (24.9%)
	Undergraduate	169 (32.7%)	259 (36.1%)
	Postgraduate	212 (41.0%)	280 (39.0%)

Ethnicity	White	427 (82.8%)	578 (80.5%)
	Black	8 (5.4%)	14 (2.0%)
	Asian	28 (5.4%)	32 (4.4%)
	Other	55 (10.6%)	94 (13.0%)

A2.12 Scree plot showing eigenvalues and results of non-graphical tests to determine optimal number of factors to extract from the PPA.



A2.13 Item loading patterns (EFA)

Factor Matrix[a]				
	K-E	**P-R**	**I-P**	**S-P**
I had done some of my own research into the effects of the psychedelic substance (e.g., reading articles/books, watching videos, listening to podcasts etc)	0.72	0.02	0.18	-0.11
I had learned about the effects of the substance through conversations with other people	0.24	0.22	-0.14	-0.11
I understood that the experience could evoke a range of intense emotions, from bliss to horror	0.71	-0.09	0.02	-0.08
I was unaware of what to expect from the experience	0.60	0.22	0.10	-0.08
I should have known more about the substance I was going to take	0.52	0.29	0.17	-0.03
I had a clear intention for the psychedelic experience	0.04	0.15	0.64	-0.05
I was sure that keeping my intention in mind would help guide the psychedelic experience in a helpful direction	0.49	0.3	0.02	-0.11
I had carefully contemplated my reasons for taking a psychedelic substance	0.29	0.17	0.72	-0.23
I expected the psychedelic experience to change my life	0.07	0.21	0.22	0.02
I was expecting the psychedelic experience to be easy and fun	0.14	0.03	-0.07	0.29
I understood that events from my past could surface into the psychedelic experience	0.68	0.06	0.16	-0.05
I knew that my experience would be somewhat unpredictable	0.63	0.10	-0.09	-0.13
I spoke with a therapist/counsellor as part of my preparation for the psychedelic experience	0.18	-0.17	0.74	0.11
I went into the experience willing to learn more about the meaning behind my thoughts	0.11	0.27	0.51	0.01
I went into the experience with a curiosity about my own mind	0.18	0.27	0.51	0.2
I felt ready for the psychedelic experience	0.16	0.15	0.29	0.25
I had significant doubts before going into the psychedelic experience	0.23	0.06	0.43	0.17
I felt afraid going into the psychedelic experience	0.23	0.12	0.34	0.16
I felt comfortable going into the psychedelic experience	0.11	0.06	0.32	0.31
I was ready to experience whatever 'came up' during the psychedelic experience	0.03	0.66	0.12	0.14
I was prepared to deal with uncomfortable and challenging aspects of the psychedelic experience	0.12	0.65	0.14	0.01
I felt ready to surrender to whatever the psychedelic experience would be	0.18	0.65	-0.01	0.04
I felt psychologically prepared for the psychedelic experience	0.08	0.63	0.05	0.01

A2.13 (continued)				
I was prepared for the physical effects of the psychedelic	0.11	0.62	0.15	0.08
I felt as though my mind and body would be 'strong enough' for the upcoming experience	0.10	0.68	0.32	0.02
I felt a trusting, positive connection with the people who were going to be around me during the experience	0.18	-0.17	0.13	0.74
I felt the substance would be safe to take	0.16	-0.13	0.14	0.68
I trusted the quality and purity of the of the substance	0.27	-0.20	0.21	0.67
I trusted my own mind and body to safely process the experience	0.04	0.58	0.04	-0.09
I was aware that the psychedelic experience might change me in some way	0.47	0.16	0.16	-0.01
I felt ready to accept some big changes that might occur in myself as a result of the psychedelic experience	0.25	-0.06	0.2	0.67
My family and/or friends were prepared and well-informed about the changes that could occur in me	-0.1	0.17	0.08	0.68
My friends and/or family were ready to support me through any changes I experienced	-0.26	0.21	0.10	0.25
I was worried about becoming too different as a person after the psychedelic experience	-0.09	-0.15	-0.25	0.33
I was afraid that I might change in a negative way after the psychedelic experience	0.26	0.19	0.25	0.33
I dedicated time to preparing for the psychedelic experience	0.10	0.11	0.25	0.29
I engaged with specific preparation practices before the psychedelic experience (e.g., meditation, yoga, breathwork, journalling, diet, exercise)	-0.12	0.01	0.73	0.20
I had made a plan for what I would do in the hours and days after the psychedelic experience	0.16	-0.02	-0.03	0.56
I told close/trusted friends and/or family that I was going to be taking a psychedelic substance	0.24	0.17	0.29	0.03
I didn't do anything in particular to prepare for the psychedelic experience	0.39	0.01	0.02	0.33
I had prepared some strategies in case things started to get difficult during the psychedelic experience	0.16	0.06	-0.15	0.56

A2.14 Items removed from PPS

Significant cross-loadings >0.20:

1. I was unaware of what to expect from the experience
2. I should have known more about the substance I was going to take
3. I was sure that keeping my intention in mind would help guide the psychedelic experience in a helpful direction
4. I went into the experience willing to learn more about the meaning behind my thoughts
5. I went into the experience with a curiosity about my own mind
6. I had significant doubts before going into the psychedelic experience
7. I felt afraid going into the psychedelic experience
8. I felt comfortable going into the psychedelic experience
9. I felt as though my mind and body would be 'strong enough' for the upcoming experience
10. I trusted the quality and purity of the of the substance
11. I felt ready to accept some big changes that might occur in myself as a result of the psychedelic experience
12. I was worried about becoming too different as a person after the psychedelic experience
13. I was afraid that I might change in a negative way after the psychedelic experience
14. I didn't do anything in particular to prepare for the psychedelic experience

Factor loadings < .30:

1. I had learned about the effects of the substance through conversations with other people
2. I expected the psychedelic experience to change my life
3. I was expecting the psychedelic experience to be easy and fun
4. I felt ready for the psychedelic experience
5. My friends and/or family were ready to support me through any changes I experienced
6. I dedicated time to preparing for the psychedelic experience
7. I told close/trusted friends and/or family that I was going to be taking a psychedelic substance

A2.15 Reliability analysis

Reliability analysis hypothesised 4-factor model with sub-scale ω values if an item is removed and correlations of each item with the total of all other items in the subscale. Values in bold indicate items where overall reliability rises if the item is dropped. N=718.

Subscale reliability (McDonald's ω, 95% CI)	Item text	McDonald's ω if item dropped	Item-rest correlation
Knowledge-Expectation (ω=0.890, 95% CI=0.880-0.900)	I had done some of my own research into the effects of the psychedelic substance (e.g., reading articles/books, watching videos, listening to podcasts etc)	0.870	0.714
	I understood that the experience could evoke a range of intense emotions, from bliss to horror	0.867	0.740
	I understood that events from my past could surface into the psychedelic experience	0.879	0.676
	I knew that my experience would be somewhat unpredictable	0.864	0.755
	I was aware that the psychedelic experience might change me in some way	0.857	0.781
Intention-Preparation (ω=0.865, 95% CI=0.854-0.877)	I was ready to experience whatever 'came up' during the psychedelic experience	0.847	0.639
	I was prepared to deal with uncomfortable and challenging aspects of the psychedelic experience	0.909	0.735
	I felt ready to surrender to whatever the psychedelic experience would be	0.812	0.794
	I felt psychologically prepared for the psychedelic experience	0.825	0.752
	I was prepared for the physical effects of the psychedelic	0.818	0.768
	I trusted my own mind and body to safely process the experience	0.828	0.738
Psychophysical-Readiness (ω=0.828, 95% CI=0.813-0.844)	I had a clear intention for the psychedelic experience	0.799	0.617
	I had carefully contemplated my reasons for taking a psychedelic substance	0.812	0.588
	I spoke with a therapist/counsellor as part of my preparation for the psychedelic experience	0.765	0.709
	I engaged with specific preparation practices before the psychedelic experience (e.g., meditation, yoga, breathwork, journalling, diet, exercise)	0.758	0.704
Support-Planning (ω=0.799, 95% CI=0.782-0.817)	I felt a trusting, positive connection with the people who were going to be around me during the experience	0.787	0.477
	I felt the substance would be safe to take	0.794	0.467
	My family and/or friends were prepared and well-informed about the changes that could occur in me	0.734	0.647
	I had made a plan for what I would do in the hours and days after the psychedelic experience	0.736	0.647
	I had prepared some strategies in case things started to get difficult during the psychedelic experience	0.750	0.624

A2.16 Group descriptives for high/low prep groups on the MEQ, CEQ, EBI, PPGI-SF, COES, and SWEBWBS outcomes

	Preparation Group	N	Mean	SD	t	p
MEQ	High	611	149.339	24.818	14.654	< .001
	Low	625	120.675	41.660		
CEQ	High	451	72.636	16.385	-8.647	< .001
	Low	523	83.874	23.024		
EBI	High	611	424.989	157.150	11.945	< .001
	Low	625	310.963	177.570		
PPGI	High	611	39.858	7.916	14.437	< .001
	Low	625	31.174	12.639		
COES	High	611	55.043	9.517	17.235	< .001
	Low	625	42.213	15.813		
SWEBWBS	High	611	40.291	6.189	16.692	< .001
	Low	625	31.637	11.261		

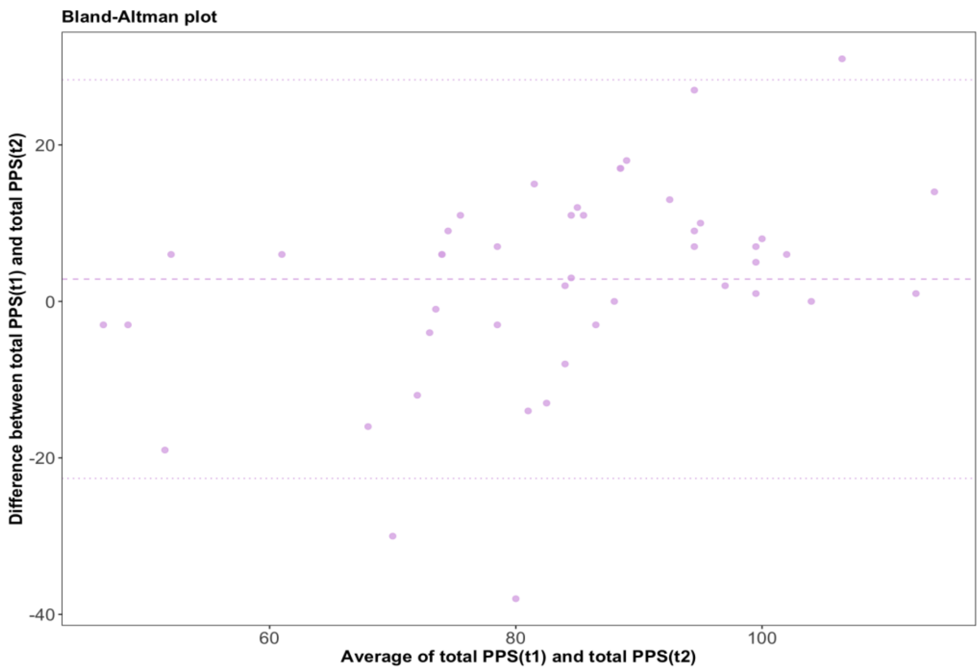
A2.17 Demographic characteristics of Retreat Survey participants

Gender (n=46)	Male	22 (47.83%)
	Female	24 (52.17%)
Mean age in years (SD)		44.02 (13.54)
Lifetime psychedelic use	Never before	25 (54.35%)
	On 1 occasion	9 (19.57%)
	On 2-5 occasions	6 (13.04%)
	On 6-10 occasions	2 (4.35%)
	On 11-20 occasions	3 (6.52%)
	On more than 20 occasions	1 (2.17%)
Religion	Not religious	25 (54.35%)
	Christian	8 (17.39%)
	Buddhism	3 (6.52%)
	Spiritual	10 (21.74%)
Education	Secondary/High School	2 (4.35%)
	Undergraduate	28 (60.87%)

	Postgraduate	16 (34.78%)
Ethnicity	White	32 (71.11%)
	Black	4 (8.89%)
	Asian	1 (2.22%)
	Latino/Hispanic	2 (4.44%)
	Mixed	6 (13.33%)

A2.18 Bland-Altman plot

Intraindividual differences (n = 46) between mean PPS scores for test–retest, plotted against the average of the two scores. The central line represents the mean difference, and the top and bottom lines display the 95% confidence interval.

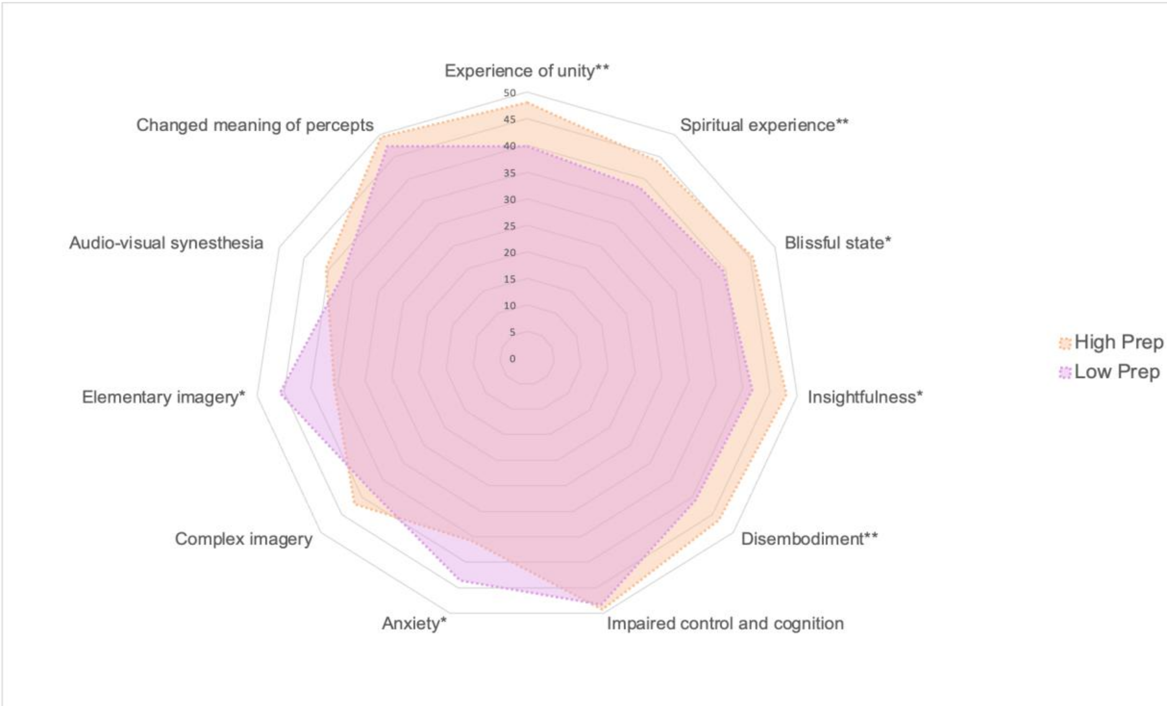


A2.19 11D-ASC group descriptives

	Preparation Group	Mean	SD	t	p
Global-ASC	High	44.067	2.635	2.106	0.041
	Low	41.834	4.350		
Experience of unity**	High	48.043	7.119	4.719	**< .001**
	Low	39.826	4.366		
Spiritual experience**	High	44.043	4.876	3.545	**< .001**
	Low	38.130	6.341		
Blissful state*	High	45.478	5.830	3.117	**0.003**
	Low	39.522	7.070		
Insightfulness*	High	48.043	7.456	3.358	**0.002**
	Low	41.739	5.047		
Disembodiment**	High	46.478	5.401	4.375	**< .001**
	Low	40.783	3.133		
Impaired control and cognition	High	49.217	12.087	0.234	0.816
	Low	48.261	15.404		
Anxiety*	High	35.826	9.099	-2.348	**0.023**
	Low	43.609	13.034		
Complex imagery	High	41.870	10.015	1.205	0.235
	Low	37.957	11.933		
Elementary imagery*	High	35.739	10.855	-3.432	**0.001**
	Low	45.783	8.893		
Audio-visual synaesthesia	High	40.565	15.356	0.813	0.421
	Low	37.217	12.428		
Changed meaning of percepts	High	49.435	7.241	0.735	0.466
	Low	47.348	11.523		

*** sig at p<0.001*
** sig at p<0.05*

A2.20 11D-ASC Radar Plot



A2.21 DASS-21 group descriptives

	Group	Mean	SD	t	p
Δ Depression	High	-9.043	6.898	-3.526	**< .001**
	Low	-2.522	5.575		
Δ Anxiety	High	-9.565	6.535	-3.202	**0.003**
	Low	-2.826	7.691		
Δ Stress	High	-8.348	5.820	-3.162	**0.003**
	Low	-3.043	5.555		

A2.22 Psychedelic Preparedness Scale (PPS) (Prospective Version)

In relation to your upcoming psychedelic experience, indicate the degree to which you agree with the following statements.

Not at all (1)	*A little (2)*	*More than a little (3)*	*Moderately (4)*	*Considerably (5)*	*Very much (6)*	*Completely (7)*

1	I have done some of my own research into the effects of the psychedelic substance (e.g., reading articles/books, watching videos, listening to podcasts etc)	1 2 3 4 5 6 7
2	I understand that the experience might evoke a range of intense emotions, from bliss to horror	1 2 3 4 5 6 7
3	I have a clear intention for the psychedelic experience	1 2 3 4 5 6 7
4	I have carefully contemplated my reasons for taking a psychedelic substance	1 2 3 4 5 6 7
5	I understand that events from my past could surface into the psychedelic experience	1 2 3 4 5 6 7
6	I know that my experience will be somewhat unpredictable	1 2 3 4 5 6 7
7	I have spoken with a therapist/counsellor as part of my preparation for the psychedelic experience	1 2 3 4 5 6 7
8	I am ready to experience whatever 'comes up' during the psychedelic experience	1 2 3 4 5 6 7
9	I am prepared to deal with uncomfortable and challenging aspects of the psychedelic experience	1 2 3 4 5 6 7
10	I feel ready to surrender to whatever the psychedelic experience will be	1 2 3 4 5 6 7
11	I feel psychologically prepared for the psychedelic experience	1 2 3 4 5 6 7
12	I am prepared for the physical effects of the psychedelic	1 2 3 4 5 6 7
13	I feel a trusting, positive connection with the people who are going to be around me during the experience	1 2 3 4 5 6 7
14	I feel the substance will be safe to take	1 2 3 4 5 6 7
15	I trust my own mind and body to safely process the experience	1 2 3 4 5 6 7
16	I am aware that the psychedelic experience might change me in some way	1 2 3 4 5 6 7
17	My family and/or friends are prepared and well-informed about the changes that could occur in me	1 2 3 4 5 6 7
18	I have engaged with specific preparation practices (e.g., meditation, yoga, breathwork, journaling, diet, exercise)	1 2 3 4 5 6 7
19	I have made a plan for what I will do in the hours and days after the psychedelic experience	1 2 3 4 5 6 7
20	I have prepared some strategies in case things started to get difficult during the psychedelic experience	1 2 3 4 5 6 7

Factors: *Knowledge-Expectation* (1, 2, 5, 6, 16); *Psychophysical-Readiness* (8, 9, 10, 11, 12, 15); *Intention-Preparation* (3, 4, 7, 18); *Support-Planning* (13, 14, 17, 19, 20)

A2.23 Psychedelic Preparedness Scale (PPS) (Retrospective Version)

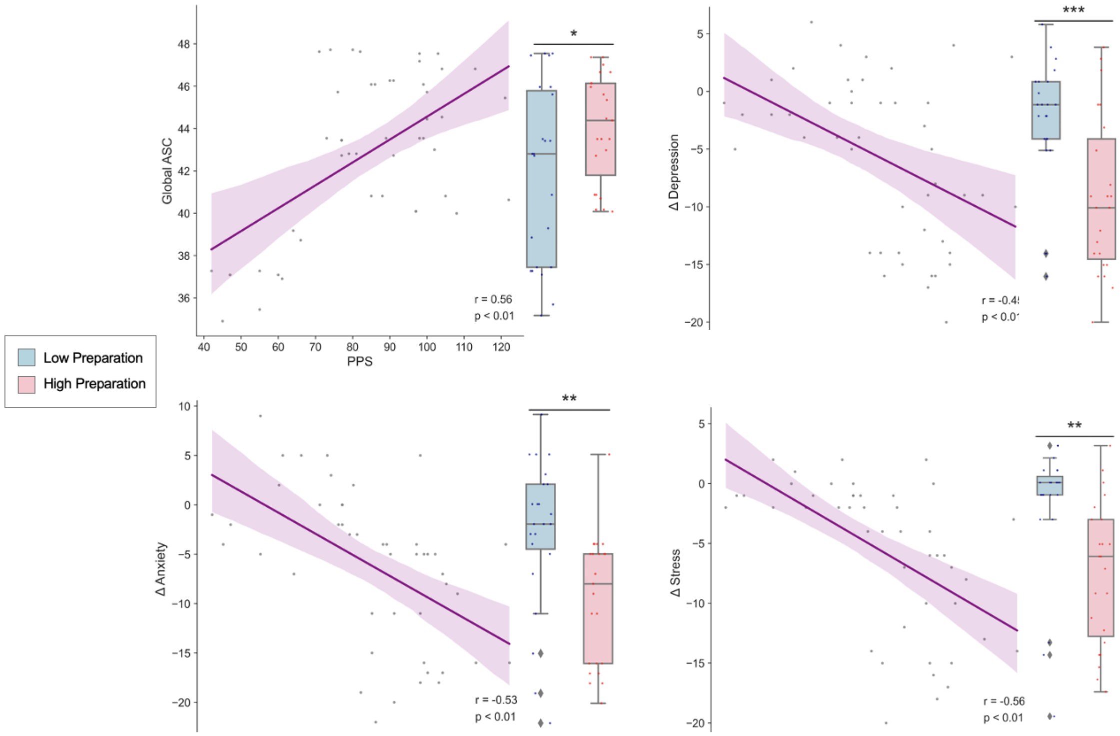
In relation to your psychedelic experience, indicate the degree to which you agree with the following statements.

Not at all (1)	*A little (2)*	*More than a little (3)*	*Moderately (4)*	*Considerably (5)*	*Very much (6)*	*Completely (7)*

1	I had done some of my own research into the effects of the psychedelic substance (e.g., reading articles/books, watching videos, listening to podcasts etc)	1 2 3 4 5 6 7
2	I understood that the experience could evoke a range of intense emotions, from bliss to horror	1 2 3 4 5 6 7
3	I had a clear intention for the psychedelic experience	1 2 3 4 5 6 7
4	I had carefully contemplated my reasons for taking a psychedelic substance	1 2 3 4 5 6 7
5	I understood that events from my past could surface into the psychedelic experience	1 2 3 4 5 6 7
6	I knew that my experience would be somewhat unpredictable	1 2 3 4 5 6 7
7	I spoke with a therapist/counsellor as part of my preparation for the psychedelic experience	1 2 3 4 5 6 7
8	I was ready to experience whatever 'came up' during the psychedelic experience	1 2 3 4 5 6 7
9	I was prepared to deal with uncomfortable and challenging aspects of the psychedelic experience	1 2 3 4 5 6 7
10	I felt ready to surrender to whatever the psychedelic experience would be	1 2 3 4 5 6 7
11	I felt psychologically prepared for the psychedelic experience	1 2 3 4 5 6 7
12	I was prepared for the physical effects of the psychedelic	1 2 3 4 5 6 7
13	I felt a trusting, positive connection with the people who were going to be around me during the experience	1 2 3 4 5 6 7
14	I felt the substance would be safe to take	1 2 3 4 5 6 7
15	I trusted my own mind and body to safely process the experience	1 2 3 4 5 6 7
16	I was aware that the psychedelic experience might change me in some way	1 2 3 4 5 6 7
17	My family and/or friends were prepared and well-informed about the changes that could occur in me	1 2 3 4 5 6 7
18	I engaged with specific preparation practices before the psychedelic experience (e.g., meditation, yoga, breathwork, journaling, diet, exercise)	1 2 3 4 5 6 7
19	I had made a plan for what I would do in the hours and days after the psychedelic experience	1 2 3 4 5 6 7
20	I had prepared some strategies in case things started to get difficult during the psychedelic experience	1 2 3 4 5 6 7

Factors: *Knowledge-Expectation* (1, 2, 5, 6, 16); *Psychophysical-Readiness* (8, 9, 10, 11, 12, 15); *Intention-Preparation* (3, 4, 7, 18); *Support-Planning* (13, 14, 17, 19, 20)

A2.24 PPS scale implementation figures



Appendix 3

A3.1 Contextual Information: Psilocybin Retreat Centres

This section provides detailed information about the psilocybin retreat centres involved in our study. While these centres vary in location and specific approach, they share commonalities in their operational framework, target population, and overall objectives. The centres are unified by their focus on offering 'healing' experiences, primarily to individuals seeking therapeutic benefits from psilocybin for conditions such as depression and anxiety. Notably, these centres predominantly cater to first-time psilocybin users. While there are differences in the specific programs of each retreat, the centres were selected for collaboration based on the similarities in their program structures and types of support offered. It is acknowledged that these variations could potentially influence participants' experiences and outcomes.

Participant Population and Screening: Each centre conducts its own screening process, aiming to create a safe and supportive environment. The primary criterion for admission is the absence of current diagnoses or family history of psychosis or schizophrenia. This screening ensures that the participants are suitable for the psilocybin experience, primarily focusing on individuals seeking healing from various psychological conditions.

Program Structure: Despite slight variations, the retreats generally follow a similar structure. This structure encompasses a preparation day at the beginning, followed by the dosing days, and concludes with an integration day. The dosing days are interspersed with various workshops, including meditation, yoga, and breathwork. These activities are designed to enhance the psychedelic experience and promote introspection and personal growth.

Sharing Circles and Participant Interaction: A critical component of these retreats is the incorporation of sharing circles. These circles provide participants with a platform to express their feelings and discuss their psilocybin experiences. This practice fosters a sense of community and mutual support, enhancing the overall therapeutic experience.

Facilitation and Support: The retreats do not include specific psychotherapy sessions; however, they are facilitated by trained individuals who offer non-directive support. These facilitators play a crucial role during the group ceremonies, which often include live music. They are also available to assist participants with practical needs and provide grounding support when necessary.

A3.2 Co-design Workshop Methodological Details

Workshop 1

The objective of Workshop 1 was to develop a prioritised list of components. Participants were first introduced to the findings from Chapter 2. Based on these findings, they were instructed to delineate potential components for the intervention. They were encouraged to draw from the findings of Study 1 and, importantly, to supplement these with any additional components they deemed relevant to the intervention's objectives. Each participant separately recorded their inputs, either in writing or through diagrams. Next, a group discussion was held to facilitate knowledge sharing and collaboration. During this session, participants evaluated and discussed the proposed components, resulting in a compiled list, presented on a single sheet of paper. The dot voting method was then employed [803–805], whereby each participant was provided with ten coloured stickers to mark the components they prioritised as most important to include in the intervention.

Workshop 2

The objective of Workshop 2 was to further refine the set of components identified in Workshop 1. This refinement was driven by the goal of achieving consistent exposure to intervention components across the intervention while mitigating the risk of diminishing engagement due to excessive repetition and general participant burden [806–808].

Informed by these considerations and underscored by the significance of user-centric design [809], we decided to select the top seven activities from this workshop to take forward into Workshop 3.

The workshop began with a presentation of the findings from Workshop 1, followed by a group discussion focusing on each of the components. This was to ensure all participants had a clear understanding of each component's objectives and principles. Emphasis was placed on assessing the relevance of each component for the digital intervention and the practicality of incorporating it. After the discussion, a refined evaluation procedure was implemented via a two-step dot voting procedure. The necessity for this modification became apparent in Workshop 1, where the initial assessment only gauged the critical importance of components without considering participants' opinions on the feasibility of embedding these components into a digital intervention. To address this, a secondary assessment step was incorporated. On a single piece of paper, participants marked activities they viewed as ‘priority’ with a green sticker. Components marked as a priority were then further evaluated by participants for their suitability within a digital intervention framework, with a secondary green sticker indicating practical ‘feasibility’.

Workshop 3

The two primary objectives of Workshop 3 were: (1) To evaluate each component in terms of its Benefits, Barriers, Risks, and projected Outcomes (BBRO) and (2) To formulate solutions for the challenges identified. The session started with a summary of the findings from Workshop 1 and Workshop 2. After a group discussion, participants were segmented into smaller teams. Each team was allocated a set of components from the top eight identified in previous workshops. Under the BBRO framework, teams listed specific points for their respective components, categorising them accordingly. Following the subgroup evaluations, participants reconvened to collaboratively discuss and propose potential solutions and strategies to address the identified challenges.

A3.3 W1 Idea Generation Phase

Activities derived from Workshop 1 (Study 3.II) thematic analysis, discerned post-hoc through the examination of each participant’s submissions. Corresponding Study 3.I components are displayed to the right.

#	Study 3.II: components (theme)	Study 3.I: corresponding components
1	Reading assignments (KE)	Educational resources
2	Journalling (IP)	Journal prompts
3	Meditation (PR)	Meditation materials
4	Physical exercise routines (PR)	Yoga/movement
5	Holotropic breathwork (KE)	Breathing exercises
6	Grounding techniques (PR)	Strategies for handling challenging experiences
7	Carving out time after the retreat (SP)[a]	Post-experience integration planning
8	Yoga (PR)	Yoga/movement
9	Dietary guidance (PR)	Lifestyle recommendations
10	Abstinence from alcohol/drugs (PR)	Lifestyle recommendations
11	Creating an integration plan (SP)[a]	Post-experience integration planning
12	Resource list (SP)	Educational resources
13	Connecting with retreat leaders (SP)	Personal check-ins
14	Hands-on workshop (KE)	•
15	Group discussions (KE)[c]	Community sharing
16	Lecture series (KE)[b]	Educational resources

17	Nature walks (PR)	Nature immersion
18	Quizzes (KE)	Educational resources
19	Connecting with retreat guests (SP)[c]	Community sharing; Real-life stories
20	Group sharing (IP)[c]	Community sharing; Real-life stories
21	Sound baths (PR)	•
22	Dance and movement (IP)	Yoga/movement
23	Documentary viewings (KE)	Educational resources
24	Panel discussions (KE)[b]	Educational resources
25	Virtual reality experiences (KE)	•
26	Sleep hygiene (PR)	Lifestyle recommendations
27	Vision board creation (IP)	•
28	Affirmation crafting (IP)	•
29	Guided visualisations (IP)	•
30	Arts and crafts (IP)	•
31	Buddy system (SP)	Personal check-ins

A3.4 GUIDED: A Guideline for Reporting for Intervention Development Studies

Item description	**Explanation**	**Page in published manuscript** [156]
Report the context for which the intervention was developed.	Understanding the context in which an intervention was developed informs readers about the suitability and transferability of the intervention to the context in which they are considering evaluating, adapting or using the intervention. Context here can include place, organisational, and wider sociopolitical factors that may influence the development and/or delivery of the intervention.	5
Report the purpose of the intervention development process.	Clearly describing the purpose of the intervention specifies what it sets out to achieve. The purpose may be informed by research priorities, for example those identified in systematic reviews, evidence gaps set out in practice guidance such as The National Institute for Health and Care Excellence or specific prioritisation exercises such as those undertaken with patients and practitioners through the James Lind Alliance.	3
Report the target population for the intervention development process.	The target population is the population that will potentially benefit from the intervention – this may include patients, clinicians, and/or members of the public. If the target population is clearly described then readers will be able to understand the relevance of the intervention to their own research or practice. Health inequalities, gender and ethnicity are features of the target population that may be relevant to intervention development processes.	27
Report how any published intervention development approach contributed to the development process	Many formal intervention development approaches exist and are used to guide the intervention development process (e.g. 6Squid or The Person Based Approach to Intervention Development). Where a formal intervention development approach is used, it is helpful to describe the process that was followed, including any deviations. More general approaches to intervention development also exist and have been categorised as follows: Target Population-centred intervention development; evidence and theory-based intervention development; partnership intervention development; implementation-based intervention development; efficacy based intervention development; step or phase-based intervention development; and intervention-specific intervention development. These approaches do not always have specific guidance that describe their use. Nevertheless, it is helpful to give a rich description of how any published approach was operationalised.	3
Report how evidence from different sources informed the intervention development process.	Intervention development is often based on published evidence and/or primary data that has been collected to inform the intervention development process. It is useful to describe and reference all forms of evidence and data that have informed the development of the intervention because evidence bases can change rapidly, and to explain the manner in which the evidence and/or data was used. Understanding what evidence was and was not available at the time of intervention development can help readers to assess transferability to their current situation.	24
Report how/if published theory informed the intervention development process.	Reporting whether and how theory informed the intervention development process aids the reader's understanding of the theoretical rationale that underpins the intervention. Though not mentioned in the e-Delphi or consensus meeting, it became increasingly apparent through the development of our guidance that this theory item could relate to either existing published theory or programme theory.	24

A3.4 (continued)		
Report any use of components from an existing intervention in the current intervention development process.	Some interventions are developed with components that have been adopted from existing interventions. Clearly identifying components that have been adopted or adapted and acknowledging their original source helps the reader to understand and distinguish between the novel and adopted components of the new intervention.	n/a
Report any guiding principles, people or factors that were prioritised when making decisions during the intervention development process.	Reporting any guiding principles that governed the development of the application helps the reader to understand the authors' reasoning behind the decisions that were made. These could include the examples of particular populations whose views are being considered when designing the intervention, the modality that is viewed as being most appropriate, design features considered important for the target population, or the potential for the intervention to be scaled up.	24-25
Report how stakeholders contributed to the intervention development process.	Potential stakeholders can include patient and community representatives, local and national policy makers, health care providers and those paying for or commissioning health care. Each of these groups may influence the intervention development process in different ways. Specifying how differing groups of stakeholders contributed to the intervention development process helps the reader to understand how stakeholders were involved and the degree of influence they had on the overall process. Further detail on how to integrate stakeholder contributions within intervention reporting are available.	5, 15-16
Report how the intervention changed in content and format from the start of the intervention development process.	Intervention development is frequently an iterative process. The conclusion of the initial phase of intervention development does not necessarily mean that all uncertainties have been addressed. It is helpful to list remaining uncertainties such as the intervention intensity, mode of delivery, materials, procedures, or type of location that the intervention is most suitable for. This can guide other researchers to potential future areas of research and practitioners about uncertainties relevant to their healthcare context.	18-23
Report any changes to interventions required or likely to be required for subgroups.	Specifying any changes that the intervention development team perceive are required for the intervention to be delivered or tailored to specific subgroups enables readers to understand the applicability of the intervention to their target population or context. These changes could include changes to personnel delivering the intervention, to the content of the intervention, or to the mode of delivery of the intervention.	26
Report important uncertainties at the end of the intervention development process	Intervention development is frequently an iterative process. The conclusion of the initial phase of intervention development does not necessarily mean that all uncertainties have been addressed. It is helpful to list remaining uncertainties such as the intervention intensity, mode of delivery, materials, procedures, or type of location that the intervention is most suitable for. This can guide other researchers to potential future areas of research and practitioners about uncertainties relevant to their healthcare context.	27-28
Follow TIDieR guidance when describing the developed intervention.	Interventions have been poorly reported for several years. In response to this, internationally recognised guidance has been published to support the high-quality reporting of public health interventions. This guidance should therefore be followed when describing a developed intervention.	24

A3.4 (continued)	
Report the intervention development process in an open access format.	Unless reports of intervention development are available, people considering using an intervention cannot understand the process that was undertaken and make a judgement about its appropriateness to their context. It also limits cumulative learning about intervention development methodology and observed consequences at later evaluation, translation and implementation stages. Reporting intervention development in an open access (Gold or Green) publishing format increases the accessibility and visibility of intervention development research and makes it more likely to be read and used. Potential platforms for open access publication of intervention development include open access journal publications, freely accessible funder reports or a study web-page that details the intervention development process.

**e.g. if the item is reported elsewhere, then the location of this information can be stated here.*

A3.5 TIDieR: Template for Intervention Description and Replication (TIDieR) checklist

Item No	TIDieR Item	Current Intervention Description
Brief name		
1	Provide the name or a phrase that describes the intervention	Self-led, digital psychedelic preparedness intervention.
Why		
2	Describe any rationale, theory, or goal of the elements essential to the intervention	Rationale: The states induced by classic psychedelics necessitate a comprehensive psychological preparation to ensure participant safety and optimise therapeutic outcomes. Despite the acknowledged importance of this preparation, current approaches often lack consistent standardisation. Theory: The core premise of our intervention is based on the hypothesis that an evidence-backed, individualised preparation can enhance the therapeutic efficacy of psychedelics while minimising risks. By improving participants' understanding, ensuring readiness, guiding introspective focus, and emphasising safety, the intervention aims to provide an optimal setting for effective psychedelic experiences. Integrating self-directed strategies with clinician-led methods is believed to better accommodate individual variability in preparation needs. Goal: The primary objective is to establish a methodical, evidence-based, and individualised preparation process for psychedelic interventions. Key components from our four-factor model include: • Knowledge-Expectation: Educating participants about psychedelics to align expectations with likely outcomes. • Psychophysical-Readiness: Preparing participants mentally and physically to effectively manage the nuances of the psychedelic experience. • Intention-Preparation: Guiding introspective reflection to ensure participants approach the experience with clear objectives. • Support-Planning: Implementing measures to ensure a secure and supportive environment throughout the psychedelic session. To achieve these goals, the intervention employs various tools and strategies, such as structured educational materials, meditation practices, and intention-setting protocols, each developed based on empirical evidence and participant feedback.

A3.5 (continued)		
What		
3	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (such as online appendix, URL)	Format & Structure: The intervention is delivered through an online platform, allowing individual user access via unique login credentials. This digital format ensures consistent delivery and facilitates tracking of individual progress. Thematic Modules: The intervention is organised into a series of three one-week thematic modules: • Week 1: 'Knowledge-Expectation' • Week 2: 'Psychophysical-Readiness' • Week 3: 'Support-Planning' An overarching module, 'Intention-Preparation,' is interwoven throughout the entire three-week period, reinforcing its pervasive importance in the psychedelic preparation process. Daily Protocols: Each day comprises: • A session of guided meditation, backed by instructional materials (detailed in a forthcoming paper). • A list of auxiliary activities resonating with the weekly theme. Participants can engage with these activities flexibly, as per their convenience within the respective week. • A concise online mood assessment, facilitating daily monitoring of participants' psychological states. Introductory Materials: Before initiating the intervention, participants are provided with an introductory program booklet. This document elucidates the course's architecture and objectives and provides comprehensive instructions for the daily meditation exercises integral to the intervention (details to be expanded upon in a forthcoming paper). Resource Library: An online resource repository is available to participants, stocked with supplementary materials tailored to each of the four thematic modules. This library serves as a reference hub, enabling participants to delve deeper into topics of interest. Lifestyle Guidelines: During the 21-day intervention span, participants are explicitly instructed to refrain from consuming drugs and alcohol. Furthermore, they receive guidelines promoting a balanced diet, regular physical activity, and adequate sleep to optimise the intervention's efficacy. Accessibility: All the intervention materials, including the introductory booklet, daily protocols, and online resource library, are hosted on our dedicated platform. Access details and further specifics will be provided in the appendices of the forthcoming study.

A3.5 (continued)		
4	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities	Intervention Initiation: Participants register on the online platform and receive unique login credentials; Upon initial login, they are directed to download and review the introductory program booklet to familiarise themselves with the course structure and objectives; They are also guided on how to navigate the online resource library and access supplementary materials as needed. Daily Protocol: Each day begins with participants logging in to the platform; They are prompted to engage in the guided meditation session and are provided access to the instructional materials; Post-meditation, they receive a list of auxiliary activities specific to the week's theme, allowing them to choose based on interest and convenience; By the day's end, participants complete the online mood assessment, providing immediate feedback on their psychological state. Weekly Thematic Engagement: Each week is categorised by its thematic module. The platform's dashboard or main page highlights the theme prominently, ensuring participants are aligned with the week's focus; The online resource library is curated to emphasise materials corresponding to the current week's theme, facilitating deeper engagement. Lifestyle Monitoring and Adherence: Throughout the 21-day period, participants receive periodic reminders, both within the platform and via email notifications, emphasising the importance of abstaining from drugs and alcohol; They also get periodic tips and guidelines on maintaining a balanced diet, engaging in physical activity, and ensuring adequate sleep. Feedback and Support: An integrated support feature on the platform allows participants to raise queries or seek clarifications on the materials or procedures; Weekly feedback forms enable the intervention team to gather insights and address any concerns promptly.
Who provided		
5	For each category of intervention provider (such as psychologist, nursing assistant), describe their expertise, background, and any specific training given.	1. Academics and Clinical Psychologists: Expertise: Specialised in the study and clinical application of psychedelics and their therapeutic implications; Proficient in developing structured educational content based on empirical evidence and best practices in psychedelic therapy. Background: Typically hold a Ph.D. in Clinical Psychology, Neuroscience, or a related field; Possess extensive experience in psychedelic research, both in clinical and academic settings. Specific Training: All contributing academics and clinical psychologists have been a part of interdisciplinary conferences and workshops focused on psychedelic therapy and its advancements; They have undergone peer-review processes and collaborations to ensure the content is comprehensive, accurate, and relevant for the intervention's intended audience. 2. Meditation Practitioners: Expertise: Experienced in guiding meditation sessions tailored for introspection, mental preparedness, and grounding; Understand the nuances of meditative practices as they relate to psychedelic experiences, ensuring participants are mentally aligned and centred. Background: Certified from recognised meditation or mindfulness institutions or have significant lineage-based training; Boast a track record, often spanning a decade or more, of leading meditation sessions, workshops, and retreats. Specific Training: All meditation practitioners involved in content creation have been briefed on the specifics of the psychedelic intervention and its objectives; They have collaborated with the clinical psychologists to tailor the meditation guides, ensuring they align with the themes of the intervention and meet the unique requirements of preparing individuals for psychedelic experiences.

A3.5 (continued)		
How		
6	Describe the modes of delivery (such as face to face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group	Platform Delivery: The primary mode of delivery for the intervention is via an online digital platform. Participants access the intervention content, materials, and activities through this platform. Delivery Mechanism: Internet-Based: The intervention's core content and resources are hosted on a dedicated online platform. This allows for uniform content presentation and easy accessibility for all participants from any location, provided they have internet connectivity. Automated Email Notifications: Periodic reminders, tips, and guidelines are disseminated to participants through email notifications to reinforce adherence to the intervention's protocols and lifestyle guidelines. Nature of the Intervention: Individually Tailored: While the content remains consistent for all participants, the digital nature of the intervention allows for individualised progress tracking. Each participant has a unique login, and their engagement with the intervention is self-paced and self-led. This ensures that the experience is tailored to each individual's pace and preferences. Group Interaction: The intervention is primarily designed for individual engagement, ensuring personal introspection and reflection. However, given the digital format, there is potential (if deemed beneficial in the future) to incorporate group forums or discussion boards for participants to share experiences or seek peer support.

A3.6 Module Structure Information

The modules are structured as follows:

- Week 1/Module 1 (Days 1-7): Knowledge-Expectation (KE) provides an in-depth education on psychedelics. Through tailored 'Reading assignments', it assesses participants' current understanding of these substances and sets their expectations regarding both immediate and prolonged outcomes of their use.
- Week 2/Module 2 (Days 8-14): Psychophysical-Readiness (PR) focuses on evaluating participants' psychological and physiological preparedness for the multifaceted nature of psychedelic experiences. This module emphasises the participants' capacity to confront potential emotional or physical challenges, fostering an acceptance of unforeseen elements of the experience, and building trust in their inherent ability to navigate these challenges skilfully. The main activities taught here are 'Grounding techniques', to provide participants with tools to use before, during and after the psychedelic experience.
- Week 3/Module 3 (Days 15-21): Support-Planning (SP) emphasises the imperative of creating a safe and supportive environment during the psychedelic session. Key aspects include cultivating trust with attendants, confirming substance safety, preparing acquaintances for possible behavioural or emotional changes, and formulating contingency strategies for any post-experience challenges. 'Integration planning', within this context, predominantly addresses strategies for post-experience reflection and coping, ensuring participants are well-prepared for the aftermath.
- Weeks 1-3/Module 4 (Days 1-21): Interwoven throughout the duration of the program is the Intention-Preparation (IP) module. Through reflective 'Journaling' exercises, this module delves into the underlying motivations and intentions for psychedelic-use, whether they be oriented towards self-exploration, therapeutic applications, or spiritual growth.

A3.7 Thematic Analysis

Theme 1: Knowledge-Expectation

The Knowledge-Expectation theme refers to activities that participants described as undertaking in order to improve their understanding of psychedelic substances and their resultant expectations regarding the potential immediate and long-term effects.

Subtheme 1.1: Acquiring knowledge about the science and history of psychedelics

Participants demonstrated a robust commitment to learning about the scientific foundation and historical background of psychedelic substances. Twelve participants (n=12) reported proactively seeking scientific literature, books, and online materials, while others made use of expert-led videos (n=5) and podcasts (n=6) as educational resources.

This self-directed education allowed participants to make more **informed decisions about psychedelic use (1.1.1)**. By improving their understanding of psychedelics, participants felt better equipped to assess their readiness for, and the appropriateness of the psychedelic experience. A solid foundation of knowledge also enabled the appraisal of potential risks, thereby addressing and clarifying initial uncertainties.

> "[Doing my own research] helped me [to] weigh out the pros and cons, before deciding whether this was something I wanted to do." (P5)

> "The more I learned about [psilocybin] […] the more I felt that my decision to go on this journey was a sensible thing to do." (P14)

Expanded knowledge also influenced participants' **perception of the safety of psychedelics (1.1.2)**. Participants who actively sought information on both the historical use and scientific understanding of these substances typically perceived psychedelics as safer than they initially believed .

> "I [discovered] that cultures have been using these substances for centuries […] It eased my concerns. It wasn't just a recent fad." (P6)

> "[This knowledge] definitely made me feel more comfortable about trying them myself […] they are literally giving them to people in dozens of [universities] around the world…" (P12)

Self-initiated education also resulted in a notable change in **participants' attitudes towards psychedelics (1.1.3).** As participants acquired knowledge on the historical, cultural, and scientific facets of these substances, initial neutrality or curiosity often evolved into variations of "respect" (P4). This change frequently coincided with a decrease in initial "misconceptions" (P7) and a more informed, positive perception of psychedelics.

> "[…] opened my eyes to how powerful these substances can be […]. There's a depth to [psilocybin] that demands respect." (P4)

> "It made me rethink everything." (P18)

> "It was like separating fact from fiction, which made me feel way less anxious about it all." (P7)

Subtheme 1.2: Acquiring information about subjective psychedelic effects

Participants leveraged multiple strategies to gain insights into the potential subjective effects of psychedelic experiences. Thirteen participants (n=13) consulted scholarly articles, books, and blogs authored by experts in the field. Four participants (n=4) found value in personal trip reports, often available on platforms such as Erowid and Reddit, while others explored multimedia resources such as videos (n=5) and podcasts (n=4) featuring personal accounts of psychedelic experiences. A smaller subset of participants (n=3) directly sought conversations with experienced peers to gain firsthand insights.

These activities greatly facilitated the **decision-making processes (1.2.1)** of participants. By understanding the potential spectrum of experiences and assimilating personal accounts, participants were empowered to make more "informed" (P9) decisions about the appropriateness of such experiences for their current situation.

> "[Knowing what to expect] helped me to make a […] decision about whether this was something for me, right now." (P16)

> "Honestly after hearing from some of these patients I was a little scared, [but] I realised [that] this was basically something I needed to do too... I [wasn't] expecting to see rainbows and fairies and I didn't even want to. I just want to heal." (P9)

Information gathering also assisted in **setting realistic expectations for their own psychedelic journeys (1.2.2).** The importance of gaining clarity on the potential experiences was emphasised, with the goal of mitigating any "surprise or shock" (P13). This understanding led participants to approach the experience with a better sense of preparedness and a realistic mindset.

> "[…] helped me set expectations that were grounded in reality, not just some abstract idea of what I thought it might be like." (P11)

> "... set me up to manage whatever came my way." (P19)

The assimilated information prompted participants to **reflect on their therapeutic goals (1.2.3).** Assessing potential subjective effects allowed several participants to delineate anticipated outcomes from the psychedelic journey, creating a "roadmap" (P3) of desired milestones. This process fostered a deliberate consideration of personal therapeutic advantages, focusing on the tangible benefits of the psychedelic experience.

> "I guess understanding what could [potentially] happen on these trips really made me consider my own [goals]." (P17)

> "[...] I was focusing on what I wanted to achieve from the whole thing. [It] kind of gave me a roadmap." (P3)

Subtheme 1.3: Undertaking experiential mind-body exercises to familiarise with potential psychedelic phenomena
Participants highlighted the role of experiential exercises in preparing for forthcoming psychedelic experiences. Some participants partook in various practices to acquaint themselves with possible psychedelic phenomena, including self-transcendence meditation techniques such as non-dual and transcendental meditation (n=7), guided imagery and hypnosis (n=3), intensive breathing exercises like Holotropic Breathwork and the Wim Hof Method (n=3), and sensory deprivation activities such as floatation tanks (n=2).

Participants noted that these practices markedly **increased their confidence in navigating the psychedelic journey (1.3.1)**. Techniques such as self-transcendence meditation and Holotropic Breathwork provided an acquaintance with the potential variability of the psychedelic experience. Therefore, initial exposure to an altered state of consciousness via these preparatory exercises appeared to improve participants' confidence in navigating the unfamiliar psychedelic experience.

> "Going through all that really helped me get cosy with the unpredictable." (P9)

> "[Meditation] gave me confidence to navigate whatever came up." (P10)

> "[...] my [training in Vedanta] gave me a bit of a warm up… I already knew what it felt like to really let go." (P11)

These activities furthered the cultivation of **adaptive coping strategies for the potential challenges of the psychedelic journey (1.3.2).** They offered a "safe space" (P6) for participants to navigate difficult situations, practise 'surrendering', and refine their capacity to 'let go'. Methods like using affirming mantras (e.g., "I am not my thoughts") and calming breathwork (e.g., pursed lip breathing, 4-6-8 breathing) were applied to address anxiety during these experiential exercises. Consequently, participants were better prepared to handle emotionally intense moments during the actual psychedelic experience.

> "[The visualisations] let me run through all sorts of scary 'what ifs' without actually being out of my head." (P2)

> "I was kind of learning to let go, to surrender, to peel back layers." (P15)

Experiential exercises were also noted to foster **familiarity with altered states of consciousness (1.3.3)**, giving participants a more nuanced understanding of potential shifts in perception and awareness during the psychedelic experience. For example, one participant expressed that they had experienced an "intricate tapestry of consciousness" (P15), enabling them to approach their psychedelic experiences with insight, openness, and readiness, rather than apprehension.

> "At first, [the effects of holotropic breathwork] were just intense and physical, but then it sort of broke open into something more [...] I started seeing patterns, feeling connected to things outside myself." (P1)

> "[...] it's like I stumbled onto a whole new side of my mind." (P3)

> "[During this meditation] you're awake, but it's not your everyday kind of awake. It's like being in this peaceful bubble where your mind can wander off into different directions […] that really helped me get a [sense] of what being on [psilocybin] might feel like." (P6)

Increased self-awareness (1.3.4) was another notable outcome of these experiential exercises. Participants reported that the practices fostered a deeper understanding of their mental processes and patterns, enabling them to approach their psychedelic journeys with a more metacognitive stance.

> "It showed me just how much control and insight I could actually have." (P3)

> "I started realising that my mind wasn't just something that things happened to." (P7)

Finally, these preparatory exercises were found to be useful in **managing expectations effectively (1.3.5).** Through such exercises, participants gained insights into the potential for profound revelations, emotional challenges, and unexpected experiences during the psychedelic journey. For several participants, this helped them to recalibrate and align their expectations to the depth and intensity of the forthcoming experiences.

> "[...] it gave me an idea that the actual experience could bring […] challenging moments." (P15)

> "[Breathwork] kind of hinted at the stuff that might come up." (P15)

Theme 2: Psychophysical-Readiness

The Psychophysical-Readiness theme describes how participants prepared themselves mentally and physically for navigating the complexities of the psychedelic experience. It encompasses the readiness to confront the emotional or physical phenomena that may arise, acceptance of potentially uncomfortable aspects of the experience, and a trust in one's mind and body to manage the journey safely.

Subtheme 2.1: Promotion of a relaxed and regulated psychophysical state

Participants utilised various practices to cultivate a relaxed and regulated psychophysical state in preparation for psychedelic experiences. These activities comprised focused-attention meditation, such as breath awareness (n=12). A fraction of participants also practised meditative-stretch yoga, such as Hatha Yoga (n=3). Some participants (n=2) engaged in slow, deep breathing exercises such as '4-6 breathing' and 'box breathing', known for inducing relaxation.

Participants identified these practices as beneficial for **stress management (2.1.1)**, regulating their mental and physical well-being, and fostering calmness during challenging situations. Hence, the practice of these techniques, particularly at the start or end of the day, was associated with significant reductions stress and emotional regulation.

> "I found a few moments every day, especially when I felt overwhelmed or needed a break […] I would sit down, shut my eyes, slow down my breathing, and try to centre myself to relax and regain balance." (P2)

> "The idea was to […] try to step away from the [stresses] of my life, creating a sense inside that everything was okay and still." (P7)

> "[Deep diaphragmatic breathing] allowed me to tap into a sense of slow, grounded stability, even during moments of real [stress]." (P2)

> "[Hatha yoga] bec[a]me my go-to escape from the craziness of life." (P2)

Many participants also emphasised that these practices led to a **quieting of the mind (2.1.2).** They described discovering a sense of stillness, slowing down the pace of life, and a reduction in internal dialogue through their engagement in these activities.

> "[I] strived to carve out a period where I could experience calmness, [quietening] the 'monkey mind'." (P1)

> "[...] that voice in my head would go away, even if just for a few moments, and I'd just be flowing and moving and breathing without any distractions or voices." (P19)

> "My main goal was to quiet my mind and find a sense of inner calm." (P3)

> "[Mindful meditation] helped me to slow down my mind and relax." (P16)

> "When I was in [yoga] flow, that voice in my head would go away, even if just for a few moments […] and I'd just be flowing and moving and breathing without any distractions or voices." (P19)

Through sustained training or extended practice, several participants reported an enhancement in **personal resilience (2.1.3)**, with an increased ability to adapt to and manage challenges as they advanced in their preparation for psychedelic experiences.

> "I basically build up the mental strength to be able to do it […] By practising staying calm and focused." (P7)

> "At first I was bored but as I kind of got better at the whole thing it started to get way more eas[ier]." (P3)

> "[...] my mind was like a hamster wheel, constantly racing with thoughts, [but] with consistent [meditation] practice I [am now able] to effortlessly enter a still state." (P15)

> "I was pretty disciplined [about yoga] because I wanted to train my mind and body to be strong and ready." (P4)

Subtheme 2.2: Cultivating present-moment awareness

Participants reported engaging in various practices to cultivate present-moment awareness as part of their preparation for psychedelic experiences. These activities included open-monitoring meditation (e.g., mindfulness, Vipassana) (n=9). Participants also engaged in reflective writing exercises (n=5) and mindful walking (n=3), often in nature.

Participants engaging in these practices reported noticeable enhancements in **attentional regulation and sustained focus (2.2.1).** For instance, the implementation of these techniques often resulted in an increased capacity to direct cognitive resources effectively and reduced the impact of intrusive thoughts. In the case of reflective writing, for instance, the slow and deliberative nature of the task requires a high level of patience and focused attention. Participants reported that this particular practice compelled them to stay closely attuned to their thoughts, thereby fostering an enriched engagement with their internal cognitive landscape.

> "Writing all those thoughts down really forces you to be patient and stay with your thoughts because you can only write as fast as you can. I had to really focus on what I was thinking and allow that to come out through the pen." (P2)

> "[FM meditation] made me less distracted, like I wasn't jumping around with thoughts." (P6)

> "[...] I would pay attention and focus on every single step and every single tree […] I could focus on everything way more clearly." (P16)

> "I felt more present [after FM meditation]. I would be having a conversation with my partner and I was actually there. I wasn't elsewhere in my mind. I was there with them, *in* that moment, focusing on what they were saying and how we were sharing words." (P13)

These practices also fostered an increased capacity for participants to **observe their thoughts (2.2.2).** Techniques such as open-monitoring meditation reportedly facilitated participants' ability to decenter from their thoughts, perceive them with objectivity, and refrain from automatic judgement or evaluation. This promoted a more mindful, nonreactive relationship with their ongoing thought processes, resulting in what one participant characterised as a "healthier relationship with [their] own stream of consciousness." (P8)

> “It was like a little peg just dropping the thoughts off in one room and letting me move onto the next.” (P4)

> “By writing all of this stuff down, I would then just have it there, in a little packaged form, and then I could shut the book and be like okay yeah that's what I felt but that’s just it [...] They are just words, they are just feelings, and I could quite literally just look at them…” (P2)

> “[...] I just could way more easily see the distractions come up and let them go.” (P16)

> “[…] and so the more I was able to learn to just listen to those thoughts and just watch them, I realised they were normal and they eventually just, kind of, went away.” (P9)

Subtheme 2.3: Cultivating awareness of body sensations

Participants utilised specific practices to enhance their awareness of bodily sensations in preparation for psychedelic experiences. Body scan meditation (e.g., FA) was a relatively common practice among participants (n=4). Some participants also engaged in specific somatic or movement practices , namely Feldenkrais Method (n=1) and Alexander Technique (n=1), to further cultivate this awareness.

Several participants reported a refined ability to **perceive internal physical sensations (2.3.1)** through these types of practices. This heightened awareness ranged from recognising the subtleties of their heartbeat, as one individual became acutely attuned to variations in rhythm and intensity, to sensing delicate shifts in posture and the gentle rise and fall of their breath. These experiences were described as contributing to an enriched sense of presence and connection with the physical body, both within daily life and throughout the psychedelic journey.

> “[...] I would just get more and more aware of my own heart and the way it was beating.” (P6)

> “I started noticing the gentle rise and fall of my breath, the slight tingling in my fingertips, and… the [sensations of] warmth or coolness in different parts of my body.” (P9)

> “I could sense the […] subtle shifts in my posture.” (P12)

> "I was able to notice tension… and areas of discomfort, and with gentle adjustments, I learned to release and realign my body." (P11)

The practice of these techniques also fostered a more nuanced understanding of the **mind-body connection (2.3.2)**. Participants were able to recognise and interpret the intricate relationship between physical sensations and psychological states. For example, some noted how physical tension in specific areas such as shoulders and jaw could correspond to feelings of stress or anxiety. Others reported that focusing attention on different parts of the body would evoke memories and feelings, signifying a deep, interconnected relationship between the physical and emotional self.

> "I [noticed that] when I was feeling stressed or anxious, my body would tense up, especially in my shoulders and jaw." (P10)

> "I learned to recognise how my body responded to different emotions." (P14)

> "[...] as I moved my attention to different parts of my body, different things would come up, like memories and feelings." (P6)

Finally, participants found that these practices equipped them with improved control over their **physical responses to stress (2.3.3).** They described gaining proficiency in regulating their nervous systems and making deliberate decisions about bodily reactions. Some expressed that this practice allowed them to notice tension or discomfort, then consciously release and realign the body. This enhanced control contributed to a more intentional and "empowered" (P6) engagement with their bodies, which was perceived to enrich their overall psychedelic experiences.

> "[...] I got better at regulating […] my nervous system.." (P9)

> "It was cool because [practising the Alexander Technique] helped me to learn how much effort I needed to move, and I could look inside and make deliberate decisions about when and how I was going to react to things and move my body." (P12)

> "I could catch myself in the moment and consciously release the tension." (P10)

Subtheme 2.4: Optimising overall physical health
Participants adopted various strategies aimed at nurturing their bodies and enhancing overall health and well-being in anticipation of their psychedelic experiences. These strategies included adopting a healthy and balanced diet (n=7), engaging in regular exercise, including cardio, strength training, and power yoga (n=7), and prioritising sufficient sleep and rest (n=6).

Participants observed **improved fitness (2.4.1)**, including weight loss and increased cardiovascular endurance, following consistent commitment to regular exercise and healthy eating habits. Rather than aiming to achieve an idealised state of physical health, participants sought a sense of feeling strong, healthy, and prepared for their upcoming experiences. This level of physical readiness served to instil confidence and contribute to an overall sense of wellbeing.

> "I actually got really fit, maybe the most fit I've been in years." (P12)

> "[My body] felt good and way lighter… I had so much more energy and actually wanted to move." (P11)

> "It wasn't about becoming some kind of health guru… It was about feeling like my body was in good shape […] strong and healthy, and kind of cleaned out, ready." (P16)

Participants also reported an improvement in their **baseline mood and wellbeing (2.4.2)**, resulting from the combined effect of regular exercise, balanced nutrition, sufficient sleep, and self-care 'rituals'. The adoption of these healthy lifestyle habits led to an increase in energy levels and positive feelings, creating an optimal emotional "foundation" (P5) for their forthcoming psychedelic experiences.

> "Cutting out all that crap [food] just made me feel good." (P18)

> "[Regular yoga] makes me feel so much better… so much more full of energy and positivity." (P14)

> "... when I started [prioritising sleep] I felt way less anxious." (P8)

Several participants found that regular engagement in physically challenging activities such as power yoga contributed to an increased **resilience to physical discomfort (4.2.3)**. The discipline cultivated during these rigorous practices was perceived to carry over into their psychedelic experiences, allowing them to manage and navigate any arising bodily sensations more effectively.

> "[...] they help me to… keep going even when it feels like I can't go on […] because I know I can do it, and I know I'll be fine." (P14)

> "It was a lot about discipline and pushing through." (P4)

Theme 3: Intention-Preparation

The Intention-Preparation theme summarises the introspective journey that underlies participants' decision to use psychedelics. This process involves thoughtful deliberation on the motivations behind the psychedelic use, such as self-exploration, therapeutic purposes, or spiritual growth. Integral to this theme is the establishment of setting clear intentions for the experience, providing a sense of direction and purpose.

Subtheme 3.1: Identifying motivations for using psychedelics

Participants engaged in reflective processes to understand their motivations for using psychedelic substances. These processes included journaling (n=8), introspection (n=6), and discussing with friends or psychedelic communities (n=4).

The process of reflecting on their motivations led participants to an increased **self-understanding (3.1.1)**. Participants reported gaining clarity regarding their personal characteristics, life circumstances, preferences, and dislikes. For instance, journaling about their reasons for using psychedelics facilitated an in-depth self-evaluation, leading to a comprehensive understanding of their personal attributes and behaviours.

> "[Journalling] made me really think about all of the parts I have to myself…" (P15)

> "I had to admit… that I wasn't this confident person I [had] made [myself] out to be." (P14)

Upon introspection of their motivations, participants found themselves better aligned with their **therapeutic goals (3.1.2)**. The act of contemplating the potential benefits of psychedelic use in relation to their current life situations aided them in identifying and clarifying the specific outcomes they intended to achieve from their psychedelic experiences.

> “[...] you start to notice, or like [to] identify, which bits of your story you want to let go of.” (P3)

> “[...] when I really thought about why I was going, it was way more dense than I first realised… and it helped me work out really what I wanted to make of this retreat.” (P16)

Subtheme 3.2: Establishing intentions for the experience
Participants frequently spoke about explicitly ‘setting intentions' for their psychedelic experiences. This was typically accomplished through journaling (n=10), meditation (n=3), and engaging in discussions with friends or psychedelic communities (n=3).

Setting clear intentions provided a heightened **sense of direction for the psychedelic experience (3.2.1).** These pre-established intentions acted as a guide or "anchor" (P14), helping maintain focus amidst the complex sensory and cognitive alterations induced by psychedelics.

> “[Journalling] gave me a clear sense of direction for my experience.” (P9)

> “It was like drawing a map for my journey.” (P18)

> “[Speaking with others] gave me a better understanding of what I wanted from my experience.” (P17)

The establishment of explicit intentions also augmented the **meaningfulness of the psychedelic journey (3.2.2)**. "Meaningfulness" was defined by participants as the personal relevance and emotional resonance of the experience. They expressed that having distinct, personal objectives before the psychedelic experience increased the perceived value and significance of the insights gained during the journey.

> “[Journalling] infused my experience with a deeper sense of purpose and meaning.” (P14)

> “[Mindful meditation] allowed me to feel the significance of it all.” (P16)

> “[Meditation] helped me to get super mindful of my intention, which helped me connect with it on a deeper level.” (P1)

> “[Engaging in discussions] added depth to the [psilocybin] journey.” (P6)

The presence of defined intentions offered a **practical framework for integration (3.2.3)** following the psychedelic experience. Participants referenced their set intentions as guiding principles or "touchstones" (P12) for interpreting and incorporating their psychedelic insights into their everyday lives.

> “It was interesting to see how my intentions changed and evolved as we got closer to the retreat and also during it… I still sometimes look back at [them] now and they really remind me of how far I’ve come.” (P7)

> “I could reflect back on my initial goals and see how they've manifested.” (P9)

Theme 4 Support-Planning
The Support-Planning theme explores the importance of ensuring a safe and supportive environment during the psychedelic experience and the need for post-experience planning. This theme focuses on establishing a trustful connection with those present during the experience, ensuring the safety of the substance, preparing friends and family

for potential changes, and making a contingency plan for possible challenging moments during and after the experience.

Subtheme 4.1: Cultivating trustful relationships
Participants prepared for their psilocybin sessions by establishing trust with those in attendance, accomplished via dialogues with facilitators or guides (n=18), preliminary conversations with peers (n=6), and participation in communal activities such as breathwork, meditation, and ecstatic dance (n=9). The importance of clear communication and respect for personal boundaries during the psychedelic session was also emphasised (n=4).

The establishment of trustful relationships **enhanced participants' sense of comfort and safety (4.1.1)**, resulting from both pre-retreat interactions and mutual respect for individual boundaries. Trust was fostered through initial discussions with facilitators and peers prior to the retreat, which served to “humanise” (P3) the forthcoming experience and cultivate a sense of familiarity. In addition, mutual recognition of and respect for personal space contributed to an environment of trust and safety.

> "Getting the chance to chat with [the facilitators/guides] before the retreat was really helpful […] [It was] relieving to talk to an actual person.” (P13)

> “Speaking to [the facilitators/guides] definitely put some of my nerves to rest.” (P6)

> “I was able to feel more comfortable around [the other guests] because I had already met them on Zoom.” (P14)

> “I think we all could feel it… like safe in this container, trusting that everyone would basically stick to what we signed up for and respect those boundaries.” (P3)

The development of relationships with fellow participants and retreat personnel enabled the **growth of a strong communal support network (4.1.2)**. This experience was often described by participants as joining a new familial structure, underpinned by reciprocal watchfulness. The reassurance derived from the presence of others, coupled with the knowledge of mutual safeguarding within the group, engendered a sense of ease, underscoring the essential role of a supportive community in the participants' experience.

> “[...] like becoming a member of a new family, with people looking out for me.” (P7)

> “It was reassuring to know that I was not alone in my journey.” (P1)

> “[...] made me feel so at ease knowing we had each other's backs.” (P15)

These relationships also significantly contributed to **promoting a sense of unity within the group (4.1.3)**. Emphasis was placed on collective experiences such as workshops and sharing circles, which swiftly catalysed the formation of close bonds among participants. This rapid development of connection often took participants by surprise. Such shared experiences proved critical in amplifying group coherence and fostering an environment conducive to empathy and support.

> “I was amazed by how tight-knit our group became in such a short span of time.” (P10)

> “Doing the [morning workshops] together definitely made us feel closer.” (P11)

> "We began to form bonds early on." (P12)

Subtheme 4.2: Verifying retreat and staff credibility

Participants engaged in thorough online research to assess the credibility of the retreat and its staff. This process included examining past participant reviews and testimonials (n=11), investigating the experience, qualifications, and skills of the retreat staff (n=4), and assessing the retreat's digital footprint, including social media presence and website content (n=3).

Rigorous scrutiny of retreat and staff credibility significantly bolstered participants' **perception of physical safety (4.2.1)**. An abundance of positive reviews and testimonials often solidified confidence in the legitimacy of the retreats. A sense of relief was noted among participants, attributable to the realisation that the staff were proficiently equipped with specialised skills and comprehensive experience, thereby fostering an environment of security.

> "They had tons of reviews […] you could tell straight away it was legit[imate]" (P11)

> "[...] everyone seemed to have a special skill […] [It] felt like I was in safe hands." (P3)

Complementing the enhanced sense of safety, this verification process precipitated a **heightened level of trust in the retreat staff (4.2.2)**. The dedication, expertise, and professionalism exhibited by the staff through their digital platforms were pivotal in nurturing this trust. Further trust development was facilitated by the staff's responsive engagement with inquiries on social media, demonstrating their expertise and commitment to the retreat.

> "Seeing their dedication, their depth of knowledge...it was so reassuring, you know. I felt...I felt secure." (P10)

> "[The retreat staff] weren't just randomly picked people... they were experienced, skilled...[I] felt I was stepping into a well-run, professional space." (P18)

> "Seeing them answer questions and interact with their followers [on social media]... I could tell they knew what they were talking about." (P7)

> "I watched some of their live sessions...their way of explaining and guiding through the process...it was really impressive." (P14)

Subsequently, the procedure of validating retreat and staff credibility effectively **alleviated pre-retreat anxiety (4.2.3)**. Online testimonials and reviews depicting transformative experiences of former participants fostered a sense of calmness among prospective attendees. The resultant trust, founded on the retreat staff's proven experience managing similar retreats and handling diverse situations, was a considerable factor in minimising participants' anxiety.

> "...when you read about other people having these [transformations] it makes you feel a lot calmer about the whole thing." (P19)

> "[I trusted them] and it took a bit of weight off… because I knew how many times they had done this and how they had seen absolutely everything." (P5)

Subtheme 4.3: Preparing in-experience support

Participants prepared for the in-experience support during the psilocybin session by acquiring a comprehensive understanding of the session's structure (n=15) and the roles of the retreat staff during the session (n=13). They also focused on the development of personal coping strategies (n=13) and actively communicated their individual support needs and preferences to the retreat facilitators (n=10).

A comprehensive understanding of the session's structure and the roles of the retreat staff significantly **enhanced the participants' sense of safety (4.3.1).** Workshops delineating the ceremony and open Q&A sessions provided valuable clarity and alleviated uncertainties. Additionally, personal consultations with facilitators about individual support needs further instilled a sense of calm among participants. The development of personal coping strategies, such as grounding and mindfulness techniques, also served as a comforting resource.

> "[The staff] spent about two hours doing a 'what is ceremony' workshop, where they explained what will happen during the [psilocybin session] [...] At the end they opened it up to questions [...] Before this meeting, I didn't really know what to expect, so it was a relief to have all my questions answered." (P2)

> "I had a long chat with one of the facilitators about my [support needs] on the second day of the retreat [...] [which] made me feel a bit calmer about the [psilocybin session] [...] I knew they were there to help and guide me." (P8)

> "It was comforting to know I could come back to my breath if things started to get difficult..." (P17)

This preparation process also expanded the participants' **capacity to manage challenging psychedelic experiences (4.3.2)**. Participants reported that guidance from facilitators, such as advice on navigating difficult moments during the ceremony, proved "transformative" (P9). Additionally, reassurances from the staff about their continual presence and watchfulness enabled participants to let go and fully engage in the experience. Participants also recalled utilising grounding techniques taught by facilitators to effectively manage intense moments during the session.

> "[...] when I [faced a difficult moment] during the ceremony, I remembered the advice from [one of the facilitators] to ask the question: "is this medicine, if not you must go" [...] It changed the whole scene." (P3)

> "[The staff] reassured me that they would keep an eye on me, and that acknowledgment… that feeling of being held… really allowed me to let go during the ceremony." (P14)

> "During a particularly intense moment in the ceremony, I felt a surge of anxiety [...] I remembered one of the [strategies] I had been told by [a facilitator]. I visualised myself as a tree, with the roots spreading deep into the earth, grounding me literally into the floor, making me immovable [...] I concentrated on my breath, imagining each exhale sending my roots deeper and deeper into the ground. The anxiety didn't disappear completely, but it became way more manageable..." (P10)

Finally, preparing and understanding in-experience support in advance of the psilocybin sessions also **optimised the use of such support resources (4.3.3)**. Participants felt empowered to actively seek help when needed, as they were well-informed about how to communicate their needs during the session. Facilitators' timely and empathetic responses to these requests further facilitated participants' navigation of the experience. This process, in turn, led to an optimised use of the support resources available to the participants.

> "... during the second ceremony I *knew* I could put my hand up and ask for some help… [A facilitator] came to me and sat by me. [They] asked if I wanted a hand… They stroked my head and helped me to slow down my breathing… and that was exactly what I needed…" (P2)

"... I asked how I should let the facilitators know if I wanted a hand hold." (P8)

Subtheme 4.4: Preparing a post-experience integration plan

Participants prepared for their post-experience integration by arranging 'integration' sessions with retreat staff to discuss and interpret their experiences (n=12). Additionally, they allocated adequate recovery and reflection time following the retreat (n=6) and created a consistent schedule for integration or contemplative practices (n=6). Participants also proactively communicated with their personal networks about potential changes following the retreat (n=5).

Efforts towards preparing a post-experience integration plan significantly **reduced participants' post-retreat transition anxiety (4.4.1)**. Participants reported that taking time off after the retreat eased their transition back into their daily routines, making the process less abrupt and more manageable. Planning to establish regular practices, such as daily meditation, even for short periods, was recognised as a significant aid in transitioning back into everyday life.

> "After the retreat, I [took] a week off just to unwind [...] It eased my re-entry into my daily routine, making it less abrupt and more... gentle." (P16)

> "Establishing a morning meditation routine [after the retreat]... even if it was only five minutes a day [...] really helped me transition back into my everyday life." (P11)

These planned post-retreat arrangements also led to **continued therapeutic benefits (4.4.2).** Participants found that integration sessions with retreat facilitators enabled them to process their experiences more effectively and apply the lessons learned during the retreat to their daily life and relationships. These sessions, combined with consistent meditation and self-reflection practices, were seen as effective strategies to tap back into the therapeutic "mushroomy" (P10) feeling and handle daily life triggers.

> "After the retreat, [meditation] became a way for me to tap back into that 'mushroomy' feeling [...] It was like a daily mood boost." (P10)

> "[The integration sessions with the retreat facilitators] helped me to understand and process the tougher parts of my experience [...] They helped me find ways to actually make changes and apply some of those lessons to my life and relationships." (P7)

> "The retreat was just the beginning. As I integrated more meditation and self-reflection into my life [...] I noticed the lessons from the retreat were helping me to handle triggers in my daily life more effectively" (P19)

This planned post-retreat integration process was also tied to an **increased motivation for personal growth (4.4.3).** Participants reported that the uncovering of new areas for healing during the integration process spurred them to delve deeper into their self-discovery journeys. This process was further supported by the accountability brought about through sharing their experiences and integration plans with friends and family.

> "[...] I began to uncover more areas for healing [...] This motivated me to delve deeper and continue on this path." (P12)

> "Telling my friends and family about my retreat experiences and [my integration plan] [...] made me accountable. Their support encouraged me to continue healing and I even ended up joining more groups and integration circles." (P1)

Lastly, by preparing a post-experience integration plan, participants were able to **strengthen support from their personal networks (4.4.4)**. Informing friends and family about their retreat experiences and subsequent integration plan ahead of time led to increased understanding and support upon returning home. The guidance received during the integration sessions was particularly beneficial for participants in communicating their experiences to those who were less familiar with their journey.

> "When I came home, my friends… already knowing about my experience… were really supportive and didn't make me feel weird about my new sort of rituals [...]" (P16)

> "The [integration] sessions with the retreat facilitators were quite useful [...] They helped me communicate my experiences to friends at home, some of whom didn't really understand my journey." (P13)

A3.8 Demographic characteristics

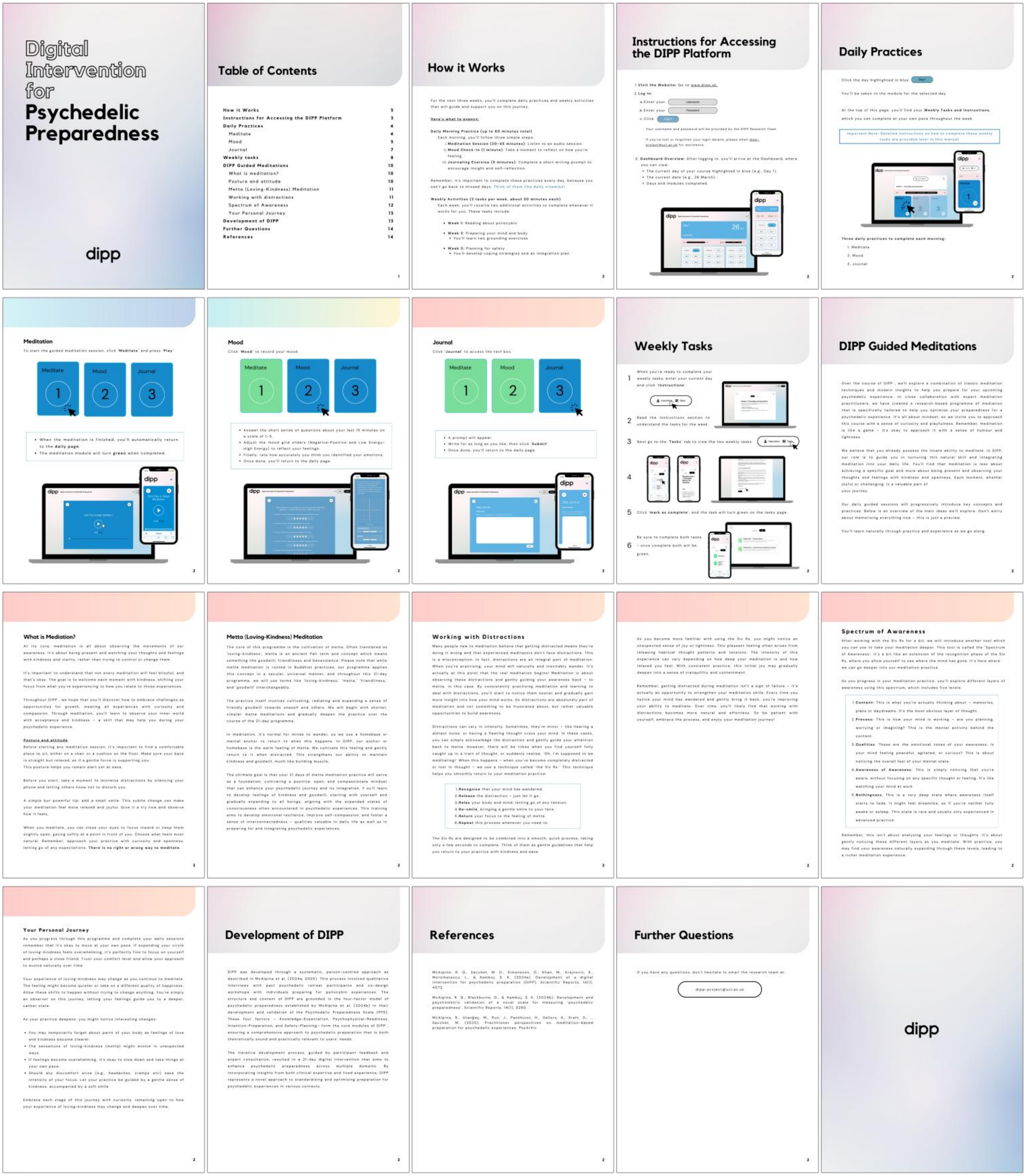
Study 3.I (Qualitative Interviews) Sample (N=19)

Variables	**M ± SD**	**Range**
Age (years)	42.37 ± 12.37	37-77
Months since retreat	3.16 ± 2.09	1-9
Days spent preparing for retreat	17.68 ± 11.29	3-40
Minutes per day spent preparing for retreat	37.63 ± 18.06	10-60
	n	**%**
Gender		
Male	7	36.84
Female	12	63.16
Education		
High school/college	1	5.26
Undergraduate	8	42.11
Postgraduate	10	52.63
Ethnicity		
White	14	73.68
Black	1	5.26
Latino/Hispanic	1	5.26
Mixed	3	15.79
Religion		
Not religious	14	73.68
Christian	5	26.32
Lifetime psychedelic use		
Never before	12	63.16
On 1 occasion only	4	21.05
On 2-5 occasions only	3	15.79
Location of psilocybin retreat		
Mexico	12	63.16
Netherlands	7	36.84

Study 3.II (Co-design Workshops) (N=28)

Demographic	**Workshop 1 (n=10)**		**Workshop 2 (n=9)**		**Workshop 3 (n=9)**	
	M	**SD**	**M**	**SD**	**M**	**SD**
Age (years)	46.11	8.33	51.13	10.47	51.88	14.32
	n	**%**	**n**	**%**	**n**	**%**
Gender						
Male	3	30.00	2	22.22	5	55.56
Female	7	70.00	7	77.78	4	44.44
Education						
High school/college	1	10.00	-	-	-	
Undergraduate	6	60.00	4	44.44	6	66.67
Postgraduate	3	30.00	5	55.56	3	33.33
Ethnicity						
White	8	80.00	6	66.67	6	66.67
Black	1	10.00	-	-	1	11.11
Latino/Hispanic	1	10.00	1	11.11	-	-
Mixed	-	-	1	11.11	2	22.22
Other	-	-	1	11.11	-	-
Religion						
Not religious	7	70.00	6	66.67	6	66.67
Christian	3	30.00	2	22.22	3	33.33
Buddhist	-	-	1	11.11	-	-
Lifetime Psychedelic Use						
Never before	6	60.00	5	55.56	3	33.34
On 1 occasion only	2	20.00	2	22.22	2	22.22
On 2-5 occasions only	2	20.00	2	22.22	2	22.22
On more than 5 occasions	-	-	-	-	2	22.22

A3.9 DIPP digital handbook



Appendix 4

A4.1 Survey measures

CAMS-R adaptation

The following items, adapted from the CAMS-R, were modified to fit the context of this survey, focusing on how meditation training might enhance a person's abilities during a psychedelic experience.

"Training in meditation before using a psychedelic would probably enhance someone's ability to…"

1. "... concentrate during the psychedelic experience."
2. "... tolerate emotional pain during the experience."
3. "... accept uncontrollable aspects of the psychedelic experience."
4. "... describe their feelings in detail during the experience."
5. "... not get distracted during the experience."
6. "... keep track of their thoughts and feelings during the experience."
7. "... notice thoughts without judgement during the experience."
8. "... accept their thoughts and feelings during the experience."
9. "... focus on the present moment during the experience."
10. "... focus on a single aspect for a long duration during the experience."

Meditative elements

In the survey, participants were provided with the following descriptions of various meditation competencies. Each item was designed to describe a distinct practice:

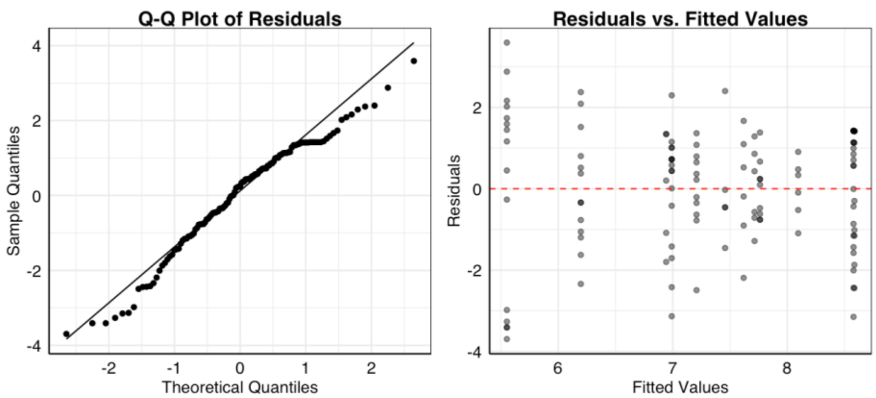
1. Observing attention - Noticing the movement of attention as it shifts from experience to another.
2. Positive emotion cultivation - Radiating feelings of goodwill and kindness towards oneself and others.
3. Relaxation/tranquillity cultivation - Nurturing a peaceful mind while releasing physical tension to achieve a state of calm.
4. Recognising and releasing distractions - Identifying distractions and gently redirecting focus back to the object of meditation.
5. Recognising interconnectedness of phenomena - Understanding the cause-and-effect relationships that bind both experiences and phenomena.
6. Non-discriminatory awareness - Adopting a neutral stance, free from judgement or attachment, while observing all experiences.
7. Ongoing awareness - Maintaining or returning to meditative practices when not formally meditating.
8. Insight - Gaining a deep, intuitive understanding of oneself and one's experiences.
9. Equanimity - Maintaining a calm and balanced mind, undisturbed by joy or sorrow, through mindful awareness and acceptance of experiences as they occur.
10. Empathy and compassion - Cultivating an understanding and kindness toward others' feelings and experiences, alongside a desire to alleviate their suffering.
11. Comfort with discomfort - Developing the ability to remain calm and endure difficult or uncomfortable situations with a composed mind.
12. Sense of humour - Approaching meditation with a light-heart; allowing for joy and spontaneity in the practice.
13. Curiosity - Nurturing interest in exploring and understanding one's inner experiences deeply and objectively during meditation.
14. One-pointed concentration - Focusing intently on a singular object, such as the breath, to foster attention without peripheral awareness or distractions.
15. Visualisation - Creating and immersing in mental images or scenarios to aid in concentration or other purposes like evoking a particular experience.
16. Mantra - Repeating a word or phrase to aid concentration and focus, or to stop discursive thinking

17. Body scan - Systematically moving attention through the body to notice sensations.
18. Noting - Verbally labelling emerging thoughts, sensations, and emotions as they arise during meditation.

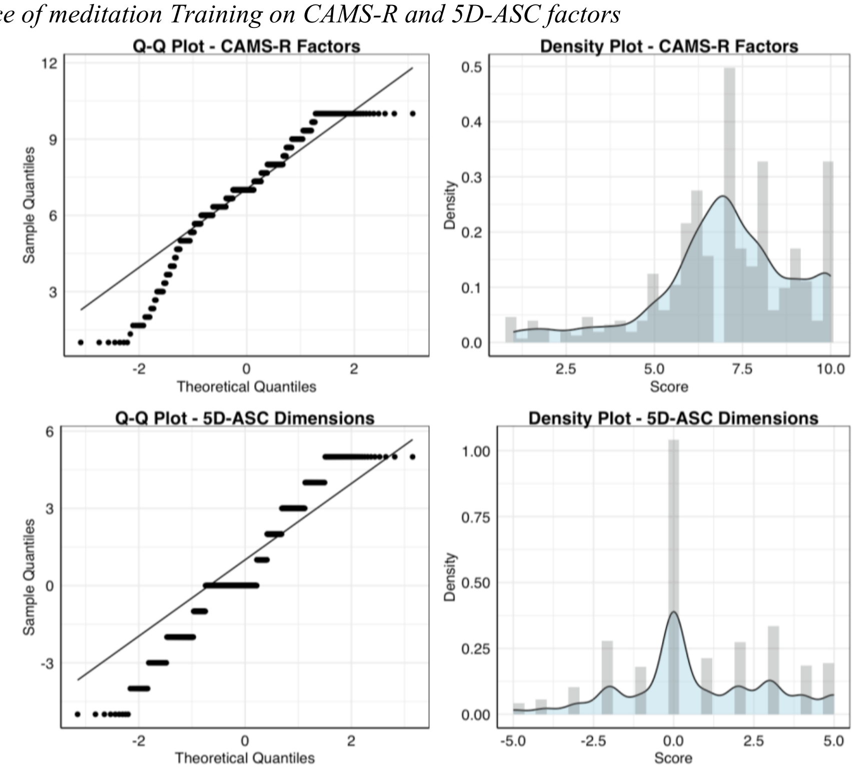
A4.2 Assumption tests

Effects of meditation tradition, meditation experience, and psychedelic use on PBMPP scores (3-way ANOVA)

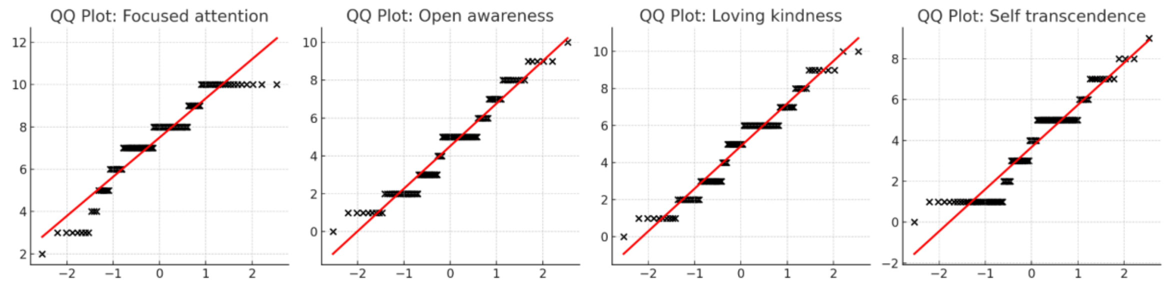
The assumptions of normality of residuals and homogeneity of variance for the three-way ANOVA were evaluated. The Q-Q plot indicated mild deviations from normality, particularly in the tails, which was confirmed by the Shapiro-Wilk test (W = 0.97, $p = 0.014$). However, the deviations were not severe, and the residuals followed an approximate normal distribution. The Residuals vs. Fitted Values plot showed no major patterns, with residuals scattered randomly around zero, however, Levene's test for homogeneity of variance was significant, $F(11, 111) = 1.91$, $p = 0.046$, indicating unequal variances across groups. Given these violations, we conducted a robust ANOVA using heteroscedasticity-consistent (HC) standard errors to account for heteroscedasticity and ensure valid statistical inference.



Expected influence of meditation Training on CAMS-R and 5D-ASC factors



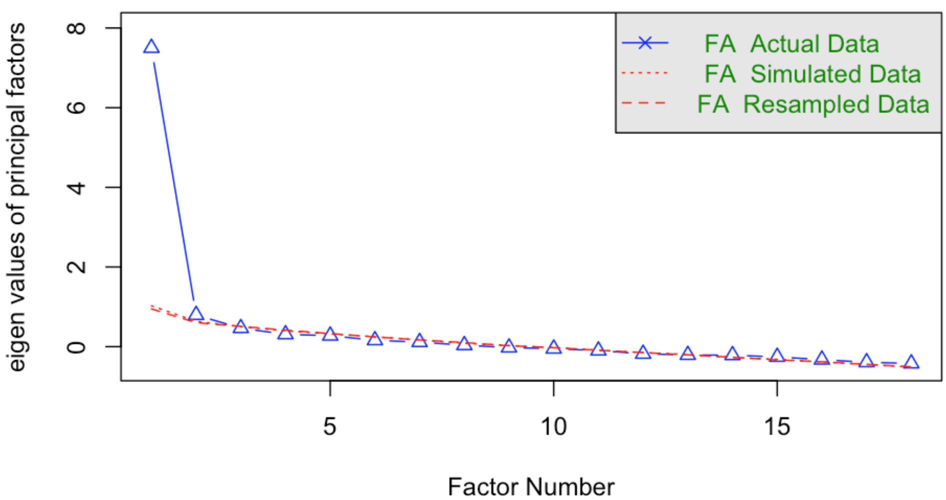
Perceived efficacy of meditation practices and processes for psychedelic preparation (repeated measures ANOVAs)
The assumptions of normality and sphericity for the repeated measures ANOVA were assessed. The Shapiro-Wilk test for normality was significant for all groups, however, Q-Q plots for each group were examined to assess the severity of the deviations from normality. While some deviations from the diagonal line were observed, they did not appear severe enough to prevent running the repeated measures ANOVA.



For the assessment of sphericity, Mauchly's test was conducted for both analyses. In the meditation practices analysis, the test was not significant ($W = 0.95$, $p = 0.289$), indicating that the assumption of sphericity was not violated. Similarly, for the meditation mechanisms analysis, Mauchly's test was also not significant ($W = 0.918$, $p = 0.324$), suggesting that sphericity was met. As a precautionary measure, Greenhouse-Geisser (GG) and Huynh-Feldt (HF) corrections were calculated for both analyses. For the practices, GG epsilon was 0.968 and HF epsilon was 0.994, while for the mechanisms, GG epsilon was 0.955 and HF epsilon was 0.989. In both cases, the GG- and HF-adjusted p-values remained significant ($p < 0.001$), confirming the robustness of our findings even if sphericity had been violated. These results support the appropriateness of using the repeated measures ANOVA for our analyses and provide additional assurance of the validity of our results.

A4.3 Factor solution evaluation

Parallel analysis scree plot



Comparison of factor solutions (1-5 factors) (Fit indices; proportion of variance explained)

Factors	ChiSquare	df	p-value	TLI	RMSEA	Prop_Var
1	288.9783	135	3.114e-13	0.8237	0.09595	0.74823
2	224.9278	118	1.128e-08	0.8590	0.08544	0.84809
3	182.9771	102	1.529e-06	0.8756	0.07992	0.91300
4	147.2125	87	5.909e-05	0.8908	0.07457	0.96321
5	113.7007	73	1.624e-03	0.9114	0.06683	1.04135

Factor loadings for 3-factor solution

Item	Factor 1	Factor 2	Factor 3
C1: Observing attention	0.643		
C2: Positive emotion cultivation	0.563		
C3: Relaxation/tranquillity cultivation	0.404		0.315
C4: Recognising and releasing distractions		0.313	
C5: Recognising interconnectedness of phenomena	0.789		
C6: Non-discriminatory awareness	0.535		0.378
C7: Ongoing awareness	0.308		0.361
C8: Insight	0.679		
C9: Equanimity	0.474		0.342
C10: Empathy and compassion	0.715		
C11: Comfort with discomfort			0.586
C12: Sense of humour			0.700
C13: Curiosity	0.619		
C14: One-pointed concentration		0.848	
C15: Visualisation		0.478	
C16: Mantra		0.507	
C17: Body scan		0.469	
C18: Noting		0.492	
SS loadings	3.730	1.946	1.571
Proportion Var	0.207	0.108	0.087
Cumulative Var	0.207	0.315	0.403

Note: Only loadings > 0.3 are shown for clarity.

A4.4 Participant characteristics (N=123)

Variables	M ± SD	Range
Age (years)	41.1 ± 13.5	18 - 78
Meditation frequency (sessions per week)	7.4 ± 4.6	1 - 34
Meditation duration (minutes per session)	46.4 ± 33.4	10 - 240
	n	**%**
Gender		
Male	82	66.67
Female	33	26.83
Non-binary / third gender	4	3.25
Prefer not to say	4	3.25
Ethnicity		
Asian	9	7.32
Black	2	1.63
Black or African American	1	0.81
Other	13	10.57
White	98	79.67
Education		
Completed Doctorate degree	12	9.76
Completed master's degree	42	34.15
Completed undergraduate degree	44	35.77
Graduated from high school / secondary school	24	20.33
Country		
Australia	2	1.63
Austria	1	0.81
Belgium	1	0.81
Britain	1	0.81
Canada	8	6.50
China	1	0.81
Croatia	1	0.81
Denmark	1	0.81
Estonia	1	0.81
Finland	1	0.81
Germany	9	7.32
India	2	1.63
Israel	1	0.81

Italy	2	1.63
Netherlands	5	4.07
Singapore	1	0.81
Slovenia	1	0.81
South Africa	3	2.44
Spain	2	1.63
Sweden	2	1.63
Switzerland	2	1.63
UK	19	15.45
USA	56	45.55
Meditation Experience		
1-3 years	46	37.40
3-10 years	30	24.39
10+ years	47	38.21
Meditation Tradition		
Does not identify with any tradition	50	40.65
Identifies with one or more traditions	73	59.35
Number of psychedelic experiences		
1-5	29	23.58
6-20	41	33.34
20+	53	43.09

A4.5 ANOVA results for PBMPP scores across meditation tradition, meditation experience, and psychedelic use

Source	df	F	p
Meditation Tradition	1	0.003	0.961
Meditation Experience	2	3.978	0.021
Psychedelic Experience	1	10.733	0.001
Meditation Tradition × Meditation Experience	2	1.438	0.242
Meditation Tradition × Psychedelic Experience	1	0.534	0.467
Meditation Experience × Psychedelic Experience	2	2.074	0.131
Meditation Tradition × Meditation Experience × Psychedelic Experience	2	3.987	0.021
Residuals	111		

Note. df = degrees of freedom

A4.6. Post-hoc comparisons: Estimated Marginal Means (EMMs) of PBMPP scores by meditation tradition, meditation experience, and psychedelic use.

Psychedelic Experience	Meditation Experience	Meditation Tradition	EMM	SE	Lower CI	Upper CI	Estimate	SE	t-ratio	p	d
1-20 occasions	1-3 years	Non-adherence	5.55	0.40	4.38	6.72	-1.44	0.56	-2.59	0.01	-0.69
		Adherence	6.99	0.39	5.86	8.12					
	3-10 years	Non-adherence	6.94	0.69	4.92	8.97	0.75	0.81	0.92	0.36	0.52
		Adherence	6.20	0.43	4.94	7.45					
	10+ years	Non-adherence	8.59	0.49	7.15	10.02	1.38	0.68	2.04	0.04	0.89
		Adherence	7.21	0.47	5.84	8.57					
20+ occasions	1-3 years	Non-adherence	7.76	0.52	6.25	9.27	0.14	0.82	0.18	0.86	0.13
		Adherence	7.62	0.63	5.77	9.47					
	3-10 years	Non-adherence	8.10	0.63	6.25	9.94	0.38	0.89	0.43	0.67	0.43
		Adherence	7.71	0.63	5.87	9.56					
	10+ years	Non-adherence	7.46	0.69	5.43	9.48	-1.12	0.77	-1.46	0.15	-0.77
		Adherence	8.58	0.34	7.59	9.57					

Note: EMM = Estimated Marginal Mean; SE = Standard Error; CI = Confidence Interval.

A4.7. Change descriptive statistics for outcome measures

Measure	Items	M	SD	95% CI
PBMPP	Positive Experience	7.50	2.24	7.10, 7.90
	Helpful Insights	7.31	2.19	6.92, 7.70
	Safe Experience	7.34	2.50	6.90, 7.79
	Smoother Re-Adjustment	7.81	2.11	7.44, 8.19
	Negative Experience	6.89	2.26	6.48, 7.29
	Access Meditative States	7.26	2.41	6.83, 7.69
	Derive Lasting Benefits	7.28	2.19	6.89, 7.67
CAMS-R	Attention	6.43	1.86	6.10, 6.77
	Present Focus	7.29	2.17	6.91, 7.68
	Awareness	6.63	1.88	6.30, 6.97
	Acceptance	7.69	1.84	7.36, 8.02
5D-ASC	Oceanic Boundlessness	2.98	1.55	2.71, 3.26
	Anxious Ego-Dissolution	-1.01	2.55	-1.46, -0.55
	Visionary Restructuralization	0.73	1.49	0.47, 1.0
	Acoustic Alterations	0.84	1.51	0.57, 1.11
	Vigilance Reduction	-0.13	1.91	-0.47, 0.21
Meditation Practices	Focused Attention	5.28	2.02	4.92, 5.64
	Open Awareness	7.29	2.11	6.92, 7.67
	Loving-Kindness	8.07	2.14	7.69, 8.45
	Self-Transcendence	6.96	2.24	6.56, 7.36
Meditation Processes	Attention Regulation	5.67	2.38	5.25, 6.10
	Body Awareness	6.80	2.21	6.41, 7.20
	Emotion Regulation I	7.74	2.19	7.35, 8.13
	Emotion Regulation II	7.87	2.10	7.50, 8.24
	Change in Perspective on the Self	7.37	2.20	6.98, 7.77

A4.7 (continued)

Meditation Competencies	C1: Observing attention - Noticing the movement of attention as it shifts from experience to another.	6.46	1.95	6.12, 6.81
	C2: Positive emotion cultivation - Radiating feelings of goodwill and kindness towards oneself and others.	7.69	2.1	7.32, 8.06
	C3: Relaxation/tranquillity cultivation - Nurturing a peaceful mind while releasing physical tension to achieve a state of calm.	7.59	2.15	7.20, 7.97
	C4: Recognising and releasing distractions - Identifying distractions and gently redirecting focus back to the object of meditation.	6.5	2.08	6.13, 6.86
	C5: Recognising interconnectedness of phenomena - Understanding the cause-and-effect relationships that bind both experiences and phenomena.	6.84	2.25	6.44, 7.23
	C6: Non-discriminatory awareness - Adopting a neutral stance, free from judgement or attachment, while observing all experiences.	7.72	1.99	7.37, 8.08
	C7: Ongoing awareness - Maintaining or returning to meditative practices when not formally meditating.	7.35	2.11	6.98, 7.72
	C8: Insight - Gaining a deep, intuitive understanding of oneself and one's experiences.	7.09	2.23	6.70, 7.48
	C9: Equanimity - Maintaining a calm and balanced mind, undisturbed by joy or sorrow, through mindful awareness and acceptance of experiences as they occur.	7.72	2.24	7.32, 8.12
	C10: Empathy and compassion - Cultivating an understanding and kindness toward others' feelings and experiences, alongside a desire to alleviate their suffering.	7.59	2.23	7.19, 7.98
	C11: Comfort with discomfort - Developing the ability to remain calm and endure difficult or uncomfortable situations with a composed mind.	7.86	1.97	7.51, 8.21
	C12: Sense of humour - Approaching meditation with a light-heart; allowing for joy and spontaneity in the practice.	8.01	1.78	7.69, 8.32
	C13: Curiosity - Nurturing interest in exploring and understanding one's inner experiences deeply and objectively during meditation.	7.5	1.92	7.16, 7.83
	C14: One-pointed concentration - Focusing intently on a singular object, such as the breath, to foster attention without peripheral awareness or distractions.	4.52	2.27	4.12, 4.92
	C15: Visualisation - Creating and immersing in mental images or scenarios to aid in concentration or other purposes like evoking a particular experience.	4.89	2.32	4.48, 5.30
	C16: Mantra - Repeating a word or phrase to aid concentration and focus, or to stop discursive thinking.	3.67	2.13	3.30, 4.05
	C17: Body scan - Systematically moving attention through the body to notice sensations.	5.33	2.6	4.87, 5.79
	C18: Noting - Verbally labelling emerging thoughts, sensations, and emotions as they arise during meditation.	4.46	2.63	4.00, 4.93

Note. For the PBMPP, scores range from 0 to 10, with higher scores indicating greater agreement. For the 5D-ASC, scores range from -5 to +5, with positive scores indicating an expected increase and negative scores indicating an expected decrease in the respective dimensions following meditation training. CAMS-R scores range from 0 to 10, with higher scores representing greater agreement. Meditation Practices, Processes and Competencies scores range from 0 to 10, with higher scores indicating greater perceived effectiveness. CI = Confidence Interval; SD = Standard Deviation.

A4.8. Final Factor Structure

Factor loadings

Item	Factor 1	Factor 2	Factor 3	Communality
C2: Positive emotion cultivation	0.85	-	-	0.74
C14: One-pointed concentration	-	-	0.80	0.67
C1: Observing attention	-	0.72	-	0.54
C3: Relaxation/tranquillity cultivation	0.67	-	-	0.57
C12: Sense of humour	0.63	-	-	0.38
C10: Empathy and compassion	0.61	-	-	0.59
C8: Insight	-	0.59	-	0.54
C5: Recognising interconnectedness of phenomena	-	0.57	-	0.59
C13: Curiosity	-	0.56	-	0.38
C15: Visualisation	-	-	0.50	0.37
C16: Mantra	-	-	0.49	0.32
C17: Body scan	-	-	0.47	0.32

Note. Factor loadings < 0.3 are suppressed. Bold numbers indicate the highest loading for each item. Factor 1 = Positive Emotional States; Factor 2 = Mindful Awareness and Insight; Factor 3 = Concentration Techniques.

Factor correlations

	Factor 1	Factor 3	Factor 2
Factor 1	1.0000000	0.7073206	0.4912163
Factor 3	0.7073206	1.0000000	0.4963664
Factor 2	0.4912163	0.4963664	1.0000000

Proportion of variance explained

	Factor 1	Factor 3	Factor 2
SS loadings	2.3639023	2.0211113	1.6344519
Proportion Var	0.1969919	0.1684259	0.1362043
Cumulative Var	0.1969919	0.3654178	0.5016221
Proportion Explained	0.3927097	0.3357626	0.2715277
Cumulative Proportion	0.3927097	0.7284723	1.0000000

Reliability analysis

Cronbach's alpha for each factor:

- Factor 1: 0.830458
- Factor 2: 0.7945582
- Factor 3: 0.7209829

Descriptive statistics of factor scores

	n	mean	sd	median	mad	min	max	range	skew	kurtosis	se
Factor 1	123	7.72	1.69	8.00	1.48	1.75	10.0	8.25	-1.21	1.88	0.15
Factor 2	123	6.97	1.64	7.25	1.11	2.00	10.0	8.00	-0.92	1.15	0.15
Factor 3	123	4.61	1.72	4.75	1.48	1.25	9.5	8.25	0.09	-0.54	0.16

Appendix 5

A5.1 The 6Rs method

Overview

The 6Rs is a structured method designed to help meditators recognise and skilfully work with distractions. This approach is central to the Digital Intervention for Psychedelic Preparation (DIPP), as it provides a systematic way to disengage from distractions while cultivating a relaxed and open awareness. Originally developed as part of the **Tranquil Wisdom Insight Meditation (TWIM)** system, the 6Rs method is rooted in early Buddhist teachings and was adapted at the Dhamma Sukha Meditation Centre as a contemporary guidance system for mindfulness training. The 6Rs cycle consists of six sequential steps that allow practitioners to navigate their meditation experience effectively without force or suppression. This process is particularly relevant for psychedelic preparation, where developing non-reactivity, equanimity, and attentional flexibility is essential for navigating altered states of consciousness.

Step-by-step breakdown of the 6Rs

- Recognise (Pali: *Janati* - जानाति): The first step is to recognise that the mind has wandered. This requires mindfulness (*sati)* - the ability to observe how attention moves from moment to moment. Distractions may arise in the form of thoughts, emotions, physical sensations, or external stimuli. Recognising them as distractions is the first step in working with them skilfully.
- Relevance to Psychedelic Preparation: Recognising shifts in attention is crucial for navigating the unpredictable nature of psychedelic experiences. Training in this skill helps participants notice and engage with arising phenomena without becoming overwhelmed or reactive.
- Release (Pali: *Vineyya* - विनेय्य): After recognising a distraction, the next step is to release it - allowing it to be without engaging further. This is done gently, without force, by letting go of any attachment to the distraction. The content of the thought, emotion, or sensation is not important; what matters is the ability to recognise its impermanent nature and avoid grasping onto it.
- Relevance to Psychedelic Preparation: Psychedelic experiences often bring up challenging or intrusive thoughts. Learning to release distractions without resistance can help participants navigate intense moments with greater ease.
- Relax (Pali: *Passambhayam* - पस्सम्भयं): Once a distraction is released, a subtle tension may still remain in the mind or body. The Relax step involves consciously softening any remaining tightness, both physically and mentally. This aligns with the Buddha’s instruction to “tranquilize” mental formations, allowing for a more effortless state of presence.
- Relevance to Psychedelic Preparation: Relaxation is key to reducing resistance and fear during a psychedelic journey. This step helps participants cultivate openness to whatever arises, preventing unnecessary struggle.
- Re-Smile (Pali: *Pasannen* - पसन्नेन): The Re-Smile step encourages meditators to cultivate an attitude of lightness and ease. By gently smiling with the mind (and sometimes physically), practitioners reinforce a sense of joy and curiosity rather than frustration. This step ensures that the process remains one of engagement rather than struggle.
- Relevance to Psychedelic Preparation: Maintaining a light-hearted, accepting approach is particularly helpful when encountering challenging or unfamiliar experiences. The act of smiling naturally promotes positive neurochemical changes, reinforcing resilience and well-being.
- Return (Pali: *Punarapi* - पुनरपि): After relaxing and re-smiling, the mind is gently returned to the object of meditation, whether it be the breath, a mantra, or the feeling of loving-kindness (*mettā*). This redirection is done effortlessly, without forcing focus.
- Relevance to Psychedelic Preparation: The ability to return to a stable anchor - such as the breath or the feeling of loving-kindness - helps participants navigate shifting states of consciousness during psychedelic experiences, providing a reliable point of reference.

- Repeat (Pali: *Bahulikaritva* - बहुलीकरित्वा): The final step is to repeat the process as needed. Each time a distraction arises, the 6Rs cycle begins again, reinforcing the habit of mindful awareness, gentle letting go, and returning to presence.

Relevance to Psychedelic Preparation: Repeating the 6Rs fosters habitual equanimity, allowing participants to develop the capacity to meet any experience - whether pleasurable or challenging - with stability and ease.

Application of the 6Rs in the DIPP program
The 6Rs method is progressively introduced and refined throughout the 21-day meditation training in DIPP. It serves as the primary technique for managing distractions and sustaining a relaxed, open awareness, which are crucial skills for both meditation and psychedelic experiences. Early in the program (Days 1-7): Participants are introduced to the basic mechanics of the 6Rs and practice them in relation to cultivating loving-kindness for themselves. Middle phase (Days 8-14): They develop a more fluid and effortless application of the method, using it to sustain positive emotions without clinging. Later stages (Days 15-21): The 6Rs become an automatic process, integrated seamlessly into meditation practice, allowing awareness to rest in stillness without forced redirection. By the end of the training, participants are deeply familiar with the 6Rs process, making it a valuable tool for navigating their upcoming psychedelic session with greater equanimity and ease. For additional details on the 6Rs method, see Dhamma Sukha Meditation Center.

A5.2 The 'Spectrum of Awareness'
Overview
The Spectrum of Awareness is a structured model for understanding how awareness deepens and expands in meditation. It provides a practical framework for recognising different levels of experience, moving from sensory and cognitive content to more subtle states of awareness and eventually to open, formless awareness. This framework is a key component of the Digital Intervention for Psychedelic Preparation (DIPP) and supports participants in developing stability, insight, and equanimity as they navigate shifting states of consciousness.

Buddhist teachings emphasise direct awareness of experience rather than theoretical explanations. In this approach, as awareness deepens, we learn to observe experience with increasing clarity and spaciousness, leading to greater freedom from reactivity and suffering. The Spectrum of Awareness helps structure this deepening process.

Phases of Awareness in the Spectrum
Each phase represents a progressively more refined level of awareness, where prior phases remain present but become part of a broader experience.

- Content (objects of awareness)
    - The most concrete level of awareness focuses on objects of experience - thoughts, emotions, sensations, and perceptions.
    - This is how awareness functions in daily life: distinguishing between a tree, a sound, a memory, or an emotion.
    - Objects with high emotional charge (e.g., fear, desire) tend to dominate attention.
    - Relevance to Psychedelic Preparation: During altered states, objects of awareness can become intensified. Training in recognising content helps participants engage with these experiences without becoming overwhelmed.
- Processes (how awareness operates)
    - As awareness relaxes and expands, we begin to see the mental processes that generate experience rather than just their content.
    - Instead of focusing on a thought, we recognise the process of thinking; instead of fixating on an emotion, we see the process of feeling.
    - This shift allows us to step back and observe without becoming entangled.
    - Relevance to Psychedelic Preparation: Noticing mental processes rather than being consumed by them reduces reactivity to intense psychedelic phenomena.
- Qualities of Awareness (the felt experience of awareness)

  - Deeper awareness reveals the qualities that shape our perception - e.g., calmness, agitation, spaciousness, clarity.
  - Awareness is no longer tied to specific objects or processes but feels into the underlying tone of experience.
  - Recognising and adjusting these qualities cultivates balance and ease.
  - Relevance to Psychedelic Preparation: Developing sensitivity to awareness qualities helps participants self-regulate emotions and responses during altered states.
- Field of Awareness (awareness as a whole)
  - At this stage, attention shifts to awareness itself rather than its contents or processes.
  - Awareness is perceived as a spacious, all-encompassing field that includes everything.
  - Instead of fixating on individual thoughts or emotions, we sense the entire field of experience.
  - Relevance to Psychedelic Preparation: This perspective supports non-dual awareness and fosters a sense of unity and interconnectedness, which are common in psychedelic states.
- Nothingness (open, formless awareness)
  - In its most refined form, awareness becomes so expansive that it begins to dissolve into open nothingness.
  - This phase manifests as gaps in perception - sometimes misinterpreted as micro-sleep but actually moments of cessation.
  - In Buddhist teachings, this is known as *nirodha* (cessation) and is linked to profound states of insight and liberation.
  - Relevance to Psychedelic Preparation: Encountering empty, formless awareness can be disorienting in altered states. Understanding this as a natural deepening of awareness helps participants navigate experiences of ego dissolution with equanimity.

The Spectrum as a non-linear model

While the Spectrum is often presented sequentially - from content to formless awareness - it is not a rigid, stepwise progression. Rather, these levels co-arise and influence each other.

- Awareness may shift dynamically between levels, especially in meditation or altered states.
- Some individuals may naturally experience higher levels first and later refine their ability to work with more concrete levels.
- Others may primarily engage with content and processes, gradually expanding into subtler levels over time.
- Rather than treating the Spectrum as a hierarchical progression, it is best understood as a fluid, interactive system where all levels can be accessed and explored.

Practical Applications in Meditation and Psychedelic Preparation

The Spectrum of Awareness is integrated into DIPP training through guided meditation and reflective exercises. The practice involves:

- Recognising where one’s awareness is currently anchored (content, process, qualities, field, or nothingness).
- Gently shifting awareness along the Spectrum without force or expectation.
- Using relaxation and expansion to facilitate movement across levels.
- Developing familiarity with these shifts to navigate psychedelic experiences with greater stability and insight.

By incorporating the 6Rs method alongside the Spectrum of Awareness, participants learn to recognise distractions, release tension, and expand awareness in a structured, accessible way.

A5.3 Informed consent form

CONSENT FORM FOR PARTICIPANTS INVOLVED IN RESEARCH STUDIES USING PSILOCYBIN

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Title of Study: Mechanisms of Tryptamines on Mental Health and Wellbeing (DIPP Study)

Department:
Clinical, Educational and Health Psychology, Psychology and Language Sciences Name and

Contact Details of the Researcher(s):
Ms. Rosalind McAlpine (Email: rosalind.mcalpine.18@ucl.ac.uk)
Ms Joanna Kuc (Email: joanna.kuc.22@ucl.ac.uk)
Miss Krisztina Jedlovszky (email: krisztina.jedlovszky.21@ucl.ac.uk)
Ms Magdalena Jaglinska (Email: magdalena.jaglinska.22@ucl.ac.uk)

Name and Contact Details of the Principal Researcher:
Dr Jeremy Skipper (jeremy.skipper@ucl.ac.uk).

Name and Contact Details of the UCL Data Protection Officer:
Alex Potts. Email a.potts@ucl.ac.uk

If you are concerned about how your personal data is being processed, or if you would like to contact someone about your rights, you can contact UCL at data-protection@ucl.ac.uk. This study has been approved by the UCL Research Ethics Committee: Project ID number: 19113/003.

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Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

I understand that by marking each box below, I am giving my consent to participate in that specific aspect of the study. If a box remains unmarked, it indicates that I do not give my consent to participate in that portion of the study. Please be aware that not consenting to certain elements may mean I am not eligible to participate in the study.

Statement	Tick
I have read and understood the Information Sheet for the above study, had the opportunity to consider the information, ask questions, and have received satisfactory answers.	
I understand that I can withdraw my data up to the end of the dosing visit.	
I consent to participate in the study under the conditions explained regarding data protection and use.	
I understand that all personal information will remain confidential to the extent explained, with some potential exceptions for legal and safety reasons.	
I understand that individuals from the University, sponsors, and funders might review my information for monitoring and audit purposes.	

I understand my participation is voluntary and I can withdraw at any time without giving a reason, with the option to have my data deleted.	
I am aware of the potential risks and the available support if I become distressed during the research.	
I understand the direct and indirect benefits of participating.	
I understand that data from this study will not be shared with commercial organisations and is the responsibility of the research team.	
I consent to have my interview audio recorded under the specified conditions.	
I understand the inclusion criteria as detailed and explained by the researcher.	
I have disclosed any potential reasons, including health and coercion concerns, that might prevent my participation in the study.	
I confirm that I am not pregnant, breastfeeding, or planning to become pregnant during the study.	
I agree to abstain from illicit drug use from the start of the preparation course to one week post dosing.	
I voluntarily agree to participate in this study.	

By ticking each box, you are confirming your willingness to participate in each integral component of the study. Please review each participation aspect carefully and indicate your agreement by ticking the corresponding box:

Participation Aspect	**Tick**
Participation in an individual screening interview	
Participant in fMRI-movie scans during Visit 2 and Visit 4	
Completion of the 21-day online preparation course	
Attendance and participation in the psilocybin dosing session at UCL	
Undergoing EEG recordings to capture brain activity	
Undergoing ECG recordings to capture heart activity	
Completing psychological questionnaires, which may involve discussing sensitive topics	
Completing cognitive tasks on a computer	
Contributing to the remote sampling of inner experience via regular voice recordings	

If you would like your contact details to be retained so that you can be contacted in the future by UCL researchers who would like to invite you to participate in follow up studies to this project, or in future studies of a similar nature, please tick the appropriate box below:

Yes, I would be happy to be contacted in this way	
No, I would not like to be contacted	

Name of participant	Date	Signature
Name of witness	Date	Signature
Researcher	Date	Signature

A5.4 Study timeline and outcome measures (SPIRIT table)

	STUDY PERIOD							
	Online		On-site				Online	
TIMEPOINT	$-t_1$	t_1	t_2	t_3	t_4	t_5	t_6	t_7
ENROLMENT:								
Online screening	X							
Telephone screening	X							
Clinical screening	X							
Informed consent	X							
Allocation	X							
INTERVENTIONS:								
Meditation-based DIPP								
Music-based DIPP								
Psilocybin (25 mg)				X				
PRIMARY OUTCOMES:								
Recruitment efficiency	X							
Study retention								
DIPP intervention adherence								

A5.4 (continued)							
SECONDARY OUTCOMES:							
Subjective Feasibility of Intervention Scale (SFIS)		X					
Theoretical Framework of Acceptability Scale (TFA)		X					
System Usability Scale (SUS)		X					
Mobile Application Rating Scale (MARS)		X					
Psychedelic Preparedness Scale (PPS)	X	X					
Altered States Consciousness Questionnaire (11D-ASC)			X				
Challenging Experience Questionnaire (CEQ)			X				
Short Warwick-Edinburgh Mental Wellbeing Scale (SWEMWBS)	X	X	X	X	X	X	X
OTHER PRE-SPECIFIED OUTCOMES:							
DIPP-based mood and meta-emotional awareness tracking	X	X					
DIPP-Bot inner speech metrics	X	X					
Heart rate variability (ECG)	X	X	X	X			
Neural activity (EEG)			X				
Neural activity (movie-fMRI)		X		X			
Computerised Restless 3-Arm Bandit Task	X	X		X			
Computerised Body Maps of Emotion Tool (emBODY)	X	X		X			
Computerised Perceptual Reality Monitoring Task	X			X			
Cognitive and Affective Mindfulness Scale - Revised (CAMS-R)	X	X	X	X	X	X	X
Sussex-Oxford Compassion for the Self Scale (SOCS-S)	X	X	X	X	X	X	X
Open and Engaged State Questionnaire (OESQ)	X	X	X	X	X	X	X
Patient Health Questionnaire 9 (PHQ-9)	X	X	X	X	X	X	X
Generalised Anxiety Disorder 7 (GAD-7)	X	X	X	X	X	X	X
Ruminative Response Scale - Short form (RRS-SF)	X	X	X	X	X	X	X

A5.4 (continued)							
Varieties of Inner Speech Questionnaire - Revised (VISQ-R)	X	X	X	X	X	X	X
Nevada Inner Experience Questionnaire (NIEQ)	X	X	X	X	X	X	X
Perseverative Thinking Questionnaire (PTQ)	X	X	X	X	X	X	X
Brief Multidimensional Assessment of Interoceptive Awareness, version 2 (Brief MAIA-2)	X	X	X	X	X	X	X
Černis Felt Sense of Anomaly Scale - Short form (ČEFSA)	X	X	X	X	X	X	X
9-item Material Values Scale (MVS)	X			X	X	X	X
Emotional Breakthrough Inventory (EBI)			X				
Positive and Negative Affect Schedule (PANAS)			X				
Drug Effects Questionnaire (DEQ)			X				
6-item Dissociative Symptom Scale (CADSS-6)			X				

A5.5 Primary, secondary and other pre-specified outcomes

OUTCOME MEASURE	DESCRIPTION	TIMEFRAME
PRIMARY		
Recruitment efficiency	Weekly rate of participant enrolment and randomisation. Success is defined as ≥1 participant per week (average) until target sample (N=40) achieved.	$-t_1$ (until end of recruitment period)
Study retention	Percentage of randomised participants completing the 2-week post-dose follow-up assessment. Success is defined as ≥70% completion rate.	t_1,t_4
DIPP intervention adherence	Task completion rates across three daily tasks (meditation/music practice, mood rating, journal entry) and two weekly tasks. Success is defined as ≥70% of participants achieving an average completion rate of ≥70% across all required tasks.	t_1,t_2
SECONDARY		
DIPP platform feasibility as measured by the Subjective Feasibility of Intervention Scale (SFIS)	The Subjective Feasibility of Intervention Scale (SFIS) measures perceived practicality, resource demands and integration into existing workflows of the DIPP protocol. Possible scores range from 9 to 45, with higher scores indicating better feasibility.	t_2
DIPP platform acceptability as measured by the Theoretical Framework of Acceptability Scale (TFA) [810]	The Theoretical Framework of Acceptability Scale (TFA) measures perceived appropriateness and satisfaction with the DIPP platform. Possible scores range from 7 to 35, with higher scores indicating better acceptability.	t_2
DIPP platform usability and engagement as measured by the System Usability Scale (SUS) [811] and Mobile Application Rating Scale (MARS) [812]	The System Usability Scale (SUS) and Mobile Application Rating Scale (MARS; functionality and aesthetics subscales only) measure platform user-friendliness and app quality respectively. Combined scores range from 16 to 80, with higher scores indicating a better usability/engagement.	t_2
Psychedelic Preparedness as measured using the Psychedelic Preparedness Scale (PPS) [155]	Between-group differences in psychedelic preparedness will be assessed using the Psychedelic Preparedness Scale (PPS), a validated 20-item self-report measure. The PPS evaluates four domains: knowledge-expectation, psychophysical-readiness, intention-preparation, and support-planning. Individual total scores (range: 20-140) and mean factor scores (range: 1-7) will be calculated, with higher scores indicating greater preparedness.	t_1,t_2
Positive quality of acute psychedelic experience as measured by the OBN dimension from the Altered States Consciousness Questionnaire (11D-ASC) [358]	The Altered States Consciousness Questionnaire (11D-ASC) measures the subjective effects of the psychedelic experience. To assess the positive quality of the experience, this study will focus on the Oceanic Boundlessness (OBN) factor to assess participants' subjective experience of unity, boundary dissolution, and interconnectedness during the psilocybin session. Possible standardised scores range from 0 to 1, with higher scores indicating a more positive quality of acute psychedelic experience.	t_3

A5.5 (continued)		
Challenging psychological experience during the psychedelic experience as measured by four subscales from the Challenging Experience Questionnaire (CEQ) [354]	The Challenging Experience Questionnaire (CEQ) measures various aspects of challenge experienced during a psychedelic experience. To assess challenging psychological experiences during the psilocybin session, this study will focus on the combined mean score on four CEQ subscales (Fear, Insanity, Isolation, and Paranoia). Possible scores range from 0 to 5, with higher scores indicating a more challenging psychedelic experience.	t_3
Mental wellbeing as measured by the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) [813]	The Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) measures psychological functioning and emotional wellbeing. Possible scores range from 14 to 70, with higher scores indicating better wellbeing.	t_1,t_2,t_3,t_4
OTHER PRE-SPECIFIED		
DIPP-based mood and meta-emotional awareness tracking	Participants will complete a daily mood check-in after each session during the 21-day DIPP, which includes (1) five questions on state mindfulness, (2) two on decentering, (3) identifying their emotion on a valence-arousal grid, and (4) rating the accuracy of their emotion identification (meta-emotional awareness).	t_1,t_2
DIPPBot inner speech metrics	The DIPP-Bot mobile app captures daily voice note samples to assess changes in spontaneous inner speech patterns. The analysis will encompass linguistic, syntactic, and acoustic domains, leveraging advanced Natural Language Processing (NLP) techniques and sound feature analysis to evaluate measurable changes in the content, structure, and vocal characteristics of participants' inner dialogue over time.	t_1,t_2
Physiological activity as measured by Electrocardiography (ECG)	Electrocardiography (ECG) measures the electrical activity of the heart. A three-lead eyes-closed ECG will be used to record cardiac activity before, during, and after the intervention. During the peak effects of psilocybin, ECG will be recorded for 7 minutes at 90 and 150 minutes after ingestion of the drug. The analysis will evaluate autonomic nervous system function based on the Heart Rate Variability (HRV) metrics.	t_1,t_2,t_3,t_4
Neural activity as measured by Electroencephalography (EEG)	Electroencephalography (EEG) measures brain electrical activity during the psychedelic experience. Eyes-closed EEG will be recorded at baseline and at 90 and 150 minutes after ingestion of psilocybin. The analysis will evaluate spectral power across frequency bands, neural complexity, connectivity, and traveling wave dynamics. Additionally, Heartbeat-Evoked Potentials (HEP) will be analysed to assess changes in cortical processing of cardiac interoceptive signals.	t_3
Neural activity (movie-fMRI)	Functional Magnetic Resonance Imaging (fMRI) data will be collected while participants watch full length feature movies at baseline and 2-week follow-up. The analysis will assess lasting changes in brain networks following psilocybin administration, and whether these changes are associated with well-being outcomes.	t_2,t_4

A5.5 (continued)		
Computerised Restless 3-arm Bandit Task [adapted from Ramaswamy et al., *(in prep)*]	The restless 3-arm bandit task asks participants to make decisions selecting different boxes (arms) that yield rewards and punishments with changing probabilities. The task provides a range of computational measures that capture clinically relevant aspects of reward sensitivity and reward seeking. Possible measures include reward learning rate, exploration rate, reward seeking and loss aversion.	t_1,t_2,t_4
Computerised Body Maps of emotions Task Computerised Body Maps of Emotions Tool (emBODY) [814]	The emBODY tool is a computerised task used for mapping emotion-dependent sensations in distinct body regions. This study uses an online version adapted from the original task. Analysis includes changes in strength of bodily sensations linked to specific emotions and emotional granularity, measured as the spatial differentiation of emotional experiences.	t1,t2,t4
Computerised perceptual reality monitoring task [adapted from [815]]	The perceptual reality monitoring task consists of participants imagining and making judgements about a set of Gabor gratings. The task yields psychophysical measures about the sensitivity of perception and mental imagery, as well as confidence in perceptual judgements.	t_1,t_2,t_4
Mindfulness capacity as measured by the Cognitive and Affective Mindfulness Scale Revised (CAMS-R) [544]	The Cognitive and Affective Mindfulness Scale Revised (CAMS-R) measures mindfulness capacity across attention regulation, emotional tolerance, and present-moment awareness. Possible scores range from 12 to 48, with higher scores indicating a better outcome.	t_1,t_2,t_3,t_4,t_5,t_6,t_7
Self-compassion as measured by the Sussex-Oxford Compassion for the Self Scale (SOCS-S) [816]	The Sussex-Oxford Compassion for the Self Scale (SOCS-S) measures self-compassion across recognizing suffering, understanding universality, feeling compassion, tolerating uncomfortable emotions, and motivation to alleviate suffering. Possible scores range from 20 to 100, with higher scores indicating a better outcome.	t_1,t_2,t_3,t_4,t_5,t_6,t_7
Psychological flexibility as measured by the Open and Engaged State Questionnaire (OESQ) [817]	The Open and Engaged State Questionnaire (OESQ) measures openness and engagement with emotions and life circumstances. Possible scores range from 0 to 40, with higher scores indicating a better outcome.	t_1,t_2,t_3,t_4,t_5,t_6,t_7
Depression severity as measured by the Patient Health Questionnaire (PHQ-9) [818]	The Patient Health Questionnaire (PHQ-9) measures depressive symptoms, including mood, sleep, energy levels, appetite, and suicidal thoughts. Possible scores range from 0 to 27, with higher scores indicating a worse outcome.	t_1,t_2,t_3,t_4,t_5,t_6,t_7
Anxiety severity as measured by the Generalised Anxiety Disorder 7 (GAD-7) [819]	The Generalised Anxiety Disorder (GAD-7) measures anxiety symptoms, including worry, restlessness, irritability, and physical symptoms. Possible scores range from 0 to 21, with higher scores indicating a worse outcome.	t_1,t_2,t_3,t_4,t_5,t_6,t_7
Rumination as measured by the Ruminative Response Scale (RRS-SF) [820]	The Short Form Ruminative Response Scale (RRS-SF10) measures the tendency to have persistent negative thinking patterns during periods of low mood. Possible scores range from 10 to 40, with higher scores indicating a higher tendency to ruminate.	t_1,t_2,t_3,t_4,t_5,t_6,t_7

A5.5 (continued)		
Varieties of Inner Speech Questionnaire - Revised (VISQ-R) [821]	The Varieties of Inner Speech Questionnaire - Revised (VISQ-R) measures different forms of inner speech, including dialogical inner speech, condensed inner speech, other voices in inner speech, evaluative/critical inner speech, and positive/regulatory inner speech. Possible scores in each dimension range from 1 to 7, with higher scores indicating a greater frequency or prominence of that type of inner speech.	$t_1,t_2,t_3,t_4,t_5,t_6,t_7$
Inner experience types as measured by the Nevada Inner Experience Questionnaire (NIEQ) [822]	The Nevada Inner Experience Questionnaire (NIEQ) measures various types of inner experiences, including inner speech, visual imagery, emotional experience, sensory awareness, and non-symbolic thought. Possible scores in each dimension range from 5 to 50, with higher scores indicating a greater frequency or prominence of that type of inner experience.	$t_1,t_2,t_3,t_4,t_5,t_6,t_7$
Perseverative thinking as measured by the Perseverative Thinking Questionnaire (PTQ) [823]	The Perseverative Thinking Questionnaire (PTQ) measures repetitive negative thinking as a response to negative experiences. Possible scores range from 0 to 60, with higher scores indicating a higher tendency for repetitive negative thinking.	$t_1,t_2,t_3,t_4,t_5,t_6,t_7$
Interoceptive awareness as measured by the Brief Multidimensional Assessment of Interoceptive Awareness, version 2 (Brief MAIA-2) [824]	The Multidimensional Assessment of Interoceptive Awareness (MAIA-II) is a 37-item self-report questionnaire measuring 8 factors of interoceptive awareness: Noticing, Not-Distracting, Not-Worrying, Attention Regulation, Emotional Awareness, Self-Regulation, Body Listening and Trust. Statements are rated using a 5 point Likert scale, with scores ranging from 0 "Never" to 5 "Always", with some items using reverse scoring. The outcome of each subscale is obtained by taking the average score of the items in each subscale, with higher scores indicating a better outcome.	$t_1,t_2,t_3,t_4,t_5,t_6,t_7$
Felt Sense of Anomaly as measured by the Short Form Černis Felt Sense of Anomaly Scale (ČEFSA) [825]	The Short Form Černis Felt Sense of Anomaly Scale (ČEFSA) measures felt sense of anomaly, as a type of common dissociative experience. Possible scores range from 0 to 56, with higher scores indicating higher severity of dissociative experience. The severity categories are Average (0-28), Elevated (29-38), Moderately severe (39-49) and Severe (49-56).	$t_1,t_2,t_3,t_4,t_5,t_6,t_7$
Materialism as measured by the 9-item Material Values Scale (MVS) [826]	The Material Values Scale (MVS) measures the level of importance that one ascribes to material goods. Scores range from 9 to 45 with higher scores indicating material values having a higher importance.	t_1,t_4,t_5,t_6,t_7
Emotional breakthroughs as measured by the Emotional Breakthrough Inventory (EBI) [68]	The Emotional Breakthrough Inventory (EBI) measures the extent and quality of emotional breakthroughs experienced during a psychedelic session. Possible scores range from 0 to 100, with higher scores indicating a better outcome.	t_3
Affect as measured by the Positive and Negative Affect Schedule (PANAS) [827]	The Positive and Negative Affect Schedule (PANAS) measures self-reported affect in two dimensions: positive and negative affect. In each dimension, possible scores range between 10 and 50, higher scores indicating higher positive/negative affect.	t_3

A5.5 (continued)		
Sobriety as measured by the Drug Effects Questionnaire (DEQ) [659]	The Drug Effects Questionnaire (DEQ) measures acute subjective responses to substances through 5 constructs (FEEL, HIGH, DISLIKE, LIKE, and MORE). Each construct is measured on a 100mm visual analogue scale. Participants are deemed as sober and ready to discharge if they score under 50 in the FEEL, HIGH and DISLIKE items.	t_3
Sobriety as measured by the 6-item Dissociative Symptom Scale (CADSS-6) [660]	The 6-item Dissociative Symptom Scale (CADSS-6) assesses dissociation as an emergent adverse event during drug dosing. Potential scores range between 0 and 20, with higher scores indicating more severe dissociative symptoms. This questionnaire is administered before dosing (as baseline) and after dosing (to provide a sobriety measure). Participants are deemed as sober and ready to discharge if their post-dosing score is below 4 and the score increase from baseline is less than 3.	t_3

Appendix 6

A6.1 5PS items

1. I experienced God
2. I experienced the source of all things
3. I left my body
4. I was floating through space
5. My ego was gone
6. I had no self
7. I felt a healing process occurring in my body
8. I experienced feelings that were not my own
9. I re-lived a memory or memories
10. I felt a movement or release of energy
11. I experienced 'pure' feelings or emotion
12. I experienced awareness and nothing else
13. It was as though I was dead
14. I experienced non-duality
15. It was as though I was in outer space
16. It was as though the world had ended
17. I experienced an empty void or nothingness
18. I experienced everything and nothing at the same time
19. It was as though my mind was broken
20. What I experienced felt pure
21. I had very positive feelings or emotions
22. I had very negative feelings or emotions
23. I lost my usual awareness of who, and where, I was
24. I no longer had the ability to think
25. I lost all awareness of my body
26. I was aware of sounds in my immediate environment
27. I no longer experienced 'self' and 'other' as separate things
28. It was as though everything and nothing was 'me'
29. I had no sense of time
30. I saw people or recognizable objects
31. I saw geometric shapes
32. I saw colour or light that had no particular pattern or shape
33. There was no sense of space in which I could locate myself or anything else
34. I was inside a space which had a certain shape (e.g., inside a tunnel)
35. I felt a sense of something (e.g., energy) moving in a particular direction or shape
36. I sensed a presence which seemed to have its own mind
37. I resisted the experience
38. I felt sexual or orgasmic

A6.2 ASCQ items

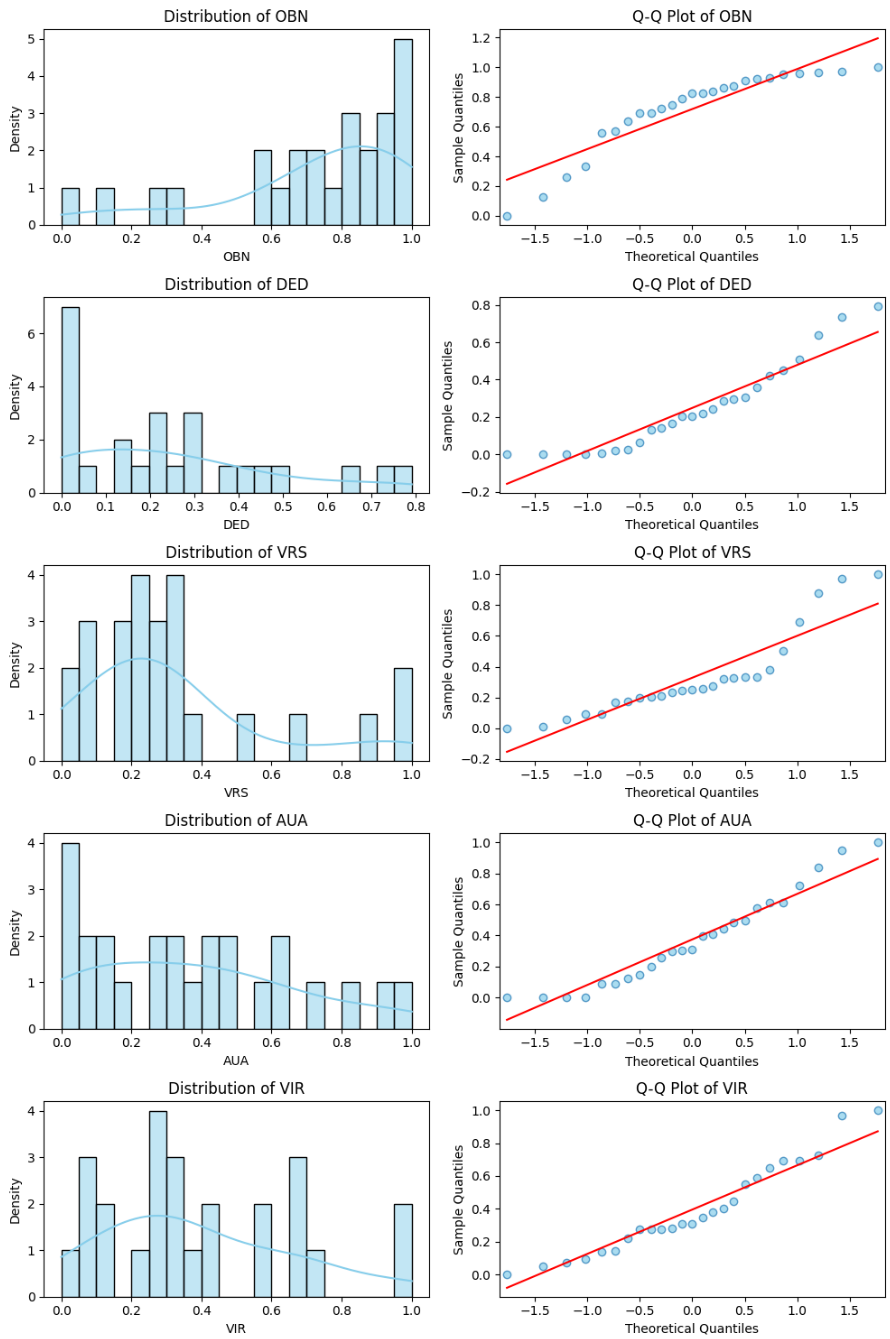
1. "My thoughts did not feel like my own"
2. "I could not tell whether I was moving or whether the world was moving"
3. "I felt a sense of unity with everything"
4. "I could not tell where I was with respect to my environment"
5. "I could not tell where bodily sensations occurred on my body"

6. "I could not tell where was up and down"
7. "My sensations did not feel connected to each other"
8. "I lost sense of my personal identity"
9. "I could not tell the difference between myself and the external world"
10. "I could not tell whether what I saw was near or far"
11. "I could not remember who I was"
12. "I felt as if I was dying"
13. "I felt as if I did not have a body anymore"
14. "I temporarily lost consciousness"
15. "I felt like I was not in control of my thoughts"
16. "I could not tell whether bodily sensations occurred on the right side or on the left side of my body"
17. "I felt as if my body was no longer my own"
18. "I felt lost in a void"
19. "I felt like I was not in control of my body"
20. "I could not feel my body"
21. "I felt as if I was no longer located anywhere"
22. "I felt as if what was happening was not happening to me"
23. "I could not think about what was happening to me"
24. "My perception had no center"
25. "My sensations did not feel like my own"

A6.3 Statistical assumption tests for scale comparisons

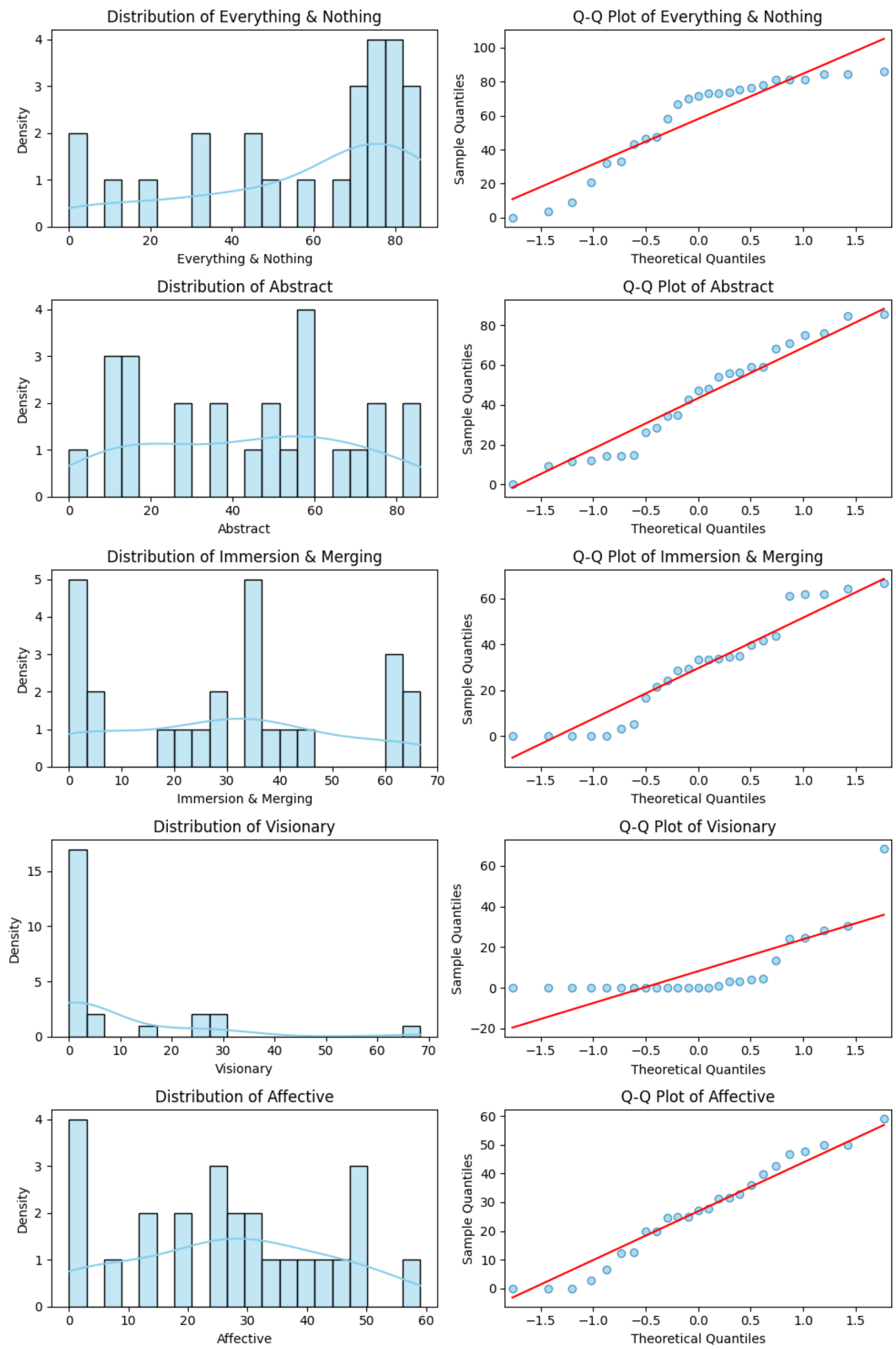
5D-ASC

Assumption tests showed normality violations in OBN ($W = 0.842$, $p = .001$), DED ($W = 0.896$, $p = .015$), and VRS ($W = 0.829$, $p < .001$), while AUA ($W = 0.938$, $p = .135$) and VIR ($W = 0.938$, $p = .132$) met normality assumptions.



5PS

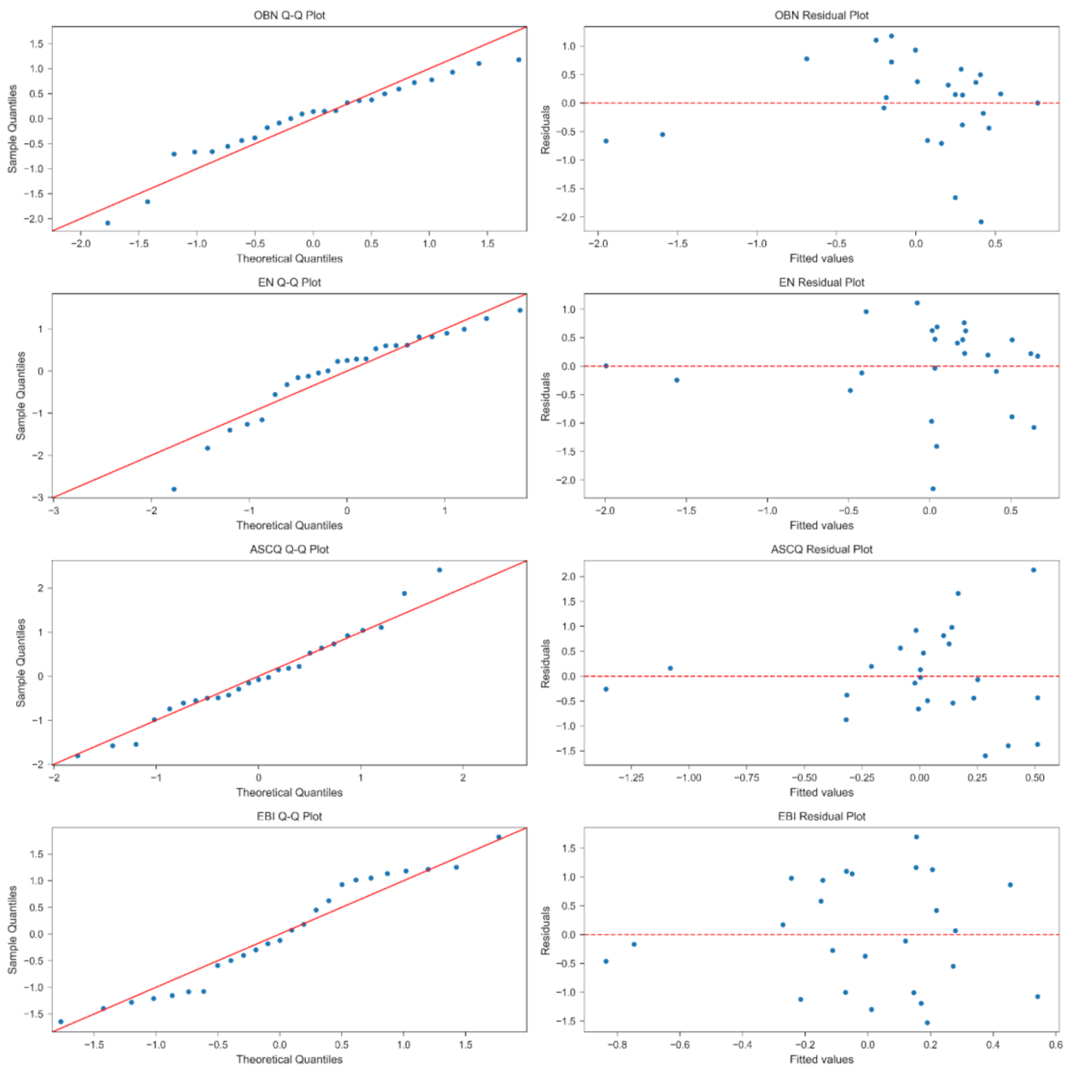
Severe normality violation in Visionary (W = 0.588, $p < .001$), with moderate violations in Everything & Nothing (W = 0.848, p = .002) and Immersion & Merging (W = 0.910, p = .030). Abstract (W = 0.946, p = .207) and Affective (W = 0.958, p = .371) met normality assumptions.


Distribution of Everything & Nothing
Density
Everything & Nothing
Q-Q Plot of Everything & Nothing
Sample Quantiles
Theoretical Quantiles
Distribution of Abstract
Density
Abstract
Q-Q Plot of Abstract
Sample Quantiles
Theoretical Quantiles
Distribution of Immersion & Merging
Density
Immersion & Merging
Q-Q Plot of Immersion & Merging
Sample Quantiles
Theoretical Quantiles
Distribution of Visionary
Density
Visionary
Q-Q Plot of Visionary
Sample Quantiles
Theoretical Quantiles
Distribution of Affective
Density
Affective
Q-Q Plot of Affective
Sample Quantiles
Theoretical Quantiles

A6.4 Regression diagnostics and detailed statistical results for pre-psychedelic predictors of acute experiences

Assumptions

Regression assumptions were tested for all models. Multicollinearity was not a concern, with all VIF values < 1.5. Normality of residuals (Shapiro-Wilk test) showed minor deviations for OBN (p = 0.049) and EN (p = 0.014) models, while ASCQ and EBI models met normality assumptions (p > 0.20). Homoscedasticity (Levene's test) was violated only in the EN model (p = 0.032). Residual plots showed no systematic nonlinear patterns. While some violations were observed in the EN model, regression is generally robust to such moderate violations with our sample size. Q-Q plots and residual plots are shown below.



A6.5 Hierarchical regression results for the PPS × BML interaction

Outcome	ΔR^2	ΔR^2 (%)	F Change	p value
OBN	0.136	13.6%	4.647	0.043*
EN	0.330	33.0%	11.288	0.003*
ASCQ	0.166	16.6%	4.277	0.051
EBI	0.020	2.0%	0.457	0.506

Note. This table shows the unique contribution of the PPS × BML interaction term when added to models containing only main effects. ΔR^2 = absolute increase in explained variance when adding the interaction term; ΔR^2 (%) = percentage of additional variance explained by the interaction; F Change = F-statistic testing the significance of the R^2 change; p value = significance level of the F Change. OBN = Oceanic Boundlessness; EN = Everything/Nothing; ASCQ = Altered Self Consciousness Scale; EBI = Emotional Breakthrough Index. Asterisks indicate statistical significance at $p < .05$.

A6.6 Electrode assignments by lobe

Frontal:
Fp1, Fp2, AF7, AF3, AF4, AF8, F9, F7, F5, F3, F1, Fz, F2, F4, F6, F8, F10, FC5, FC3, FC1, FCz, FC2, FC4, FC6

Central:
C5, C3, C1, C2, C4, C6

Parietal:
CP5, CP3, CP1, CP2, CP4, CP6, P9, P7, P5, P3, P1, Pz, P2, P4, P6, P8, P10

Temporal:
FT7, FT8, T9, T7, T8, T10, TP7, TP8

Occipital:
PO7, PO5, PO3, POz, PO4, PO6, PO8, O1, O2

A6.7 Demographic and background characteristics of participants (N = 29)

Characteristic		**N**	**%**
Gender	Female	13	44.83
	Male	16	55.17
Ethnicity	White / Caucasian	25	86.21
	Asian / Pacific Islander	1	3.45
	Hispanic	3	10.35
Nationality	Canadian	3	10.35
	American	23	79.31
	Icelandic	1	3.45
	Australian	1	3.45
	Mexican	1	3.45
Education	Master's Degree	6	20.69
	Bachelor's Degree	17	58.62
	Trade School	2	6.90
	Ph.D. or higher	2	6.90
	Prefer not to say	1	3.45
	High School	1	3.45
Religion	No	27	93.10
	Yes	1	3.45
	Not sure	1	3.45
		M (SD)	**Range**
Age		48.52 (10.44)	34-75
Lifetime Substance Use	Psilocybin	37.76 (37.44)	5–150
	LSD	34.66 (61.46)	0–300
	2C-X	1.00 (1.60)	0–6
	N,N-DMT	11.10 (23.02)	0–100
	Ayahuasca	16.14 (40.75)	0–200
	Mescaline	2.86 (5.06)	0–20
	Bufotenine or 5-MeO-DMT	39.03 (72.91)	1–300
	NBOMe	0.03 (0.19)	0–1
	MDMA	26.90 (34.50)	0–125
	Iboga / ibogaine	0.52 (1.18)	0–5
	Salvia divinorum	0.76 (1.57)	0–6
	Ketamine or PCP	8.66 (20.48)	0–100
	Datura or scopolamine	0.00 (0.00)	0–0

A6.8 Outcome descriptives for key study variables

Measure	Mean	SD	Range	95% CI
Psychedelic Preparedness (PPS)				
PPS total	124.52	10.60	103-140	[120.14, 128.90]
Knowledge-Expectation (KE)	6.7	0.42	5.6-7.0	[6.53, 6.88]
Intention-Preparation (IP)	5.58	0.94	3.5-7.0	[5.19, 5.97]
Psychophysical-Readiness (PR)	6.49	0.52	5.17-7.0	[6.27, 6.70]
Support-Planning (SP)	5.95	0.86	4.4-7.0	[5.60, 6.31]
Baseline Mindfulness Language (BML)				
BML score	4.41	1.11	2.59-7.20	[3.95, 4.87]
Altered State of Consciousness (5D-ASC)				
Oceanic Boundlessness (OBN)	0.72	0.27	0.0-1.0	[0.61, 0.83]
Dread of Ego Dissolution (DED)	0.25	0.23	0.0-0.8	[0.15, 0.35]
Visual Restructuralisation (VRS)	0.33	0.28	0.0-1.0	[0.22, 0.44]
Auditory Alterations (AUA)	0.38	0.30	0.0-1.0	[0.26, 0.50]
Vigilance Reduction (VIR)	0.40	0.28	0.0-1.0	[0.29, 0.51]
5-MeO-DMT Phenomenology Scale (5PS)				
Everything & Nothing	58.01	27.20	0.0–86.1	[47.35, 68.67]
Abstract	43.31	25.89	0.0–85.7	[33.16, 53.46]
Immersion & Merging	29.57	22.45	0.0–66.7	[20.77, 38.37]
Visionary	8.20	15.99	0.0–68.3	[1.93, 14.47]
Affective	26.84	17.30	0.0–59.0	[20.06, 33.62]
Emotional Breakthrough Inventory (EBI)				
EBI total	252.00	188.13	0-600	[178.25, 325.76]
Altered Self-Consciousness Questionnaire (ASCQ)	38.05	23.49	0-99	[28.35, 47.75]

A6.9 Regional spectral power changes following 5-MeO-DMT administration

Frequency Band	Region	Rest M(SD)	5-MeO-DMT M(SD)	t(18)	p_{FDR}	Cohen's d
Slow (0.5-1.5 Hz)	central	1.14(0.63)	4.61(3.44)	4.32	.004	1.37
	frontal	3.03(1.58)	12.68(9.49)	4.56	.004	1.38
	occipital	2.27(1.04)	7.55(5.40)	4.16	.004	1.32
	parietal	1.89(0.69)	5.83(3.16)	5.72	.001	1.68
	temporal	2.65(0.84)	12.46(10.11)	4.08	.004	1.33
Delta (1.5-4 Hz)	central	0.47(0.20)	0.87(0.60)	2.80	.044	0.88
	frontal	1.06(0.41)	1.86(1.13)	2.66	.044	0.91
	occipital	1.33(0.93)	1.54(0.84)	0.86	.447	0.22
	parietal	0.95(0.52)	1.29(0.85)	1.76	.151	0.47
	temporal	1.01(0.37)	2.13(2.06)	2.24	.074	0.74
Theta (4-8 Hz)	central	0.62(0.47)	1.01(1.46)	1.32	.245	0.35
	frontal	1.41(1.21)	1.62(1.62)	0.57	.618	0.15
	occipital	3.16(3.40)	2.33(2.07)	-1.38	.230	-0.29
	parietal	1.87(1.86)	1.95(2.13)	0.18	.860	0.04
	temporal	1.11(0.85)	2.53(4.49)	1.40	.230	0.43
Alpha (8-12 Hz)	central	0.70(0.57)	0.87(0.78)	1.69	.164	0.24
	frontal	1.79(1.66)	1.46(1.01)	-1.19	.286	-0.23
	occipital	4.88(5.04)	2.53(2.27)	-2.96	.042	-0.59
	parietal	2.63(2.58)	1.75(1.56)	-2.22	.074	-0.40
	temporal	1.29(1.08)	2.01(1.41)	2.60	.044	0.56
Beta (12-30 Hz)	central	0.20(0.21)	0.29(0.22)	1.47	.228	0.39
	frontal	0.28(0.21)	0.39(0.25)	1.76	.151	0.48
	occipital	0.59(0.61)	0.45(0.30)	-1.40	.230	-0.27
	parietal	0.38(0.40)	0.36(0.21)	-0.30	.793	-0.07
	temporal	0.31(0.22)	0.73(0.63)	2.64	.044	0.87
Gamma (30-50 Hz)	central	0.004(0.004)	0.032(0.048)	2.44	.054	0.80
	frontal	0.005(0.003)	0.037(0.049)	2.70	.044	0.89
	occipital	0.005(0.004)	0.020(0.034)	1.82	.151	0.59
	parietal	0.004(0.003)	0.024(0.032)	2.57	.044	0.84
	temporal	0.008(0.005)	0.095(0.128)	2.86	.044	0.93

Note. M = mean; SD = standard deviation; p_{FDR} = false discovery rate-corrected p-value, bold if significant. Significant results (p_{FDR} < .05) are indicated in bold. Degrees of freedom = 18 for all tests.

A6.10 Correlations between EEG significant power changes and subjective experience measures

Scale	Region	Band	r	p	pFDR
EN	occipital	alpha	-0.650	0.005	0.184
	temporal	alpha	-0.445	0.074	0.717
	frontal	delta	-0.263	0.308	0.980
	occipital	slow	0.242	0.349	0.980
	central	delta	-0.180	0.488	0.980
	central	slow	0.142	0.585	0.980
	temporal	beta	-0.137	0.601	0.980
	temporal	slow	0.121	0.645	0.980
	frontal	slow	0.111	0.672	0.980
	frontal	gamma	0.067	0.800	0.980
	parietal	gamma	-0.056	0.830	0.980
	temporal	gamma	0.042	0.872	0.980
	parietal	slow	0.031	0.905	0.981
OBN	occipital	alpha	-0.515	0.035	0.674
	central	delta	-0.320	0.210	0.980
	temporal	alpha	-0.270	0.294	0.980
	frontal	delta	-0.218	0.401	0.980
	frontal	slow	0.145	0.580	0.980
	temporal	slow	0.139	0.594	0.980
	parietal	gamma	0.134	0.609	0.980
	occipital	slow	-0.113	0.667	0.980
	frontal	gamma	0.105	0.690	0.980
	temporal	beta	-0.055	0.834	0.980
	temporal	gamma	-0.045	0.864	0.980
	central	slow	-0.040	0.879	0.980
	parietal	slow	0.002	0.995	0.995
ASCQ	occipital	alpha	-0.467	0.058	0.717
	frontal	delta	-0.296	0.249	0.980
	temporal	alpha	-0.265	0.303	0.980
	occipital	slow	0.257	0.320	0.980
	central	delta	-0.221	0.393	0.980
	frontal	slow	0.161	0.537	0.980
	temporal	beta	-0.143	0.583	0.980
	temporal	gamma	0.109	0.676	0.980
	central	slow	0.109	0.676	0.980

	parietal	gamma	-0.097	0.710	0.980
	frontal	gamma	0.059	0.822	0.980
	temporal	slow	-0.019	0.942	0.992
	parietal	slow	0.011	0.966	0.992

A6.11 Images of EEG setup, 5-MeO-DMT administration, and retreat environment

Note. (a) EEG setup with two researchers and two facilitators present. (b, c) Seven-minute EEG resting-state scan before dosing. (d) Psychedelic administration setup arranged for participant comfort. (e) 5-MeO-DMT administration with one facilitator present and a researcher monitoring EEG behind the supine participant. (f) Argon gas-powered piston vaporizer used for 5-MeO-DMT inhalation.

A6.12 Clinicaltrials.gov exported table of existing 5-MeO-DMT trials

Trial ID	Title	Status	Target Population	Sponsor/ Institution	Study Design	Study Design
NCT06816667	Safety, Tolerability, and Efficacy of Sublingual Microdoses of 5-MeO-DMT for Depression and Anxiety	ACTIVE NOT RECRUITING	Healthy Volunteers	Biomind Labs Inc.	INTERVENTIONAL	Allocation: RANDOMIZED|Intervention Model: PARALLEL|Masking: TRIPLE (PARTICIPANT, CARE_PROVIDER, INVESTIGATOR)|Primary Purpose: TREATMENT
NCT06810765	Trifecta Research Study	NOT YET RECRUITING	Post Traumatic Stress Disorder, Cognitive Dysfunction, Brain Trauma, Brain Injuries	Johns Hopkins University	INTERVENTIONAL	Allocation: NON_RANDOMIZED|Intervention Model: PARALLEL|Masking: NONE|Primary Purpose: TREATMENT
NCT06812221	Efficacy of Sublingual 5-MeO-DMT for Reducing Anxiety and Depression in MCI	ACTIVE NOT RECRUITING	Mild Cognitive Impairment, Anxiety State, Depression Anxiety Disorder	Biomind Labs Inc.	INTERVENTIONAL	Allocation: RANDOMIZED|Intervention Model: PARALLEL|Masking: TRIPLE (PARTICIPANT, CARE_PROVIDER, INVESTIGATOR)|Primary Purpose: TREATMENT
NCT06624137	Computer Game, Qualitative, and MEG/EEG Assessment of Serotonergic Psychedelics	RECRUITING	OCD, Major Depressive Disorder, Alcohol Use Disorder, Healthy Volunteer, Migraine, PTSD, Opioid Use Disorder	Yale University	OBSERVATIONAL	Observational Model: |Time Perspective: p
NCT06511947	Pharmacokinetics of GH001 Delivered Via a Proprietary Aerosol Delivery Device in Healthy Subjects	RECRUITING	Healthy Volunteers	GH Research Ireland Limited	INTERVENTIONAL	Allocation: NON_RANDOMIZED|Intervention Model: PARALLEL|Masking: NONE|Primary Purpose: TREATMENT
NCT05839509	Phase 2 Clinical Trial of GH001 in Bipolar II Disorder	TERMINATED	Bipolar II Disorder	GH Research Ireland Limited	INTERVENTIONAL	Allocation: NA|Intervention Model: SINGLE_GROUP|Masking: NONE|Primary Purpose: TREATMENT

A6.12 (contined)

NCT05804708	Phase 2 Clinical Trial of GH001 in Postpartum Depression	TERMINATED	Postpartum Depression, Postnatal Depression	GH Research Ireland Limited	INTERVENTIONAL	Allocation: NA|Intervention Model: SINGLE_GROUP|Masking: NONE|Primary Purpose: TREATMENT
NCT05800860	A Trial of GH001 in Patients with Treatment-resistant Depression	ACTIVE NOT RECRUITING	Treatment-resistant Depression	GH Research Ireland Limited	INTERVENTIONAL	Allocation: RANDOMIZED|Intervention Model: PARALLEL|Masking: QUADRUPLE (PARTICIPANT, CARE_PROVIDER, INVESTIGATOR, OUTCOMES_ASSESSOR)|Primary Purpose: TREATMENT
NCT05753956	Safety and Pharmacokinetics of GH002 in Healthy Volunteers	COMPLETED	Healthy Volunteers	GH Research Ireland Limited	INTERVENTIONAL	Allocation: RANDOMIZED|Intervention Model: PARALLEL|Masking: TRIPLE (PARTICIPANT, INVESTIGATOR, OUTCOMES_ASSESSOR)|Primary Purpose: TREATMENT
NCT05698095	Pharmacokinetics, Safety, and Tolerability of Intramuscular 5-MeO-DMT in Healthy Volunteers	COMPLETED	Pharmacokinetics, Safety, Tolerability	Usona Institute	INTERVENTIONAL	Allocation: RANDOMIZED|Intervention Model: SEQUENTIAL|Masking: TRIPLE (PARTICIPANT, CARE_PROVIDER, INVESTIGATOR)|Primary Purpose: OTHER
NCT05516823	Personality and Drug Use	UNKNOWN	No Conditions Study Focus on Substance Use and Personality	Psychedelic Data Society	OBSERVATIONAL	Observational Model: |Time Perspective: p
NCT05180149	Personality and Drug Use (PDU)	WITHDRAWN	Personality	Quantified Citizen Technologies Inc.	OBSERVATIONAL	Observational Model: |Time Perspective: p

A6.12 (contined)

NCT05163691	Pharmacokinetics of GH001 in Healthy Volunteers	COMPLETED	Healthy Volunteers	GH Research Ireland Limited	INTERVENTIONAL	Allocation: RANDOMIZED|Intervention Model: PARALLEL|Masking: TRIPLE (PARTICIPANT, INVESTIGATOR, OUTCOMES_ASSESSOR)|Primary Purpose: TREATMENT
NCT05032833	Single Ascending Dose Study With 5-MeO-DMT in Healthy Subjects	COMPLETED	Pharmacokinetics in Healthy Adults	Beckley Psytech Limited	INTERVENTIONAL	Allocation: RANDOMIZED|Intervention Model: SEQUENTIAL|Masking: QUADRUPLE (PARTICIPANT, CARE_PROVIDER, INVESTIGATOR, OUTCOMES_ASSESSOR)|Primary Purpose: TREATMENT
NCT04698603	Clinical Study of GH001 in Depression	COMPLETED	Treatment Resistant Depression, Major Depressive Disorder, Depression	GH Research Ireland Limited	INTERVENTIONAL	Allocation: NON_RANDOMIZED|Intervention Model: SEQUENTIAL|Masking: NONE|Primary Purpose: TREATMENT
NCT04640831	Safety of GH001 in Healthy Volunteers	COMPLETED	Healthy Volunteers	GH Research Ireland Limited	INTERVENTIONAL	Allocation: NON_RANDOMIZED|Intervention Model: SEQUENTIAL|Masking: NONE|Primary Purpose: TREATMENT

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