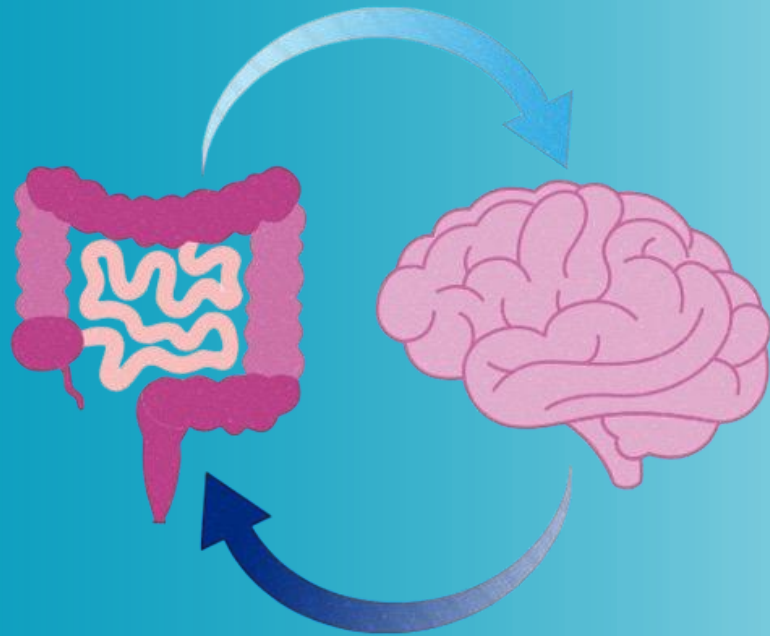




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# Psilocybin-Assisted Therapy for Irritable Bowel Syndrome



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# Disclosures



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I have the following relevant financial relationship with a commercial interest to disclose:

Research funding – Tryptamine Therapeutics

# The Gut-Brain Axis Mediates Mood and Behavior



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*The Treatment of Melancholia by the Lactic Acid Bacillus.* (1) By J. GEORGE PORTER PHILLIPS, M.B., B.S. (Lond.), M.R.C.S., L.R.C.P., Assistant Physician, Bethlem Royal Hospital.

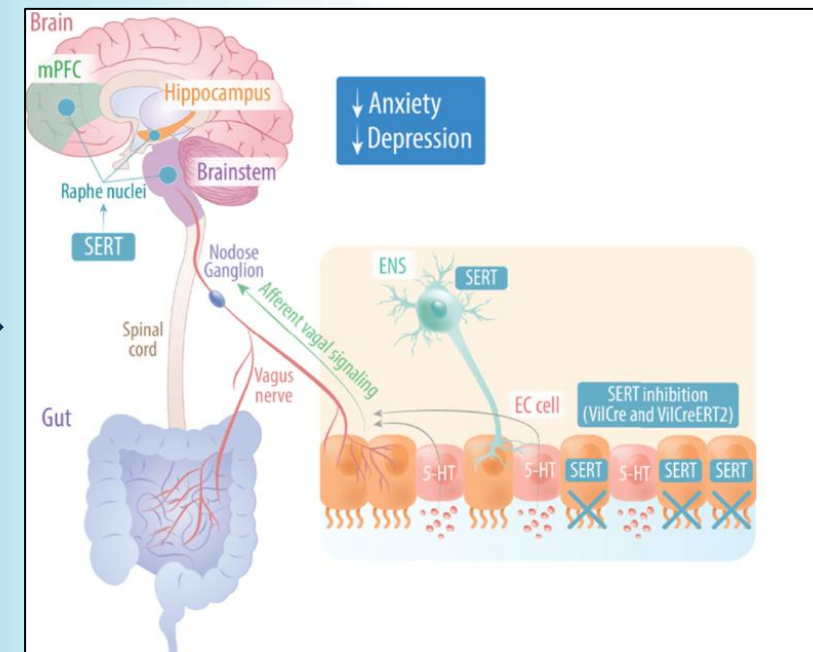
MELANCHOLIA, with its attendant constipation and faulty alimentation, lends itself at once to a dietetic form of treatment.

Whether the constipation is dependent on defective innervation and is a direct symptom of melancholia or is the initial cause of this mental disturbance, it matters not so far as our endeavours in treatment are concerned.

It is obvious that the melancholiac, in the acute stages of his illness, struggles against great odds owing to the following facts: His alimentation is defective, his excretions are diminished, and, moreover, his whole system is in a state of auto-intoxication. In other words there is a general clogging of the metabolic processes. The disturbance of the alimentary tract tends to form a vicious cycle hindering the nervous system from obtaining an efficient and pure food supply.

*Journal of Mental Science* 1910

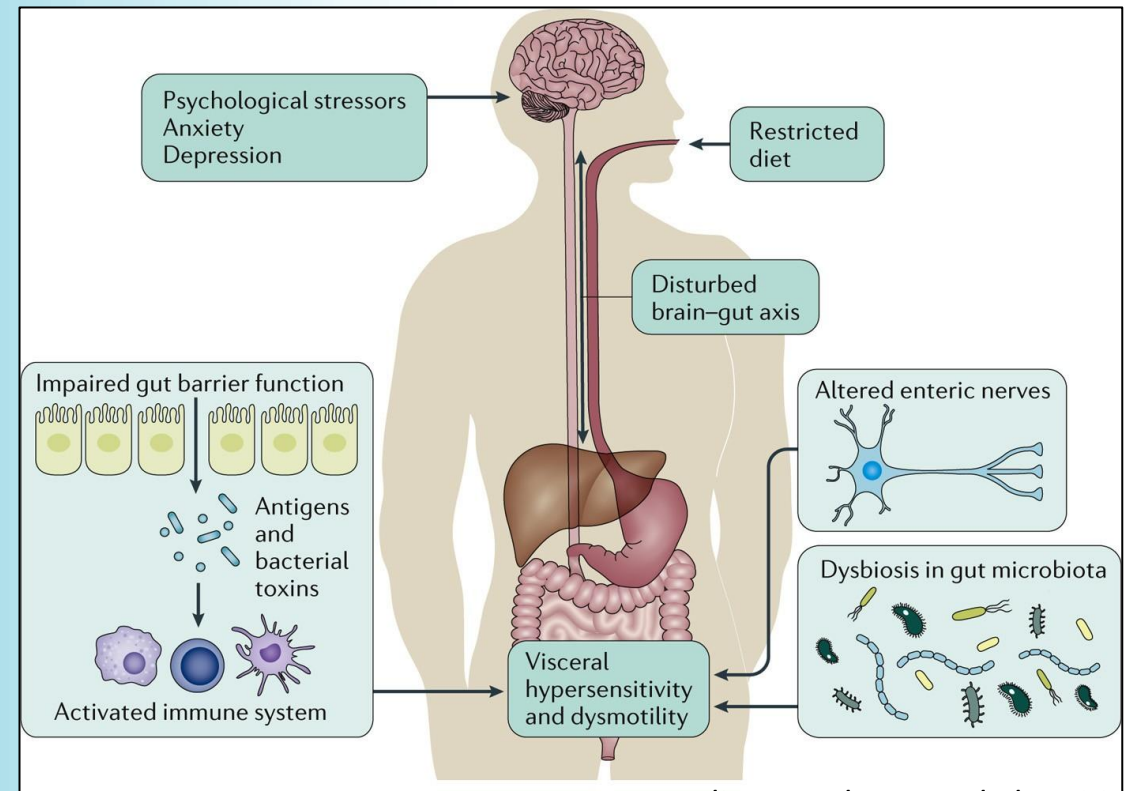
## Intestinal Epithelial Serotonin as a Novel Target for Treating Disorders of Gut-Brain Interaction and Mood



*Gastroenterology* 2025

# Irritable Bowel Syndrome (IBS) is a Pain Disorder Shaped by Trauma

- **5 – 10%** of the population
- Abd. pain + gut motility/defecation changes
- **Visceral hypersensitivity**: lower threshold for pain in GI tract
- **2-3X** as likely to have **anxiety +/- depression**
- **Early life trauma** → permanent changes to gut-brain axis



*Aliment. Pharmacol Ther.* 2019

*Nat. Rev. Gastro* 2016

*Neurogastro & Motility* 2016

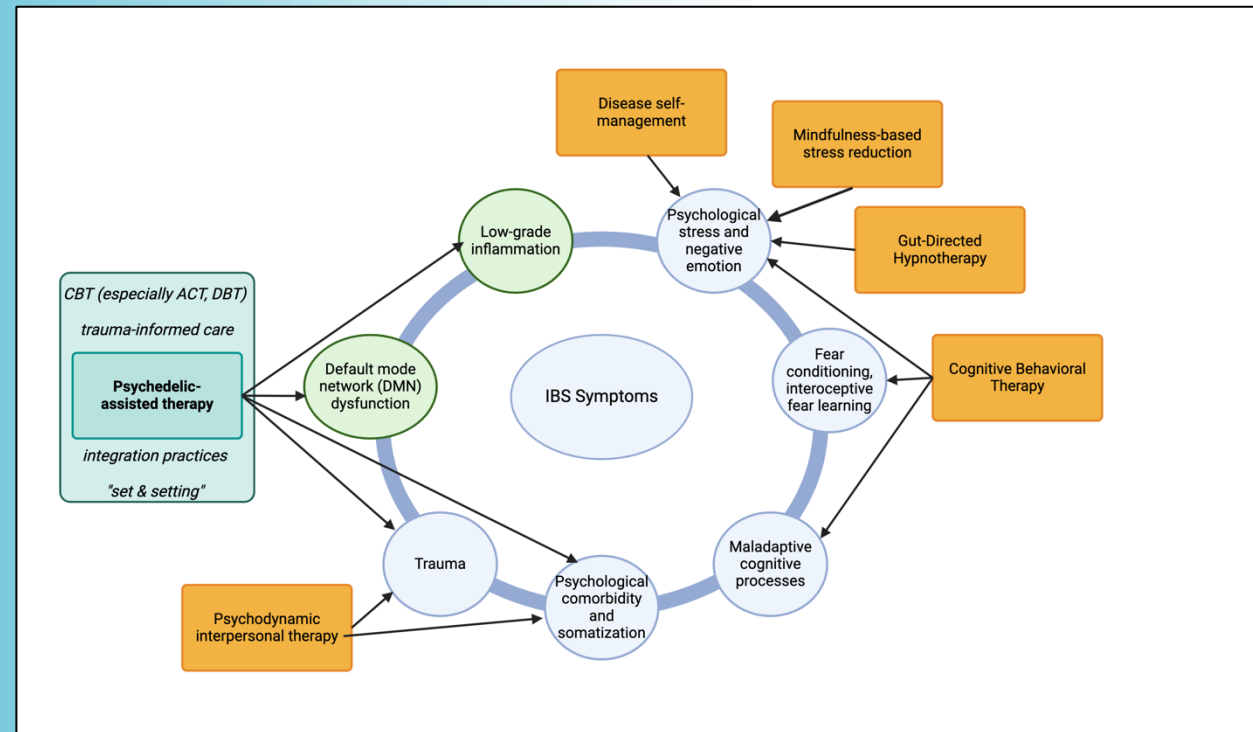
# Why Psychedelic Therapy for IBS?

## Psychedelic-assisted Therapy as a Promising Treatment for Irritable Bowel Syndrome

Mauney, Erin MD<sup>\*</sup>; King, Franklin IV MD<sup>†</sup>; Burton-Murray, Helen PhD<sup>‡</sup>; Kuo, Braden MD<sup>‡</sup>

[Author Information](#)

*Journal of Clinical Gastroenterology* 59(5):p 385-392, May/June 2025. | DOI: 10.1097/MCG.0000000000002149



*Journal of Clinical Gastro.* 2025



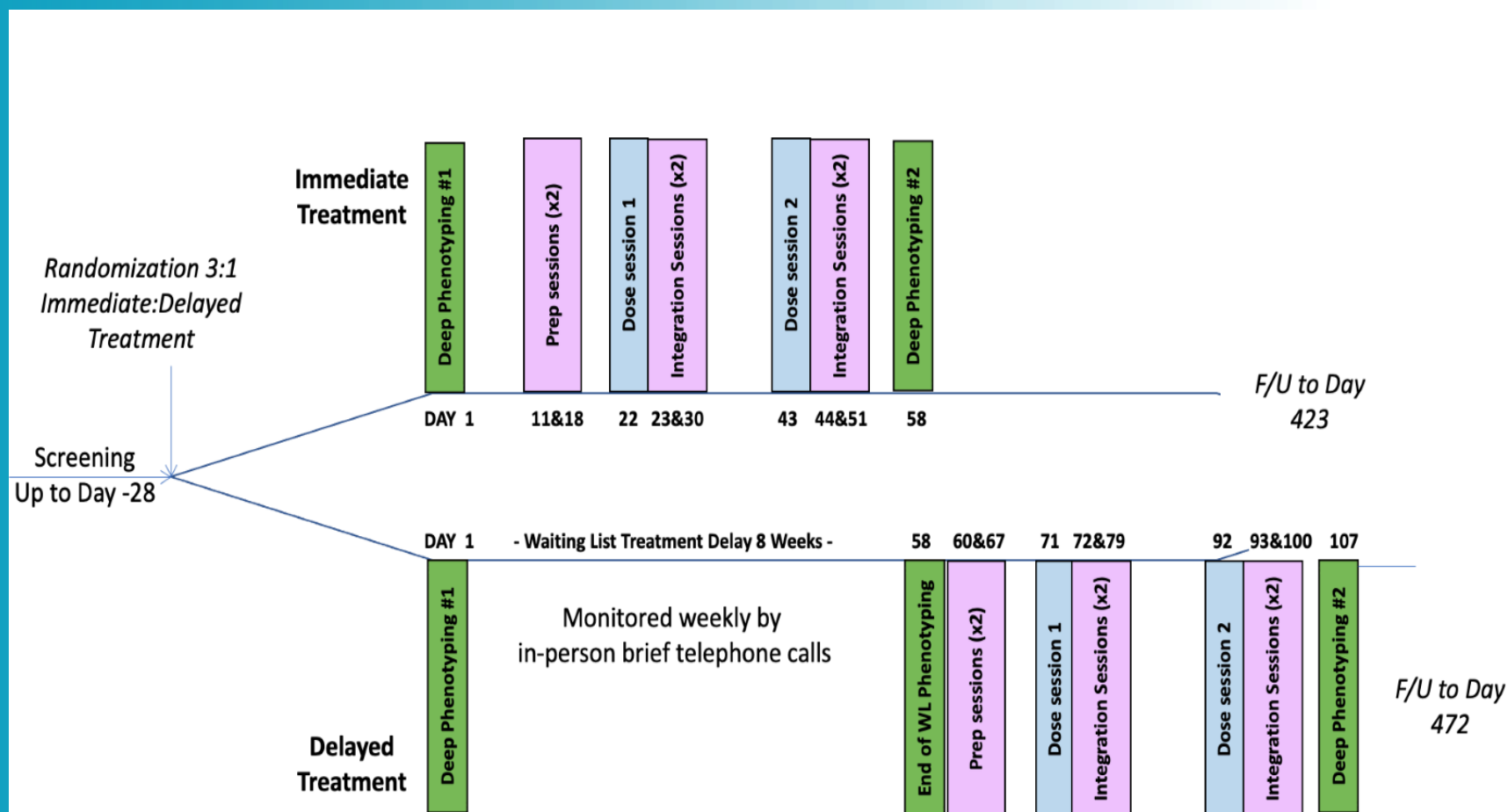
# Phase 2 Pilot Study Design:

Open-label, two-dose protocol with psychotherapy integration

- **Single-center**
  - 14 participants
  - Inclusion criteria: Treatment-refractory IBS, age 21+
- **Intervention:** Two sessions of 25mg psilocybin-assisted psychotherapy (~ACT) + prep/integration vs. waitlist control (3:1)
- **Outcomes:**
  - Primary: safety, feasibility
  - Mixed methods



# Study Schema







# Exploratory Outcomes

Wristwatch tracking (HRV, sleep)

Daily pain/stool diaries

Neuroimaging

Surveys (IBS-SSS, psychological flexibility, anxiety/depression, visceral sensitivity)

Qualitative (writing, interviews)







# Enrollment and Dosing

- Screened 447 → 12 enrolled → **3 completed 12-month follow-up** → **6 active** → 3 partial completion/drop-out after enrollment

## Demographics:

### *Race:*

8.3% Asian

8.3% Black or African American

83% White

### *Sex Assigned at Birth*

75% Female

25% Male

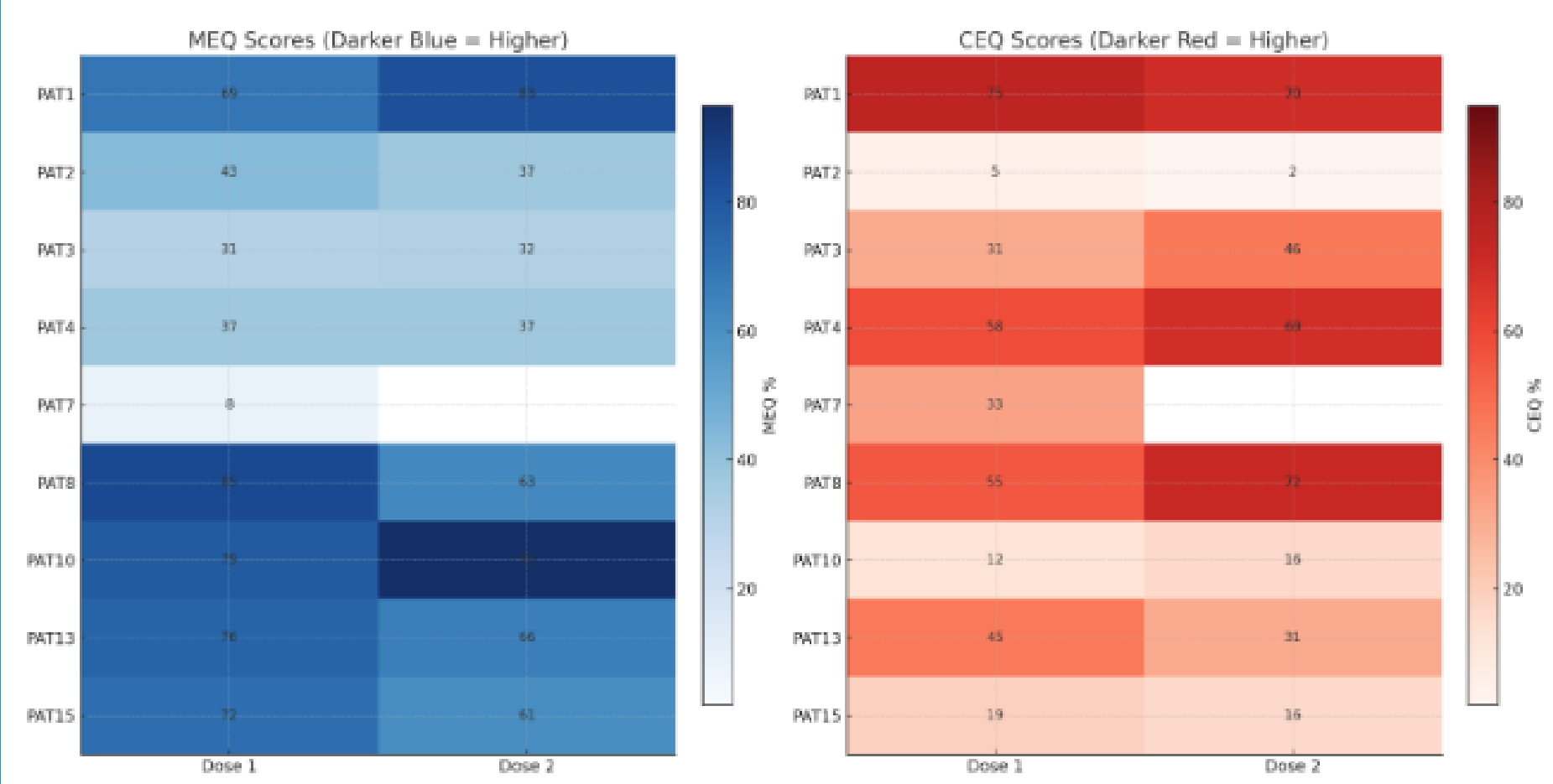
### *Ethnicity:*

17% Hispanic

83% Non-Hispanic or Latino



# Patients Described Intense, Variable Dosing Experiences

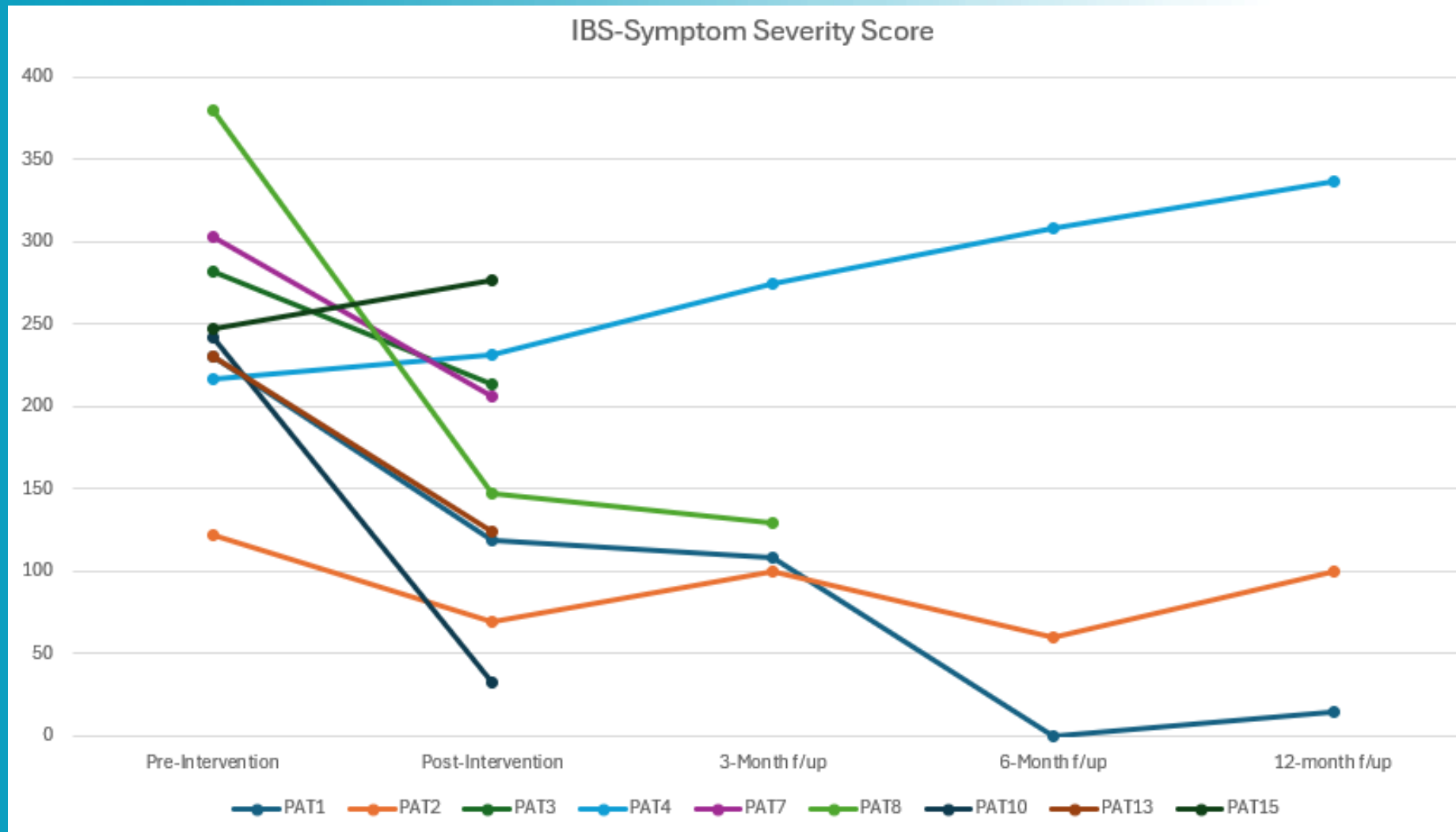


# IBS Symptoms Improved After Dosing



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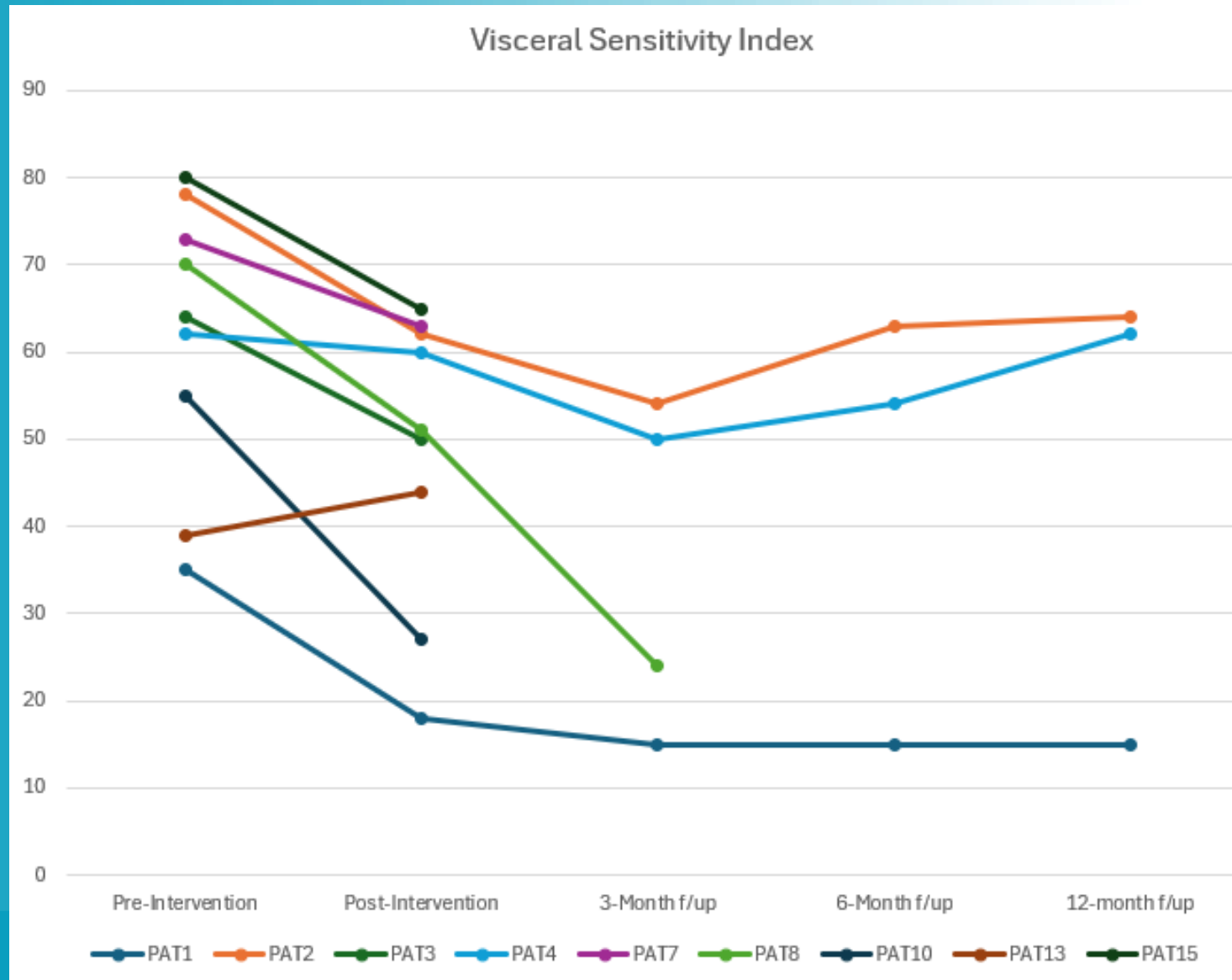


# Visceral Sensitivity Improved After Dosing



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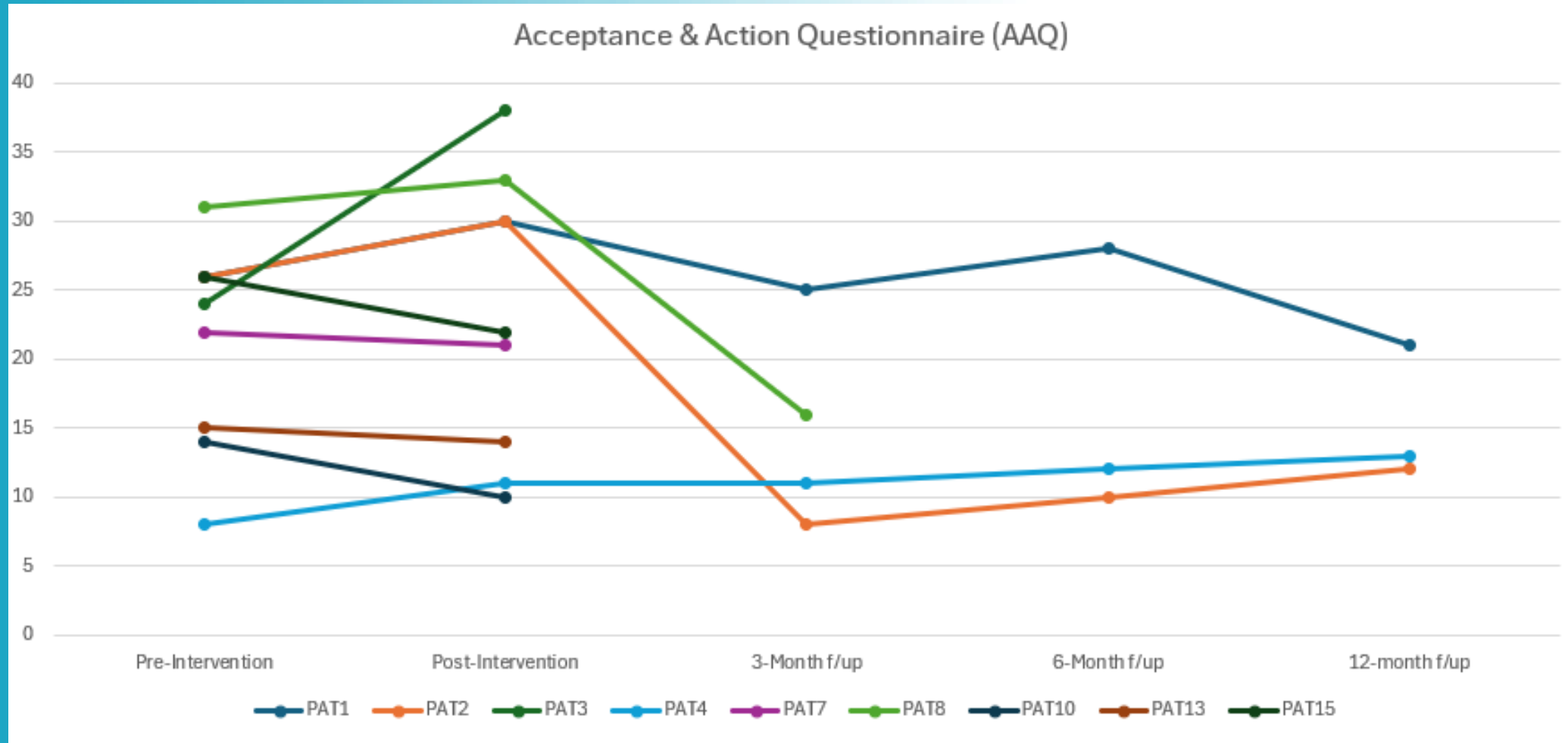


# Psychological Inflexibility After Dosing



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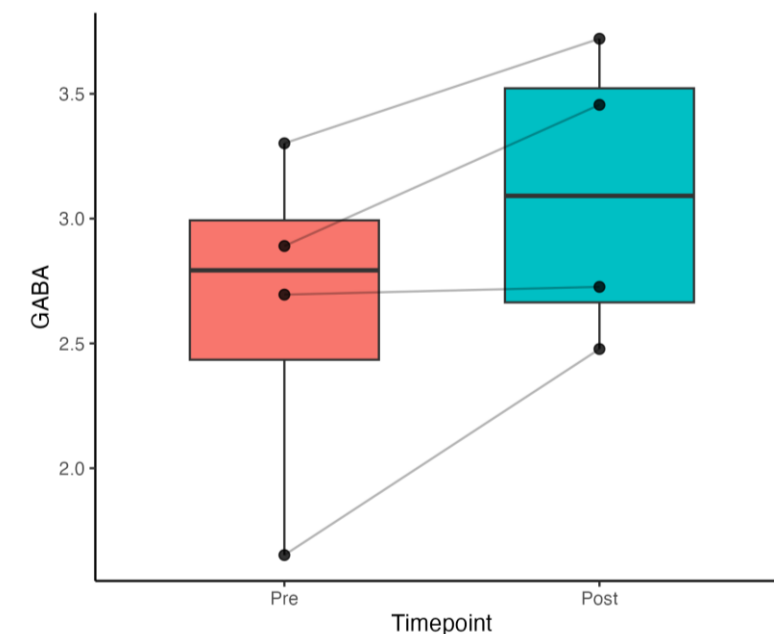
# GABA increased in the anterior insula pre- vs. post-intervention ( $p = 0.06$ , $n = 4$ )



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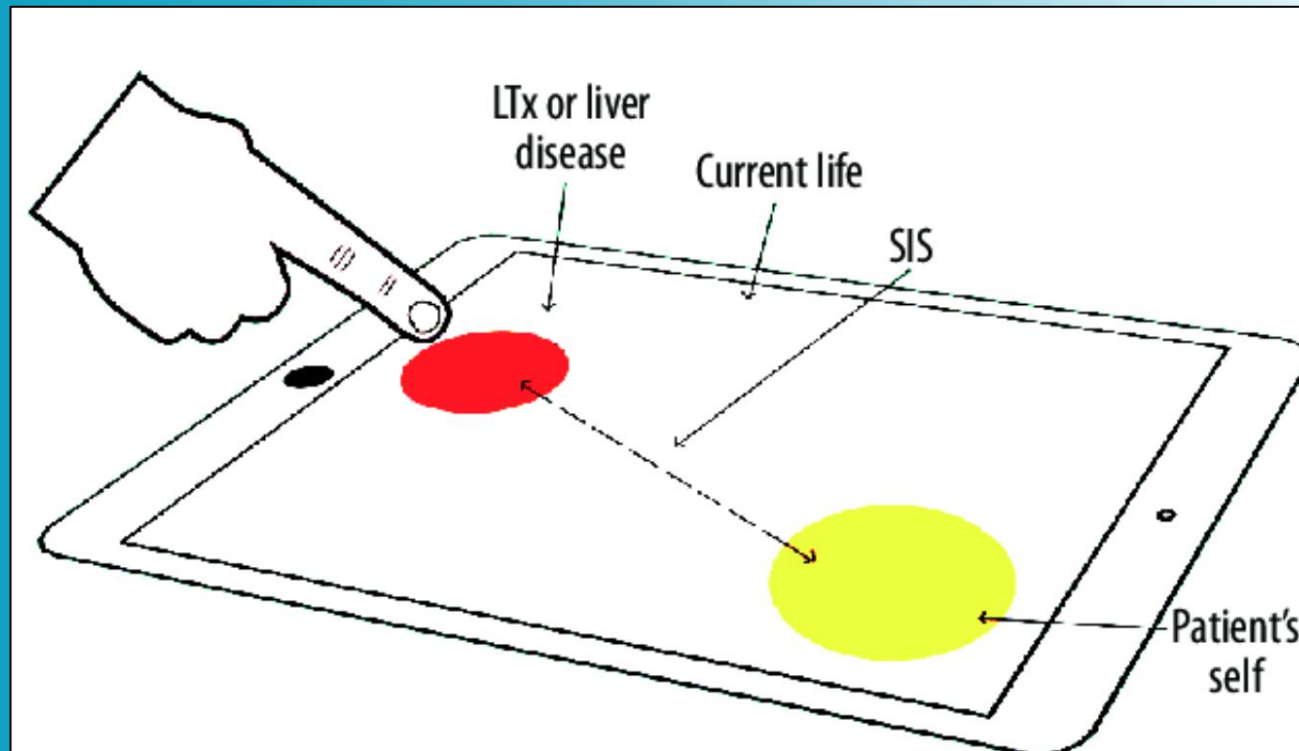
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Anterior Insula – Integration of internal bodily signals, sensory signals, and pain





# Shifting Identity: Self vs. Illness

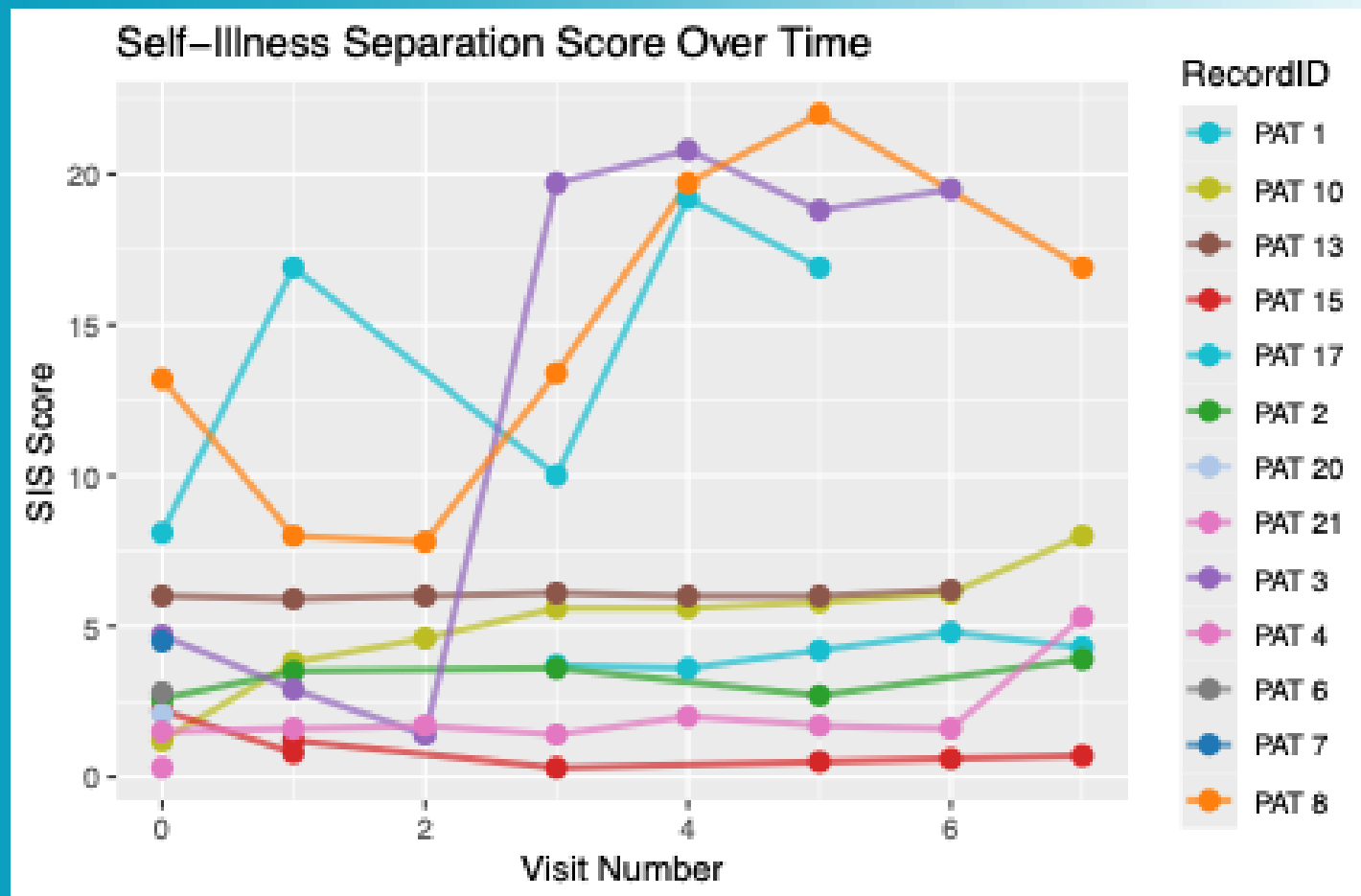


# Increased Separation Between Self and Symptoms After Dosing



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# One Case of Post-Dosing Destabilization Led to Protocol Refinement

- One episode of **suicidal ideation** lasting six weeks post-dose #2
  - Managed with additional integration sessions, medication bridge, ED eval and cleared for outpatient. In ongoing therapy (outside of study)
- IRB and FDA review → added SI to consent form, added additional pre-enrollment interview, allow participants on SSRIs into study



# Deep Change: PAT1's Story

This heron was ancient and very wise. **He taught me to take my IBS pain and discomfort, and turn it inside out, and push it out. I had a small, soft bird belly. I could take the sensations and turn them inside out, and they left my body in a shower of small white downy feathers.**

Post-Dose #2 Journal

I still think about [the study] every day...  
**I think that I have a much better awareness of what I need for self-care and implementing it.** And yeah. And you know being able to engage in those things really helps to manage my stress overall....  
So interestingly, **in the past two months, maybe, [my IBS] is gone...** I haven't really had any issues whatsoever, which is like really weird because life has been very stressful

6-Month Follow-Up



# PAT8's Qualitative Reflections on Somatic Opening

At another point I felt **a strong feeling of being overwhelmed and that it needed to get out of my body**. [The therapists] helped me get it out by making me feel like I was pulling my chest open, which seemed to work. At another point I **felt this hard shell around my chest, which represented a little me of stored emotions, just dissolve and flow out of my body**.

Post-Dose #2 Journal

I just had things that I felt like were like stored in there that I needed to get out. And I felt like both of my sessions had **some very clear both physical things that were like getting things out of my body and also like kind of emotional releases** of just like literally and physically like getting things out of my body, which was just **fascinating to kind of see that I had kind of talked about that in my prep session and then to see that kind of manifest in these dosing sessions**, which I thought was really interesting.

Additional reflections at the end of active intervention



# PAT4 Qualitative Reflections

It seems notable that I had these intensely powerful experiences across both medication days but never cried or burst out in rage. **I wonder to what extent I feel feelings with my body instead of feeling them with my mind.** I noticed that [the therapist] often asks, "how are you feeling?" and **I usually answer with some physical indicator and not how my emotions feel**

Immediate Post-Treatment

And so I think about that quite often in terms of **am I being open or closed right now? Am I pursuing that approach that I felt like maybe that was an answer about how to orient my life?** And so there are things like that that pop up quite often.

6-Month Follow-Up





# Preliminary Conclusions

## 1. Feasible & physiologically safe

- - Risk of destabilization, especially in patients with a trauma history & little psychological mindedness.

## 2. Extremely variable intensity of dosing experiences

## 3. PAT can decrease IBS symptoms and GI-specific anxiety -- ? not mediated by psych. flexibility

- **Limitations:** small N, open-label, highly self-selected population



# Where Do We Go From Here?

- Increasing diversity, generalizability
- Managing/incorporating GI “side effects”
- Matching patient + drug + therapy – cyclic vomiting, functional dyspepsia, ARFID
- Mechanisms: motility, microbiome, food diaries, mediating effect of trauma history

# Acknowledgements



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**Co-PIs:** Franklin King, Erin Mauney, Brad Kuo

**Study Therapists:** Emily Sorg, Albert Yeung, Trevor Stevens, Lisa Summer, Juliana Zambrano, Deborah Meisel, Halsey Niles, JJ Hermina Perez

**Clinical Research Coordinators:** Andy Bolender, Victoria Beck, Seneca Ellis, Blythe Peterson, Lara Gardiner, Kyla Gary

**GI Psychologist:** Helen Murray

**Spaulding/Neuroimaging Team:** Vitaly Napadow, Alessandra Anzolin, Michael Datko, Arvina Grahl

**Cardiology Team:** Jeremy Ruskin, Acile Nahlawi, Leon Ptaszek, Galal Ramadan, Ghazal Sanadgol, Mohammadhossein Yazdanpanah

**Biostats:** Nora Horick

**Funding Sources:**

Tryp Therapeutics, Atai life sciences fellowship, Center for the Neuroscience of Psychedelics, Center for Integrative Pain Neuroimaging, Center for Cardiac Arrhythmias, Center for Neurointestinal Health



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