

Therapists' Perspectives on the Psychotherapeutic Support in Psilocybin Treatment for Major Depressive Disorder: Insights from a Randomized Controlled Trial

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Abstract

Psilocybin treatment has emerged as a promising intervention for Major Depressive Disorder (MDD). However, the contribution of psychotherapeutic support to treatment outcomes remains unclear. This study explored therapists' descriptions of their work during a randomized, double-blind, placebo-controlled psilocybin treatment phase II trial for MDD. Nine therapists participated in semi-structured interviews focusing on (a) specific psychotherapeutic activity, (b) treatment structure and content, and (c) treatment active components and outcome. Data were analyzed using thematic analysis.

The analysis resulted in four themes. The first involves the therapists' reflections on the role of the psychotherapeutic support. The second includes their functions and specific approaches and techniques used. The third describes how the therapists experienced providing psychotherapeutic support within a clinical trial. The final theme describes various aspects of the therapists' experiences with the double-blind study design.

Therapists considered psilocybin treatment beneficial for psychotherapy and described the psychedelic experience as facilitating therapeutic processes. They also described how they used specialized psychotherapeutic skills during sessions. Current research has yet to determine whether psychotherapeutic support is an essential component of psilocybin treatments. Future research should clarify the role and optimal structure of psychotherapeutic support.

Introduction

Major Depressive Disorder (MDD) is one of the most prevalent and burdensome psychiatric conditions worldwide, affecting an estimated 332 million individuals globally according to the World Health Organization's 2025 estimates [1]. Despite the availability of both pharmacological and psychological interventions, a substantial proportion of patients with MDD do not receive any form of treatment, and many of those treated continue to experience insufficient symptom relief [2].

Against this background, psychedelic substances – particularly psilocybin – have gained recent interest as a potentially promising approach in depression treatment. Several small-scale and some larger randomized controlled trials have demonstrated that psilocybin treatment may provide rapid and profound relief from depressive symptoms [3].

To date, due to the temporary altered state of consciousness typically induced by psychedelic substances, clinical studies involving psilocybin have usually been conducted within a structured psychotherapeutic support model comprising three key components (i.e., preparation, dosing and integration) [4]. It is generally assumed that also this component of treatment plays a potentially critical role in treatment outcomes [5]. However, the mechanisms by which psychedelics exert their therapeutic effects remain a topic of ongoing research and there is currently no definitive understanding of whether the subjective experiences [e.g. 6,7] or the psychotherapeutic support [e.g. 8,9] are essential to treatment efficacy.

In contemporary psilocybin trials, within the three-component model, the specific content of the psychotherapeutic support and the professional background of the practitioners delivering treatments have demonstrated considerable variability and the interventions are often insufficiently described according to the rigorous methodological standards required in clinical research reporting [e.g.10,11]. These variations hinder identification of the specific skills and competencies required for effective treatment and complicate the isolation of individual contributions of different factors when interpreting treatment outcomes. The research has also been primarily focused on the pharmacological effects, and to date, no direct comparisons of the psychotherapeutic support have been published. Nevertheless, preliminary evidence suggests that the therapeutic alliance may play an important role in psychedelic treatments [12]. Two recent meta-analyses examined the association between psychotherapeutic support and treatment outcomes in psychedelic treatments. Findings have been mixed, with some studies reporting associations between preparatory support and symptom reduction, whereas others found no significant relationship between therapy quantity and outcomes [13-15].

There are also some previous qualitative studies that have explored therapists' experiences of conducting psychedelic treatments; however, none provide detailed descriptions of the psychotherapeutic processes or the specific psychotherapeutic skills employed during sessions [16-20].

To inform therapist training and generate testable hypotheses on the optimal content and structure of psychotherapeutic support, this study examined the perspectives and experiences of therapists who provided the psychotherapeutic support within a randomized, double-blind, placebo-controlled phase II study, designed to evaluate the efficacy and tolerability of psilocybin treatment for MDD.

Methods

Study Design

This study is a qualitative secondary analysis of semi-structured interviews with therapists providing psychotherapeutic support in the PSIPET trial, a randomized, double-blind, placebo-controlled phase II study evaluating psilocybin for moderate to severe recurrent major depressive disorder (MDD) [21]. Although conducted within the context of PSIPET, the present study was not a clinical trial and does not report clinical outcomes. PSIPET was approved by the Swedish Ethical Review Authority (Dnr: 2020–03700) and the Swedish Medical Products Agency (Dnr 5.1-2020-57521). Data collection was conducted at the Northern Stockholm Psychiatric Clinic between January 2021 and February 2024. The semi-structured interviews for this study were conducted in the middle of the study period.

All participants in the PSIPET clinical trial provided informed consent. In addition, informed consent was obtained from all therapists before participating in the semi-structured interviews included in the present study.

Participants

Nine of the eleven PSIPET study therapists consented to participate in the interviews. They were all clinical psychologists, five men and four women, with ages ranging from 38 to 56 years (mean age = 45.67 years, $SD = 6.42$). Two therapists held dual qualifications as licensed psychologists and licensed psychotherapists. The average professional experience ranged from 9 to 17 years, with a mean of 13.00 years ($SD = 3.24$). Seven therapists reported Cognitive Behavioral Therapy (CBT) as their primary psychotherapeutic orientation. One therapist reported using both CBT and Intensive Short-Term Dynamic Psychotherapy (ISTDP), and one reported Acceptance and Commitment Therapy in combination with ISTDP.

PSIPET

PSIPET included 35 patients, randomized (1:1) in a double-blind manner to receive either a single oral dose of psilocybin (25 mg) or an active placebo (niacin, 100 mg). The study met its primary endpoint with a significant between-group difference in the change in Montgomery–Åsberg Depression Rating Scale (MADRS) [22] scores on day eight in favor of psilocybin. The difference remained significant on days 15 and 42, but not at day 365. For the self-reported MADRS, a significant antidepressant effect was observed from days 2 to 102. Most treatment-emergent adverse events were transient and mild to moderate in severity, with no related serious adverse events reported. Two patients in the psilocybin group experienced persistent severe anxiety requiring medical attention [21].

Both groups in PSIPET underwent five sessions of psychotherapeutic support over the course of three weeks. In accordance with the study guidelines, all therapists were licensed clinical psychologists with experience in treating MDD and in mindfulness-based approaches, recruited through snowball sampling in professional and research networks at Karolinska Institutet (KI). Prior to the initiation of treatment, all therapists completed PSIPET-specific training, which included self-study of the treatment manual adapted from USONA PSIL201 and a three-day hybrid course provided by the Usona Institute. The training covered the study protocol, including inclusion and exclusion criteria, adverse event management, and data handling procedures. Additionally, the training introduced the Set and Setting methodology [23] for guiding the psychedelic sessions, emphasizing non-directive, supportive interactions to foster patients autonomy and psychological safety. The manual also detailed psychotherapeutic support techniques, including grounding strategies and approaches for managing challenging experiences, but no descriptions addressing expected experiences for the placebo group was provided. Throughout the study, all treatment sessions were recorded and evaluated for adherence to the manual, and all therapists participated in monthly group supervision sessions.

Each patient was assigned both a lead and a co-therapist, comprising one male and one female. All sessions, including dosing, were conducted in a dedicated room equipped with a bed, seating, adjustable lighting, and music equipment. The psychotherapeutic support was provided within the structured framework comprising three kinds of sessions: preparation, dosing and integration. The psychotherapeutic approach was non-directive and supportive, grounded in mindfulness principles. Therapists were instructed to cultivate patient trust by demonstrating empathy, openness, and

acceptance and to encourage inner exploration without influencing the dosing experience. Both positive and challenging experiences were validated by the therapists to facilitate psychological growth. The first session served as a two-hour preparatory session one day prior to dosing, aimed to establish trust and rapport, assess the patient's history of depression and readiness for treatment, and provide psychoeducation regarding the intervention. In the single, 7–10 hours dosing session, patients were encouraged to lie down and focus their attention inwards. Eye masks and headphones were made available for use at their discretion. Therapists maintained a supportive presence, prioritizing patient safety while fostering openness and curiosity. Verbal interactions were intentionally minimal, with therapists focusing on nonverbal presence and subtle emotional guidance. Grounding techniques were employed as needed to address anxiety or agitation. The first follow-up session was scheduled the day after dosing, with the remaining two with one-week intervals. Each session lasted approximately 1–2 hours and was designed to assist the patients in processing their dosing experiences and fostering lasting change. Therapists encouraged self-reflection without interpreting the patient's experience, guiding them to explore insights and emotions related to their depression. The overarching goal was to support the patients in integrating their experiences into daily life and promoting enduring psychological change.

Data Collection

The data collection was guided by a semi-structured interview protocol developed specifically for the PSIPET study at the Centre for Psychiatric Research, KI (Appendix 1). The protocol comprised 22 questions designed to explore the therapists' perspectives on treatment, focusing on (a) psychotherapeutic activity, (b) treatment structure and content, and (c) treatment active components and outcome. All PSIPET therapists ($n = 11$) were invited verbally and by email to participate in the interviews. The nine therapists who consented to participate were interviewed individually via telephone. Each interview lasted approximately 45 minutes and was recorded using a voice recorder and transcribed immediately afterward. All therapists in the study were blinded to whether their patients had received psilocybin or placebo. Prior to the interviews, therapists were instructed to focus their responses on patients whom they believed had received the active substance rather than placebo. This instruction was given because the primary aim of the interviews was to explore therapists' experiences in working with patients who received psilocybin treatment for depression.

Thematic Analysis: Step-by-Step Overview

The thematic analysis of the interview material was conducted in six phases, following the approach outlined by Braun and Clarke [24]. This iterative process involved continuous movement between the phases and regular consultation of the raw data to ensure that the emerging themes were firmly grounded in the data and captured the essence of the dataset as a whole.

Phase 1: Familiarization with the Data. All interview transcripts were read at least twice to gain a comprehensive understanding of the dataset's breadth and depth. During this initial phase, preliminary thoughts and ideas were noted in the margins, forming the basis for later coding.

Phase 2: Generating Initial Codes. The entire dataset was then systematically reviewed and segmented into the smallest meaningful units – text excerpts in which the respondent's narrative conveyed new or significant meaning. Each excerpt was assigned a numerical code and a corresponding descriptive label summarizing its semantic and latent content, referred to as a "coded element" (CE). A total of 1,050 CEs were identified. These were then manually sorted into categories based on similarity and meaning. Further analysis and refinement aimed to increase the level of abstraction, ultimately resulting in 26 categories that captured the essence of the initially coded elements.

Phases 3–5: Searching for, Reviewing, and Defining Themes. The next steps focused on identifying overarching themes that could meaningfully address the research questions. Each category was summarized in a few sentences and grouped into potential (proto-)themes. As preliminary themes emerged, the process slowed to ensure that each theme was firmly grounded in the raw data. To reach consensus, a synopsis was written for each theme, clarifying how the data within each theme were coherent and sufficiently rich. This process culminated in four final themes, each presented with its associated categories in the Results section. The analysis was guided by an iterative and reflexive approach [24] and followed trustworthiness criteria as outlined by Nowell et al. [25]. A rich and detailed account of the therapists' experiences was provided to support the assessment of transferability to other contexts.

Phase 6: Producing the Report. The final phase involved composing a written synthesis of each theme, describing the patterns identified in the data and illustrating them with representative quotations from the interviews.

Results

The four themes derived from the thematic analysis are presented here, along with some illustrative quotations from the therapists.

Psychotherapeutic support together with psilocybin - why and how?

This theme describes the therapists' reflections on their work with the psychotherapeutic component of PSIPET. It includes the therapists' perspectives on how treatment may facilitate change and how patients' expectations and attitudes toward the intervention could influence treatment outcomes.

All therapists identified psilocybin as a valuable component in future treatments for patients with MDD. Universally, they expressed positive emotions such as joy, gratitude, and a sense of meaningfulness in being part of the psychedelic research field. Even those therapists who observed intense and sometimes

painful emotional reactions during dosing maintained a strong belief in the substance's psychotherapeutic potential: *"(...) and I am very positive about what I consider to be the contribution of the substance. It's true that not all patients have a good experience, but I still have confidence in the substance."*

This belief in the psychotherapeutic potential of the treatment was grounded in the therapists' observations that the psychedelic experience appeared to help the patients overcome ingrained depressive thought and behavior patterns. Some therapists suggested that this effect was mediated by increased access to emotions, which could subsequently facilitate psychotherapeutic processes. Through this process, the patients seemed to be able to access previously inaccessible emotions. After dosing, the therapists also observed changes in the patients' thought patterns, leading to new perspectives on themselves and their lives: *"(...) so I think that the induced experience can create a shift in perspective that allows patients to break out of their habitual thought patterns and look at things from a new perspective."* As an example, feelings of sadness about the way life had unfolded were described, including painful emotions that the patient more or less consciously had controlled or avoided. Engaging with these feelings and thoughts was described as an opportunity to foster a desire to live more authentically and in accordance with one's emotional life and personal values. Furthermore, as patients were encouraged to reflect on and express their experiences and perspectives, these processes were described as being able to instill hope and confidence regarding the future:

It opens up the possibility of connecting with the body and emotions in a new way. This can reduce avoidance and increase openness, which, if properly integrated, can lead patients to start living more in line with their values.

The therapists' observations regarding the impact of psilocybin were also related to a sense of wonder at the substance's potent capacity to elicit a range of responses in the patients, along with the subsequent psychotherapeutic possibilities. It was described as seeming to force or unlock a spectrum of emotions and thoughts, for which patients should be prepared and then receive assistance in processing and managing afterward:

(...) even with some patients who are highly functioning, who often have a quite clear understanding of what is problematic in their lives and what they should do differently, but the challenge lies in being able to live by that knowledge.

Furthermore, the therapists noted that the substance sometimes also appeared to facilitate a deeper, more embodied connection to patients' emotions. Some therapists described that when the patients experienced their emotions more physically, their rational and intellectual understanding of what actions they needed to take to improve their well-being became more substantial and impactful. This bodily aspect of the experience was seen as capable of awakening intrinsic motivations and prompting behavioral changes: *"(...) but they experience it more deeply, and that makes it easier to act in line with that existing inner understanding."*

Additionally, some therapists emphasized that patients' willingness and readiness to engage in psychotherapeutic processes seem to be crucial for achieving enduring changes. As an example, patients who seek immediate relief without a foundational understanding of the necessary psychotherapeutic work before, during, and after dosing were described:

(...) thus, there is always the risk that individuals seek quick fixes – you want to take that pill, and you want to feel better. But it might not be that simple, as it often requires adjusting various aspects of one's life.

Therapists' function and methods

The second theme outlines the therapists' perspectives on their roles in the study, alongside challenges and opportunities identified regarding the psychotherapeutic aspect of PSIPET. The interviews revealed, among other things, the function that therapists considered most central.

All therapists expressed that their primary task during treatment was to establish a robust psychotherapeutic alliance, ensuring patients felt sufficiently safe and secure throughout the entire process. Key approaches emphasized included authenticity, openness, genuineness, and maintaining a non-judgmental stance through validating and normalizing the patients' experiences. The therapists also highlighted the significance of attentive presence and empathy, demonstrated by active listening and non-verbal cues such as eye contact and a relaxed, calm body language. Some therapist also emphasized the importance of being able to contain their own emotional reactions during sessions: *"(...) to pay attention to what might be triggered in me by patients or co-therapists, and to not judge those experiences, and ensure they don't impede the psychotherapeutic process."// "I believe it involves addressing and managing one's own triggered responses, and handling those feelings internally."*

Moreover, all therapists emphasized feeling safe and secure as necessary conditions for the patients to be able to let go during dosing, allowing them to fully engage with the experience without attempting to direct or regain control: *"It's a bit paradox, because you guide them to be safe by not being safe."* The therapists described that they provided this reassurance by ensuring that the patients received adequate emotional and practical support and assistance throughout treatment. This psychotherapeutic technique was described as fostered by a range of approaches. Initially, it involved informing the patients about both the practical and relational aspects of the dosing day (e.g., toilet visits, physical contact), and explanations of the types of inner experiences that the dosing day may induce. The therapists' competence in the effects of psychedelic substances was also highlighted as important, alongside the psychological preparations for dosing: Through psychoeducation and various exercises, the patients learned about and were motivated to engage with their inner experience and remain open and curious toward whatever came up:

(...) if you are prepared to face whatever happens, it will be less distressing. Much of what can be frightening with these substances is when you resist the experience.

Making the patients feel safe and secure was described as essential also after dosing, so that they could feel comfortable sharing and reflecting on their experiences. This relational variable was thus described as also facilitating the integration by enabling the patients to process what they encountered during dosing and contextualize these experiences within the framework of their personal history, current circumstances, and wishes and needs for a possible future. The therapists' statements illustrate the interdependence between ensuring safety and security and facilitating the psychotherapeutic process:

(...) supportive people and follow-up afterwards help transform difficult experiences into something comprehensible.

The therapists also emphasized the importance of validating and normalizing the patients' emotional reactions during the integration process: *"It is crucial to show understanding, validate their feelings, normalize their experiences, and demonstrate that you have listened to and comprehended their situation. Additionally, it is important to convey a sense of hope and the possibility of change".*

Emotion regulation strategies, such as helping the patients identify, name, and curiously explore their emotions, were also emphasized, given the centrality of the emotional experiences during dosing. However, several therapists described the patient-centered approach specified in the study's manual as unclear and somewhat limiting to their psychotherapeutic work. Some therapists even felt that this approach rendered them passive, lacking the mandate to fully implement the interventions they would typically use during psychotherapy. The therapists particularly expressed uncertainty, and in some cases frustration, regarding the handling of the emotional components within the patient-centered framework. One therapist remarked, *"I am very curious about how this could be integrated as an adjunct to regular therapy. For example, what would it be like if therapists could be more active?"*

Additionally, many therapists described the treatment arrangement involving two therapists as positive. Working in pairs was seen as enjoyable, and in some cases, synergistic effects due to the inclusion of two perspectives instead of one were mentioned. However, a recurring theme was that personal chemistry and a shared theoretical foundation were crucial for achieving such synergistic effects. There were also accounts of therapist pairs that functioned less effectively and/or were guided by differing theoretical orientations. In these cases, the importance of clearly defined roles and responsibilities was emphasized, particularly the need to establish which therapist holds overall responsibility for the treatment: *"(...)I think it is crucial to have a unified perspective and also to establish who has the final say and interpretive priority."*

Being a therapist in a clinical drug trial

The third theme describes how the study's principal investigator (PI) and some of the therapists partially entered the trial with different perspectives.

Some of the therapists described how those responsible for the study had differing frames of understanding in relation to the study design. A recurring sentiment was that the therapists viewed the

trial as reductionist, with the emphasis placed primarily on the effect of the substance. In contrast, several therapists adopted a more holistic perspective, emphasizing the psychotherapeutic component, including the preparation before dosing, the integration of the experience, and the impact of the experiences during dosing: *"(...)because I get the feeling that in this trial, somehow you have to let the substance just have its effect, but I think in the future it will be used more as an adjunct to the forms of therapy that we already know work"*. A common view was thus that the psychotherapeutic elements had not been prioritized sufficiently, and that the treatment plan, which included one preparation session and three integration sessions, was perceived as insufficient.

In addition, several of the therapists, while acknowledging the importance of comprehensive data collection, emphasized that the study's extensive and sometimes demanding somatic examinations and data collection might have had a negative impact on the treatment results: *"It must be suboptimal to initiate an experience like this with discomfort."* Aspects of the study's setting were also raised, such as the choice of location within a distinctive hospital environment. Suggestions for improvement included better views and incorporating elements of nature. An additional issue raised was the possibility of group interactions during dosing and integration.

Another reflection that emerged during the interviews was whether it is appropriate for therapists to have personal experience with the substance administered. Some therapists reported prior experiences using psychedelic substances and unanimously maintained that such firsthand experience is advantageous for a therapist in these kinds of treatments. They argued that psychedelic experiences are inherently indescribable and cannot be fully understood without direct personal experience.

A major frustration for me in this study has been that I feel that those responsible for the study do not have that first-hand experience. And I think that affects how you think about the study design, the organization of the study, how you treat the patients, the data collection, the therapist training, and the interactions within the therapist group... pretty much everything.

Thus, own experience with psychedelics was perceived to provide an idea of the type of experience patients face and the support that can be helpful. While each psychedelic encounter is unique, these therapists found that their personal experiences made them more confident in supporting patients during treatments. In contrast, a therapist without personal experience cautioned that personal experiences may lead to preconceived ideas about what patients may experience, and that basing treatments on personal experience can make it difficult to provide unbiased psychotherapeutic support during treatments.

The Blinding – an Achilles heel

In the fourth and final theme, various facets of therapists' experiences with the study's double-blind design and its impact on the psychotherapeutic aspect of treatment are described.

Skeptical remarks concerning the effectiveness of blinding emerged repeatedly during the interviews: *“That’s the nature of a substance like this. You can’t blind it very well, and in many cases, not all, but many cases, it’s fairly obvious to both the patient and the therapist whether it was the active substance or placebo.”*

The therapists also recounted instances where the patients, believing they had received a placebo rather than an active substance, experienced profound disappointment:

For instance, one patient failed to attend an appointment last Friday, citing fever and chills. Despite subsequent text messages, she remained unresponsive. This situation underscores the underlying disappointment – she felt that she had not received the substance she had hoped for. Coping with such challenges is daunting, particularly considering that individuals struggling with depression must endure this emotional turmoil.

As the quote highlights, the therapists faced recurring challenges of managing the patients’ disappointments, especially since most patients had heard about the research and formed expectations regarding the substance’s effects. Additionally, the therapists emphasized the vulnerability of this patient group and the relatively demanding test battery, which included procedures like lumbar punctures – described by one therapist as *“borderline traumatic”* for some of the patients who believed they had received placebo. Several therapists also described making every effort to help the patients derive value from their sessions despite disappointments, noting that these integration sessions often centered on processing and working through these feelings. Some therapists also expressed that a cross-over design would have been better, giving all patients active substance at some point:

They could have received the substance a month later or at some other point. Just to take the edge off the disappointment. This is almost like we are testing psilocybin against disappointment, which is not ideal. We should be testing psilocybin against a neutral baseline. As it is now, some patients’ conditions may have worsened after the experience.

However, this bleak picture bears nuance as there have also been patients where the therapist express uncertainty about which substance was administered:

I would say that sometimes it is very obvious, but I would also say that sometimes you actually have no idea. I am super curious about the unblinding when we will find out which patients received active substance and which did not, because I think it will be surprising, and it speaks to the fact that then the blinding actually works.

Discussion

This study qualitatively analyzed therapists’ descriptions of their work in providing psychotherapeutic support in a psilocybin treatment trial for MDD. The thematic analysis resulted in four key themes. The first involves the therapists’ reflections on the role of the psychotherapeutic support within the trial. The

second includes the therapists' perspectives on their function and the specific approaches and techniques used, including challenges and opportunities involved in providing psychotherapeutic support in the study. The third describes how the therapists experienced providing psychotherapeutic support within the context of a clinical drug trial. The fourth and final theme describes various aspects of the therapists' experiences with the double-blind study design and its impact on the psychotherapeutic support in the trial.

All therapists expressed confidence in the psychotherapeutic potential of the treatment, describing how the psychedelic experience appeared to foster change by enhancing access to cognitions and emotions – sometimes even at a deeper, somatic or bodily level. According to the therapists, such experiences seemed to facilitate psychotherapeutic processes through enhanced intrinsic motivation for behavioral changes. Additionally, the importance of patients' willingness and readiness to actively participate in the psychotherapeutic process was highlighted as crucial for achieving persisting changes. Embodied cognitions refer to the complex interplay between bodily structures, dynamic interoceptive and sensorimotor states, and their associated neural and computational representations, including conscious awareness [26]. Disruptions in embodied processes are characteristic of several psychiatric disorders, including depression [27]. Previous qualitative psilocybin studies have reported on participants' subjective bodily experiences, such as disembodiment, embodiment of emotions or alterations of the bodily self, often also described as highly significant by participants [28, 29, 30]. The therapeutic relevance of these experiences remains uncertain, as does the identification of psychotherapeutic behaviors that would most effectively support them. Even those therapists who observed intense and sometimes painful emotional reactions in their patients during treatment maintained a strong belief in the substance's psychotherapeutic potential. However, it is worth noting that research has yet to establish whether the therapeutic effects stem from the psychedelic experience and the psychotherapeutic context [e.g. 7, 31], from pharmacological mechanisms alone [e.g. 6,], or from a combination of these or other factors.

The therapists emphasized building a strong psychotherapeutic alliance and providing adequate emotional and practical support as their primary responsibilities to ensure that patients felt safe and secure throughout the treatment. Specific approaches and techniques at different stages of the process were also described: Before dosing, therapists emphasized the importance of treatment-specific psychoeducation, including both practical preparations and psychological readiness. Various exercises to facilitate patients' dosing day experience were also included. During dosing, therapists highlighted the importance of a composed, attentive and supportive yet non-intrusive presence, but that they also used agreed physical contact and verbal and non-verbal cues to help the patients fully engage with their experience. After dosing, the therapists described working with open, non-judgmental, empathic active listening, including validating and normalizing the patients' experiences, to build rapport and facilitate reflection of the experience in relation to their history, present circumstances and possible future. In addition, the therapists described continued efforts to guide the patients in identifying and curiously exploring thoughts and emotions, as well as prompting behavioral changes in line with their personal goals during this final stage of treatment. Altogether, this represents a description of highly specialized

psychotherapeutic skills. Due to the inherent unpredictability and individual variability of the psychedelic experience, the therapist's professional approach and psychotherapeutic competencies may play a critical role in supporting patients in integrating the experience in a constructive and meaningful way. However, there is currently no consensus regarding how the support in these treatments should be structured, which professionals are best suited to provide such support, or how they should be adequately trained [32]. Monitoring sessions through recordings and structured analyses of therapists' in-session behaviors in relation to treatment outcome may provide further insight into these issues.

One aspect of the psychotherapeutic support that is sometimes emphasized concerns the potential role of personal, first-person experience of the subjective effects of psychedelic in therapist training [e.g 33] – a consideration also highlighted by several of the therapists in this study. From the standpoint of regular psychiatric practice, this would be considered highly unconventional. The idea may have origins in recreational use practices and was also a widely held view among psychedelic researchers during the 1950s to early 1970s [34]. Similarly, early perspectives in treating substance use disorder suggested that personal experience with addiction was essential for effectively providing treatment – an assumption that has since been disproven [e.g 35]. Conversely, it can be argued that an overreliance on personal experience in therapeutic settings may negatively influence clinical judgment and patient care. In the context of psychedelic treatments, there are also clear both practical and ethical concerns associated with requiring therapists to undergo a psychedelic experience as part of their professional training.

The analyses also included reflections on conducting treatment within the framework of a clinical drug trial, revealing differing views on the study design. Particular attention was given to the role of the psychotherapeutic component, the effectiveness of blinding, the comprehensiveness of data collection and how these factors may have influenced the patients' experiences and overall treatment efficacy. Managing disappointments emerged as a key challenge. A recent meta-analysis of control-group outcomes in psilocybin, SSRI, and esketamine trials reported lower control-arm improvement in psilocybin trials than is typically observed in antidepressant studies [36]. One interpretation is that functional unblinding may contribute to attenuated placebo responses. In PSIPET, interviewed therapists expressed concerns that disappointment among participants who recognized that they had been allocated to placebo could lead to clinical deterioration. However, such deterioration was not supported at group level [21]. Nevertheless, therapists' efforts to mitigate individual participant's disappointments may have helped counteract this risk. The therapists' reflections on conducting treatment within a clinical drug trial may partly stem from preconceived notions regarding the appropriate framework for administering the substance and/or reflect the strong beliefs in the therapeutic potential of these treatments. At the same time, they also raise critical questions about how findings from clinical drug trials can be translated into regular practice and how substances historically used in non-clinical contexts should be integrated into Western healthcare systems.

Limitations

This study involved a small number of patients, with approximately half receiving placebo. Consequently, the therapists' experiences must be regarded as limited in scope, both in terms of the number of treatment sessions conducted and the diversity of patient responses. Another limitation of this study is the lack of information regarding whether the therapists held neutral, positive, or negative attitudes and beliefs toward the treatment prior to their engagement in the study. Such pre-existing dispositions may have influenced their responses during the semi-structured interviews. Finally, as the therapists were blinded to treatment allocation, their reflections on treatment effects were based on perceived rather than confirmed allocations.

Despite these limitations, the therapists provided a considerable amount of detailed professional insights and experience-based knowledge regarding the psychotherapeutic support of psilocybin treatment for MDD. Their accounts offer valuable perspectives on the psychotherapeutic support component and process, the dynamics of the patient-therapist interactions, the psychotherapeutic skills used, and the challenges encountered during treatments, even within the constraints of a small-scale clinical trial.

Conclusion

This study is among the first to examining therapist's perspectives on psychedelic-assisted psychotherapy within the context of a randomized clinical trial. The therapists in this study conveyed a strong belief in the psychotherapeutic potential of treatment, noting that the psychedelic experience appeared to facilitate psychotherapeutic processes by enhancing access to cognitions and emotions, sometimes reaching deeper, somatic or bodily levels. They also reported employing highly specialized psychotherapeutic skills during sessions. The precise mechanisms underlying therapeutic effects in psilocybin treatments remain unknown and current research has not yet established whether psychotherapeutic support constitutes an essential component of treatments. Moreover, if required, uncertainties remain regarding the most effective type and structure of such support, the professional background best suited to deliver it, and the training necessary to ensure its quality. Future studies should be designed specifically to address these questions.

Declarations

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Author Contributions

MB and JL contributed to the conception and design of the study. TL and FS conducted the interviews and contributed to the analyses. MB and AK contributed to the analyses and drafted the manuscript. All authors contributed to writing the paper and approved the final manuscript.

Data availability

The datasets generated during and/or analyzed during the current study are not publicly available due to privacy and confidentiality concerns involving participants but are available from the corresponding author on request.

Ethical approval

This study was approved by the Swedish Ethical Review Authority (Dnr 2020-03700) and the Swedish Medical Products Agency (Dnr 5.1-2020-57521). This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Informed consent was obtained prior to all interviews.

Clinical Trial Registration

The parent clinical trial (PSIPET: The Effect of Psilocybin in MDD Symptom Severity and Synaptic Density) was registered at ClinicalTrials.gov (Identifier: NCT04630964, registered on November 12, 2020).

Competing interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article

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