# Phenomenological qualitative analysis of participants' experience of the first clinical trial of psychedelic-assisted therapy for a disorder of gut-brain interaction

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## Background

The psychedelic agent psilocybin is a serotonin agonist that has shown remarkable promise for the treatment of refractory psychiatric conditions, leading to its designation as a "breakthrough therapy" by the United States Food and Drug Administration.

Amongst its scope, psychedelic-assisted therapy (PAT) is a historical and now re-emerging modality for treatment of chronic pain. Psilocybin has effects on brain networks associated with subjective experience of personal narrative and of pain and has yet unexplored effects on the brain-gut axis, making it an intriguing therapeutic for irritable bowel syndrome (IBS).

**We aim to investigate psilocybin-assisted therapy as a novel treatment for treatment-refractory IBS.**

The phenomenological, qualitative analysis of participant's experience may allow us to evaluate subjective experiences and perceived mechanisms of change and healing of this novel therapeutic approach.

## General Study Design

A multidisciplinary study team comprising experts in neurogastroenterology, psychiatry, psychology, cardiology, and neuroimaging was assembled to design a pilot trial of psilocybin-assisted therapy (PAT) for IBS.

- The study design is an open-label, waitlist-controlled trial of 14 participants.
- Participants will receive two doses of 25mg oral psilocybin in conjunction with psychotherapy.
- The parent study's primary outcomes are feasibility and safety.
- It will also explore IBS severity, daily reported abdominal pain, and pain responsiveness on fMRI, changes in inflammatory biomarkers and heart rate variability.
- Qualitative data will be collected at end of therapy, 3-, 6-, and 12-months of follow-up.

## Qualitative Study Methods

This study received the first ever investigational new drug (IND) approval granted by the FDA's Division of Gastroenterology.

An Acceptance and Commitment Therapy (ACT)-based psychotherapy manual was developed and training in disorders of gut-brain interaction (DGBI) was delivered to nine psychiatrists who will serve as study therapists.

A qualitative written response will be collected of each participant after each dosing session

A semi-structured interview guide was developed and approved by IRB.

For the phenomenological qualitative evaluation, semi structured interviews will be analyzed using interpretative phenomenological analysis framework to examine patient's experiences, themes, mechanisms of change, and evaluation of the intervention and help guide further interventions.

## Results

**We have successfully enrolled 7 participants thus far, four of which have concluded the intervention.**

*"…I do not care at all about IBS symptoms. I am noticing sensations and processing them as sensations rather than pain or indicators of something wrong. I am not worrying about going to the bathroom before I go or dwelling on it after I go. It is a tiny event in my day rather than something that consumes my thoughts for most of the day. I am less strict about my diet. I'm able to accept that sometimes comfort food is comforting and that outweighs the discomfort I feel after eating it. I'm not villainizing certain foods anymore. I am breaking long standing routines and releasing some of my rigidity around things that I have done in a certain way for years. "*

*"I think really maybe just like right off the bat, like from right after the first session. I can't remember exactly, but sometime within the first few days, definitely like things changed a lot with just having like a lot more like regularity with my bowel movements and like not having any pain, which is really good."*

*"I felt feelings of anxiety about what was happening and resisted an intense urge to tear off the eye shades and headphones. I wondered if the point of the therapy was to exert agency to "awaken" from IBS, and tearing off the eye shades and headphones could be symbolic of my choice to do that. But I reminded myself to trust the therapists since they seemed to generally encourage keeping those things on (although they always said it was okay to take them off, too)."*

*"I'm less sensory avoidant in SO many ways. Most notable are my improved tolerance for cold plunges and my ability to use both hands to apply my skincare routine. I've always only been able to have 1 finger "dirty" at a time or my skin starts to crawl. Now I can use both hands and multiple fingers and it's saving so much time."*

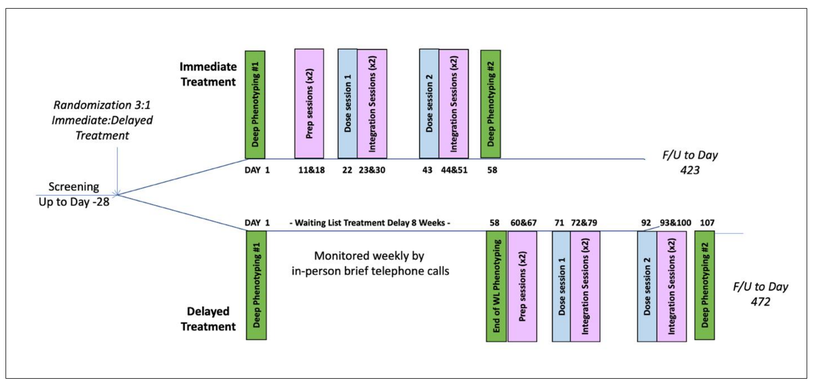


Figure 1: Protocol:

*"I am struggling with how to reconcile the concept of acceptance (this is the plane of reality within which I exist; surrender to it) and commitment to curating goals for a better life. And I still wonder: can we somehow tell my subconscious to shift from the IBS plane to the healthy plane?"*

*"I mean, I think I've changed a lot of things in my life as far as like I think self-care is probably like the biggest one and prioritizing that and thinking about it in a really different way than I did before. I would say generally, relationships are improved with most people in my life."*

*"I kept hearing someone scream "I hate you" and couldn't tell if they were yelling at me or the music. I now think that was me as a child yelling at me. She's mad that I never took care of her the way I take care of others. I'm curious now about this internal drive to be a caretaker and why it doesn't extend to me. I will go above and beyond for my patients and get in trouble at work for poor productivity because I'm handing out juice and cookies on the dementia floor instead of working but I won't let myself feel things deeply or be needy. I think I am a lot more emotionally complex or need than I want to be and focusing on others or on physical ailments helps me push that away."*

## Conclusion

PAT shares several mechanisms of action with existing brain-gut behavioral and medical therapies for IBS and may be efficacious in treating refractory forms of DBGI, particularly when comorbid with psychiatric conditions. We hypothesize that our approach to treating DGBI with PAT will be safe and feasible, and that and that our multidisciplinary analysis will drive understanding of the therapeutic mechanisms of PAT for somatic symptom disorders more broadly. The qualitative analysis of participant's experience of this study will drive development of full-scale clinical trials of PAT for various IBS subtypes. Future studies of psychedelic agents for other DGBI may lead to additional treatments for disorders with few effective therapies.

## References

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