Sydney Medical School
University of Sydney
Sydney, NSW, Australia
itod2305@uni.sydney.edu.au

December 11, 2025

Editor-in-Chief
Translational Psychiatry

Dear Editor,

We submit our manuscript "**Psychedelics as Dimensionality Modulators: A Cortical Reservoir Theory of Serotonergic Plasticity**" for consideration as an Article in *Translational Psychiatry*.

Clinical significance. As psychedelic-assisted therapy enters mainstream psychiatry, clinicians face a critical challenge: how do we quantify the neural mechanisms that distinguish therapeutic response from mere drug effect? Our work provides a direct answer: MEG-derived oscillatory coherence serves as a real-time, mechanism-specific biomarker for "psychedelic depth."

Key findings with immediate translational relevance:

1. **Mechanism-specific biomarker.** Analysis of 136 MEG sessions across four compounds reveals a striking dissociation: classical psychedelics (psilocybin, LSD) produce significant oscillatory desynchronization (psilocybin: -15%, $p = 0.003$, $d = -0.78$), while ketamine shows no effect ($p = 0.29$). This specificity—psychedelics desynchronize, dissociatives do not—provides a neural signature that distinguishes therapeutic mechanisms at the neurophysiological level.
2. **Clinical decision support.** The MEG biomarker enables three immediate clinical applications: (i) real-time monitoring during therapeutic sessions, (ii) precision dosing based on neural response rather than fixed milligrams, and (iii) patient selection by identifying likely responders through baseline cortical flexibility.
3. **Mechanistic framework for treatment optimization.** Our three-phase model (overshoot $\rightarrow$ refractory $\rightarrow$ recanalization) provides a principled basis for integration timing, session spacing, and adjunctive interventions during the critical plasticity window.

Why Translational Psychiatry. This work bridges basic neuroscience (eigenmode dynamics, reservoir computing) with clinical application (biomarkers, dosing protocols). The dimensionality framework moves psychedelic research from "entropy increases" to quantitative, testable predictions about therapeutic mechanisms. *Translational Psychiatry*'s readership—spanning psychiatrists, neuroscientists, and clinical researchers—is ideally positioned to evaluate and implement these findings.

Scope and novelty. While dimensionality metrics have been applied descriptively to psychedelic neuroimaging, our contribution is fundamentally different: we propose that effective dimensionality is not merely a correlate but the *computational function* of psychedelic therapy. The MEG validation provides the first compound-comparison evidence that oscillatory desynchronization is mechanism-specific, with direct implications for distinguishing psychedelic-assisted from ketamine-assisted therapy.

All data analyzed are publicly available (OpenNeuro ds003059, ds006072; Muthukumaraswamy

MEG repository). Code is available at `https://github.com/todd866/lsd-dimensionality`. The author declares no competing interests.

Respectfully submitted,

Ian Todd
Sydney Medical School
University of Sydney