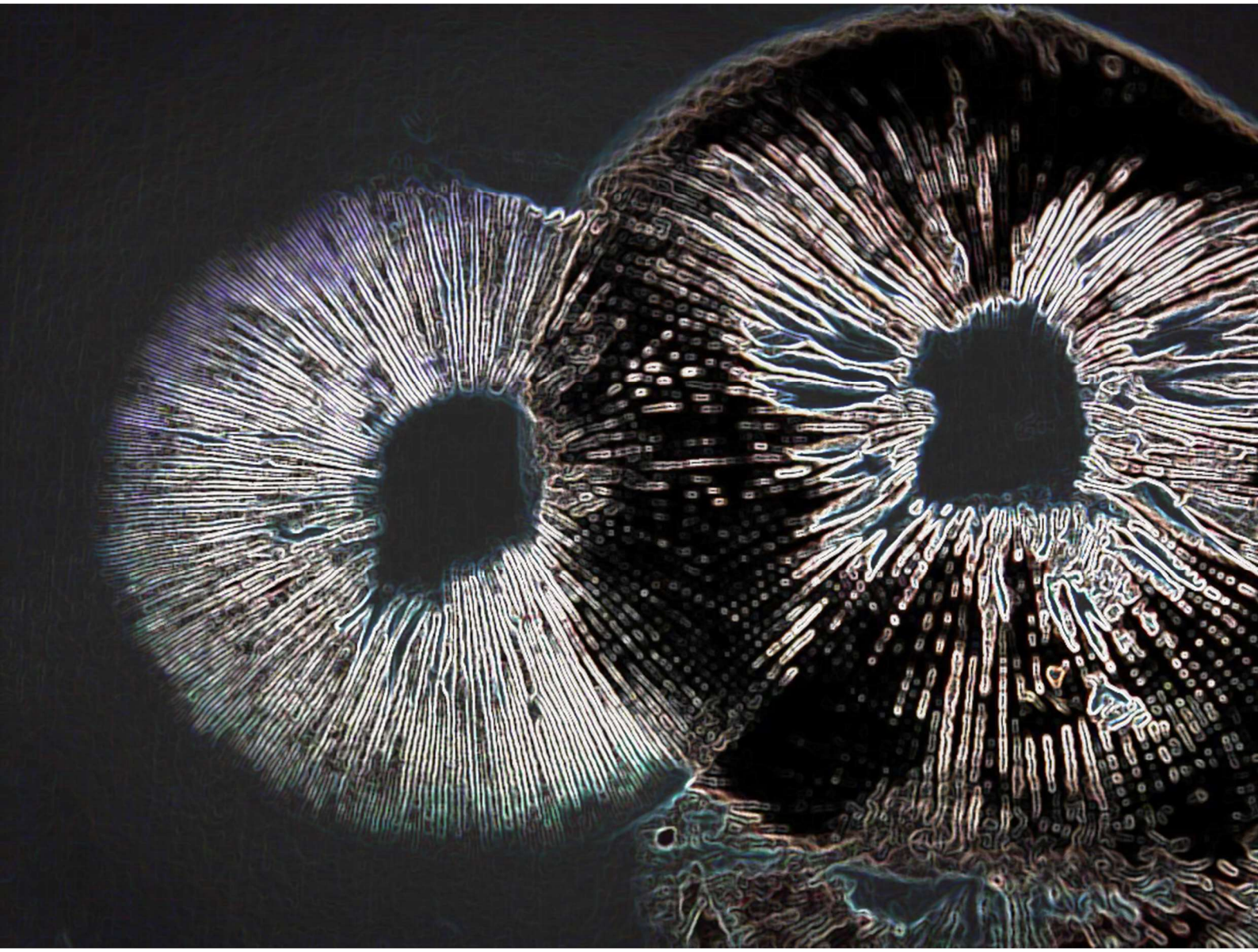
TRUST, SURRENDERENCE AND THE INABILITY TO ARTICULATE THE EXPERIENCE –

A QUALITATIVE INVESTIGATION INTO PSILOCYBIN THERAPY FOR DEPRESSION



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Abstract

Introduction: Depressive disorder is a common mental disorder affecting people across all levels of society worldwide with current treatment being insufficient for almost one-third of all patients. Renewed interest in the role of psychedelic substances in the treatment of psychiatric disorders has caused revival in research on this topic. Although our knowledge on the working mechanisms is rapidly increasing, little is known about how patients experience psychedelic therapy and what the role of this experience is for the outcome. This study investigates the lived experience of psilocybine therapy in patients with refractory depression.

Method: Participants who underwent psilocybin therapy were asked for a one-time in-depth interview about their experiences. These semi-structured interviews were transcribed verbatim. Four interviews were analyzed using Interpretative Phenomenological analysis**.**

Results: Through analysis we found common themes in participants' lived experience of the psilocybin sessions, namely: trust in therapists, inability to surrender to the experience and trouble putting the experience into words.

Conclusion: The formation of a bond of trust might play an important role for participants' experience during psilocybin therapy and should thus be one of the priorities during introductory sessions. It seems to facilitate participants in feeling at ease and surrendering to the psilocybine-induced experience.

Introduction

Depressive disorder is a common mental disorder affecting people across all levels of society worldwide (1-4). Current treatment of the mood disorder at hand is insufficient for almost one-third of all patients (5,6). In recent years a revival of interest for the potential role of psychedelic substances in the treatment of different psychiatric disorders has taken place (7,8,9). For depression in particular, research has already shown the potential effectiveness of ketamine, a psychedelic substance that can also illicit intense personal experiences during the acute phase after ingestion. (10,11,12).

At the moment, a phase 2b randomized clinical trial was conducted on psilocybin for treatment-resistant depression at three sites in the Netherlands, namely the University Centre for Psychiatry (UCP) at the University Medical Centre Groningen, the University Medical Centre Utrecht (UMCU) and the Leidse University Medical centre (LUMC). Here the safety and efficacy of psilocybin treatment is investigated. There is increasing evidence that this psychedelic substance is both safe and effective in patients suffering from refractory depression (13). On top of that, our understanding of how psilocybin affects different brain regions and cognitive mechanisms is growing (14,15).

However, little is known about how patients perceive the psilocybin treatment, and which conditions might facilitate optimal outcome. In order to improve and optimize the potential outcome of psilocybin therapy understanding the patient's perspective is thus crucial. The aim of this paper is to explore the different perspectives of patients with refractory depression who participated in the experimental oral psilocybin treatment. This exploration will take place through semi-structured interviews which will be transcribed verbatim and afterward qualitatively analysed using an Interpretative Phenomenological Analysis framework.

Through analysis of the interviews we found common themes in participants' experiences, namely: trust in therapists, inability to surrender to the experience and trouble putting the experience into words. On top of that we discuss one participant's challenging experience, because it emphasizes the need to adequately inquire into and explore these experiences. Especially in participants that lack the vocabulary to do so.

Bases on the four analysed interviews we conclude that the formation of a bond of trust might play an important role for participants' experience during psilocybin therapy. In the bigger picture this might point towards the importance and its potential functions as a cornerstone in psilocybin therapy. Without trust participants seem to feel ill at ease and are unable to surrender to the experience. For the formation of a bond of trust time is needed to for the therapist(s) and participants to get acquainted. Although time is scarce we believe investing enough time during introductory sessions prior to the psilocybin treatment will eventually pay off.

Methods

Design

Individual in-depth interviews were held with participants in order to explore their experiences and perspectives regarding the psilocybin trial they had partaken in. An Interpretative Phenomenological Analysis (IPA) framework was used for data collection and analysis (16,17). This phenomenological approach was chosen since it can yield detailed descriptions on a variety of aspects of participants' lived experience of the studied phenomenon in this qualitative study, i.e. the psilocybin trial, that are often underexamined in detail (18). IPA is designed to deal with the concrete and unique, i.e. ideography, allowing the investigator(s) to explore the individuals' perspectives in more detail. Instead of directly seeking to understand how these experiences relate to or differ from those within the group of participants. The aim was to get a more comprehensive understanding of how patients interpreted, understood and lived their experiences of the psilocybin trial.

Treatment setting

The psilocybin trial consisted of a fixed number of appointments prior to the dosing day in order to inform participants about the design of the study, filling out questionnaires for baseline information and meeting with the study's accompanying therapists. This took place in one of three University Medical Centre's as noted above. For this study only participants in UMC Utrecht and UMCG were included.

Study participants

After partaking in the psilocybin trial program participants were asked (without obligation) for a one-time interview about their experience regarding the clinical trial. Eleven study participants agreed to be interviewed. Individual semi-structured interviews were conducted either in person at one of the research or treatments sites. If this was not possible teleconferencing software was used. This depended on feasibility due to SARS-COV-2 measures and convenience for participants

Data collection

Interviews were conducted at least 14 weeks after they received treatment, after the final follow-up meeting and after the official study closing date. due to the study protocol guide lines. Eleven in-depth interviews were conducted by the second author (Joost Breeksema). He was not involved in the treatment nor had contact with participants prior to the interview. The interview was conducted using an interview guide for inquiry into participants' expectations, experiences and perspectives of the psilocybin trial altogether. This included open-ended questions and refraining from close-ended ("yes-or-no") questions in order to

Data analysis

The interviews explored patient's expectations, experiences, perspectives and outcomes after psilocybin treatment. These audio interviews were than transcribed verbatim and analysed digitally following an Interpretative Phenomenological Analysis (IPA) framework. Iterative and emergent design are inherent to qualitative research meaning that analysis and data collection take place simultaneously and evolve over the course of research. For this particular paper, four interviews were selected and used for analysis. The interviews were

elected on quality and the richness of information that was gathered. These were interviews in which themes emerged naturally over the course of the interview. This stood out during transcription and reading of transcripts. On top of that, they had the same sorts of themes which presented the opportunity to compare them and create a more elaborate understanding of these themes.

Results

In the following section we will discuss the results that were found analysing four of the transcripts. The emerging themes were: trust in therapists, surrendering to the experience, putting the experience into words. On top of that we will discuss one participants' challenging experience. We will now go through these themes separately.

Trust in therapists

The theme 'trust' emerged frequently during the interviews without being mentioned explicitly. One of the participants noticed that during the introductory sessions leading up to the dosing day there was actually too little time to discuss certain aspects of their life that might play an important role in their illness or might come up during the psilocybin session. Since these experiences reached far back into childhood it would take an extensive amount of time to give a detailed description of their history. They felt there was not enough time to do so:

"I don't know to what extent all of this was discussed in … detail. It has been discussed that I have had a [some]what boisterous youth … but not very detailed. I also think there isn't time for it, because of course they are not your regular therapists which makes it different too." [P9]

According to them, this particular issue arose, because during the study duration participants are not accompanied or treated by their regular therapists, who have known them for years; furthermore, most of the therapy sessions take place after the dosing day, which leaves less time to get acquainted beforehand. This also let them to hypothesize about the influence this could have on the bond of trust between the therapists and the participants during this study. Which is a very important aspect and necessary to be able to openly tell therapists what you struggle with, what are you afraid of and so on. This can, in turn, potentially influence the course of the session:

"[M]aybe in some situations […]there is a lack of a certain bond of trust. In order to let go completely. […]. You have to surrender to it, because otherwise you won't get out of it what you could have. […]. However, I can imagine that there are people who experienced very intense things during their youth with a lot of trauma and […] that that it will become harder to talk about it, because it's very sensitive. [P9]

The importance of a bond of trust is not only necessary in order to talk openly and let go completely. It is also needed to feel a sense of safety since you are lying on a bed, blindfolded with headphones on, taking an experimental drug that, in this case, participants had no experience with and of which the dose is unknown:

"In the room, there are two people next to you in the room uh that alone feels weird. Also weird that you are then lying down in a bed and there are two people, one on either side, in a chair who than just [watch]. […] It was uncomfortable. […], because there are strangers sitting next to you in your bedroom so to speak. [P3]

Another participant noticed that if there would not have been a bond of trust they would have never taken psilocybin to begin with, because it would be too risky for them to experiment with a substance in a setting in which they do not feel safe. One interviewee mentioned that they felt a conflict of interest in the therapists making it hard to fully trust them. This felt conflict of interest lay between informing people adequately and convincing

them to partake in the trial. The participant mentioned that they felt like they were only informed about aspects of the trial that were convincing them to participate. This made them sceptical about the information handed to them and caused them to look for information and case reports online, because they felt like they were not properly informed.

In order to quicken the forming of a bond of trust with the new therapists one participant benefited from asking questions about their therapist's personal life to get a better idea of who they were dealing with making her more comfortable:

"Definitely during a psilocybin session you are so vulnerable. So, then it is nice that, for example, questions that arise are answered even if they are questions about [the therapist] as a person. […] Look with someone else that you […] have been in therapy with for a long time you know something about: "oh this I can expect, but [here] you don't have that." [P9]

It was also remarked that a potential obstacle could arise with the introduction of a second therapist on the dosing day itself, because then a bond of trust has to be built in a couple of minutes or hours.

Another participant mentioned how a procedural problem, i.e. their blood sample was lost, led them to doubt whether they wanted to continue with the trial. Even though during the interview they did not explicitly mention that this played a role in their contemplation, the event nonetheless appeared to have made an impact on their trust leading to doubts about proceeding to the dosing day.

When asked about potential improvements, a participant stated that they believed future treatment would have a better outcome when taking place with one's own therapist. There already is a connection and a bond of trust, because you will often have known each other for quite some time, making it easier to directly build upon past problems or experiences during therapy instead of losing time on getting to know one another and trying to trust a new therapist.

Inability to surrender to the experience

Besides a trusting relationship, other aspects contributed to patients' ability to let go and surrender to the possible effect of psilocybin. Participants remarked that the artificiality of the setting, the course of the session, the music, unawareness of the dose and its effect played a crucial role in their experiences of the dosing day as well. It made them self-conscious and aware of their surroundings. This distracted them from the whole experience. It was mentioned as a potential adjustment for future psilocybin therapy that it would help participants to feel more at ease and fully surrender to the experience if they would start with a low dosage in order to get to know the drug and its potential effects.

All participants were exposed to music during the session. Some experienced it as soothing, relaxing or hardly were aware of it looking back on their session. However, another participant seemed to be distracted by it:

"[W]hat I […] also noticed was, maybe it's not that weird, that in the beginning I […] had to laugh a little about the music.. Of course it was very fitting for something in this nature, but maybe also a little cliché, […] pleasant to listen to, but that you're almost thinking: oh jeez, […]it's obvious that these two things have to be connected and maybe they reinforce one another or so, […]but I had to chuckle about it a bit […]." [P1]

Later in the interview they mentioned how they were constantly trying to figure out what songs they had heard and how they wanted to remember the tracks they had recognized in order to listen to it again after they had returned home.

Furthermore, it was remarked that the whole setting of the dosing day, e.g. people sitting next to you while you're lying in a bed, made participants ill at ease. One person even mentioned that they had to tell themselves that there is nothing they can change about the setting and they just have to make do with how things were in that moment in order to relax:

"And then you just go and lie down and then you are lying there in the dark listening to music… so that was very unusual, because… well you are lying there and there are two people just sitting there. Uhm, however, at a certain point you just have to snap out of it a little. […]. Accepting I think, yeah, that this is what it is." [P9]

Here the unusual setting was clearly experienced as something that initially bothered participants and stood in their way of surrendering to the possible effect of psilocybin. Nonetheless, all participants understood why it was necessary that there were therapists with them in the room during the session and even pointed out the importance of their presence for safety and potential guidance:

"*I also think that it's good that someone was with me, because otherwise I think that you can think [or] do pretty weird things. […] That moment when I thought I had my head together […] then took of the mask and that you realise that you're not back on earth at all. […] That was really weird, but […] they immediately said that [it's] part of it. But I think if no one would be there that you can get really weird.* [P4]

There also were positive aspects mentioned that helped some participants feel more at ease and facilitated surrendering to the experience during the session. These were mainly the well-organized course of the whole study, the fact that they were informed very thoroughly and detailed about the proceedings of the trial. Therefore, they felt prepared and safe when the session started. Participants also mentioned that they felt more comfortable during the session, because they were allowed to visit the session room beforehand. Other participants mentioned how looking up videos and stories on the internet about psilocybin beforehand helped them relax during the session. Lastly, a participant mentioned that it might help if they were able to talk to people who had already undergone a psilocybin session in order to hear an experience from someone who has actually experienced it.

Putting the experience into words

Most participants noticed that they had some difficulty putting the whole experience of the psilocybin session into words. For some, this hindered their ability to talk about it with their therapists or share it with people close to them. For two participants this difficulty arose, because they had little to no recollection of what really happened that day:

"In my view I went to sleep and woke up again and in the meantime I have no idea what happened in my head or in my feeling. I have no idea […]Basically, I went to sleep and now I'm better, […] but what happened? How is it possible that I feel like this from one moment to another? […] How do you explain that?[P3]

Another participant recalled a very intense experience, but they still were unable to put it into words properly:

It was very intense, feeling-wise. […]. What it is I don't know, because I didn't see anything [and] heard nothing. It is so difficult to explain, because it really was a feeling. […] It's really a pure experience. [S]o how do you explain something like that? [P4]

This basically vacant experience was hard to put into words in order to share it with family and friends who would inquire about their experiences. This inability to verbalize their experience bothered participants and also made them less eager to share their potential experience with other patients, because they felt like they were lacking a proper story to tell. This difficulty of putting the experience into words extended to explaining the mechanism of action when asked about by the interviewer. They would use phrases and metaphors of which they had heard from their therapists, e.g. "breaking down old connections and making room for new ones", "shaking loose faulty connections", "fluffing up a pillow".

Dark feeling

Just one participant described adverse effects both during and after the psilocybin session. This respondent experienced the whole session as very intense and dark. They felt like they were strapped to the bed and could not move. They also could not convey their experience to the therapists during the session which made them feel alone and helpless. This had two reasons: firstly, they could not put the experience into words at that moment; secondly, they were completely overwhelmed by it. On top of that, this feeling returned after the psilocybin session, and lingered for days and weeks afterwards:

"[…] I have this constant dark feeling with me now. [It] is the only thing that emerged and stayed with me. […]In hindsight I think that it all simmered too long and that I sunk deeper than I actually should have. […] Yeah, that is really tough […]." [P4]

This participant also mentioned doubts about participating in the trial in hindsight, because they were completely overwhelmed by the intensity. It was not what they had expected and also not something they could have imagined experiencing in spite of thorough preparations leading up to the session. Although it was not stated explicitly by the respondent one can infer that the follow-up appointments after the sessions were too little or too late. They mentioned that the adverse effects were "simmering for too long" and that they were "sinking too deep".

Discussion

We will now proceed discussing the results found in the analysis of the interviews, thinking about the possible implications for future psilocybin trials and linking them to existing literature on this topic.

Trust and time

During the interviews it became clear that the formation of a bond of trust between participants and the accompanying therapists plays a crucial role. This is particularly salient since participants seem to experience their position during the session as vulnerable, and the role of the therapists during sessions is to provide support (19). It follows that this building of trust should then preferably take place before the actual session.

One can hypothesize that one of the factors for trust is time. Time to get to know each other, to talk about what is important for and goes on in a participant's head. Time to talk about their history and how this might play a role in the psilocybin experience. As we saw, some respondents found that asking (personal) questions about the therapists helped building trust more quickly. In the end trust is essential for every well-functioning relationship in order to and create a safe space in which one can feel at ease (20). Therapeutic relationships during psilocybin therapy will probably not be an exception to this. However, as we found out some participants experienced too little time to build a proper bond of trust. And the problem of time shortage might be particularly present in this specific patient group as noted by one of the participants. Since these are individuals that have struggled with depression for many years, tried a variety of pharmaceuticals, and had contact with many healthcare professionals without a satisfactory result. In short, these will be patients with a long history and might struggle with building trust. On the one hand this means, that more time is needed, since they have a longer relevant narrative which needs to be explored in order to properly understand them. Yet, the question remains whether or not this is needed in psilocybine therapy per se. On the other hand, it means that their ability to trust might be less and thus there is more time needed to build a bond of trust. One can hypothesize that these two factors influence each other from which a lack of trust, because of time shortage, can arise standing in the way of feeling safe and at ease and ultimately letting go.

One can find insightful scientific literature on the importance of therapeutic alliance and preferred characteristics of psychedelic carers. Both subjects are of course closely related to trust. Therapeutic alliance is best understood as a patient's and therapist's mutual engagement in therapy and the working bond between them (21). It is regarded as a crucial component (and predictor) of treatment success in psychotherapy in general, but can be extrapolated to psychedelic therapy as well. On top of that, it may play a crucial role in surrendering to, facing or overcoming challenging experiences during therapy sessions (22). In this regard the importance of plentiful preparatory sessions is stressed again.

Forming an adequate therapeutic alliance is of course dependent on trust (20). A recent study identified two trust enhancing factors, namely a) a pre-existing relationship to the carer, and b) predictability (23)**.** The first factor was also noted by subjects in this study and is very understandable from a logical point of view. However, a pre-existing relationship can also be achieved by expanding the number of preparatory sessions. Predictability means subjects entrust that carers will stay with them as long as it is needed and they understand and anticipate the behaviours of the participants (23). This can also be established during preparatory sessions with detailed description of how psychedelic therapy sessions take place and explaining the role of the therapist.

Music

In the interviews one participant found the music during the session distracting. On the one hand, this could mean that apparently the music did not connect with their needs. On the other hand, this may translate to an inability to let go and surrender to it. In line with the latter, this participant also remarked that they were ill at ease and very aware of their surroundings during the session. This could explain why they were resistant to the music. These findings seems to be in line with other studies on the subject of music during psychedelic therapy. Since they found that music plays a key role for participants if they are able to surrender to it (24,25). However, future research should be conducted into particular selections of music and how they influence the experience (and outcome) of patients in order to further optimize the usage of music during psychedelic therapy. If music is really emphasised as a therapeutic aid during psychedelic therapy due to its profound influence then it is worth investigating the possibility of individually tailoring the music to patient's therapeutic needs (26).

Sleep

Multiple participants mentioned they slept through the greater part of the session. On top of that, some participants had less trouble sleeping afterwards for some time. That psilocybin, a serotonergic drug, affects sleep in some way or another is nothing new. Since it follows from our current knowledge about the role of this neurotransmitter and our circadian rhythm (27,28). However, it is incompletely understood. In recent scientific literature there is little to no mention about sleeping during psilocybin sessions. One can ponder whether subjects fell asleep, because they were handed a placebo or whether they were at ease because of the setting, i.e. waited blanket, blindfold, music and so on. Furthermore, many patients suffering from depression have trouble sleeping at night, making them tired during the day and eventually more prone to falling asleep. Yet, these are just speculations and future research into this subject should be conducted in order to understand these mechanisms properly.

Challenging experiences

One participant had serious challenging experiences during the session that even lasted until weeks after the dosing day. They noted that they had difficulty telling the therapist what they were experiencing, because they could not find the words to do so. Therefore, they found that they could not ask for help. This resulted in prolonged adverse effects, which they would describe as the result of "the psilocybin simmering too long", which they understood as experiencing the adverse effects without adequate help.

Clinical literature suggests a possible shared profile of adverse effects between psychedelic substances and categorized them as follows: fear, panic, paranoia, sadness, depressed mood, anger, cognitive effects, perceptual effects and physiological effects (19). In general, these challenging experiences can be minimized and successfully managed through extensive screening, preparations of subjects and the setting the session takes place in (29). Especially, preparing subjects for the possibility of adverse effects and how to behave when they are encountered, i.e. notifying therapists, might play a crucial role in their management. Since challenging experiences can also occur after psychedelic therapy, subjects should be informed about this as well. (30). There are tools that can be used to identify and classify different challenging experiences in order to adequately tackle them. These tools could be used to inform participants about the possible adverse effects beforehand and also to evaluate the experience after a session (31). The Challenging Experience Questionnaire (CEQ) was developed and validated as a new valuable tool for identifying difficult experiences during psilocybin sessions (30**).** This not only increases

the precision of our understanding of these experiences. It also might help us understand and facilitate treatment optimization and tackling difficult experiences when they occur during or after psychedelic therapy.

Limitations

One of the limitations is the methodology of this study. Particularly the amount of time between the participant's psilocybin session and the moment they were interviewed, which was three months. This raises the question how accurate and truthful the shared experiences during the interview were compared to the lived experience at the time. Since participants might already have interpreted their experiences in a certain way giving rise to a biased recollection of the events. However, due to study design and logistics there was no other option, making this limitation inevitable for the current study. Yet, it might be beneficial to interview participants sooner after the session in order to obtain a more precise recollection of their experiences during the trial. However, interviewing participants too soon after the session will most likely also result in a distorted recollection of the events since the experience also needs time to settle in. Ultimately, the question remains whether there is an optimal point in time after the session in which participants should be interviewed. Another limitation is the relative small sample size (n=4) used in this paper. For a more extensive and thorough understanding of the variety of experiences a larger sample size is definitely needed.

Conclusion

We conclude that trust in therapists is a crucial factor in shaping participants' experience during psilocybin therapy. Without trust participants seem to have trouble feeling at ease and surrendering to the psilocybin induced experiences. Furthermore, they might be distracted by the music or become very self-aware instead of trying to let go. This can potentially influence the outcome for the worse. In order to build trust, time is of the essence. How much time is needed differs per person and is, among other things, related to their history. Although time might be scarce, the investment of it is necessary in order to facilitate a more optimal course of the treatment. Participants experienced the preparatory sessions during which they got elaborate information about the treatment and possible effects of psilocybin as very pleasant and helpful in order to surrender more completely. Lastly we saw that participants had difficulty putting their experience into words, either because they slept through the session or found that they were unable to capture the feeling in words. Although this might complicate sharing their experience with others, they mostly noted that what is important is whether or not they benefited from the treatment.

We suggest that more research is needed into several aspects of psilocybin therapy. Firstly, it should be investigated when participants can best be interviewed after their session in order to give the best and most detailed account of their experience. Secondly, the effect of psilocybin on falling asleep during sessions and whether or not this is dose depended needs clarifying as well. Lastly, it might be valuable to increase our understanding of the role of music and whether or not more individualized playlists may enhance the experience.

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