

What Should Neurofeedback Control in Psychiatry?

A Low-Dimensional Brain-State Framework for State-Dependent Intervention

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Introduction

Real-time neurofeedback has shown promise as a method for modulating brain activity, yet its clinical application in psychiatry remains limited. A central challenge is the lack of principled definitions of clinically meaningful internal states that should be targeted for closed-loop intervention. While dimensional psychiatry has begun identifying biologically relevant symptom dimensions, existing approaches primarily focus on stable differences between individuals and largely overlook dynamic symptom fluctuations within individuals over time.

Methods

To address this gap, we investigated whether post-traumatic stress disorder (PTSD) symptoms are organized by a latent low-dimensional structure shared across both between-individual heterogeneity and within-individual temporal dynamics. Based on our previously proposed reciprocal inhibition model (Chiba et al., *Mol Psychiatry* 2020), we hypothesized that symptom variation is governed by a common regulatory circuit involving reciprocal interactions between the amygdala and ventromedial prefrontal cortex (vmPFC). We analyzed symptom covariance structures across nine independent PTSD cohorts using principal component analysis and identified universal symptom dimensions. We then examined associations between these dimensions and resting-state functional and effective connectivity within the amygdala-vmPFC circuit.

Results

Across cohorts, we identified a reproducible secondary symptom dimension (uPC2) that captured severity-independent imbalance between re-experiencing and avoidance symptoms, consistent with predictions of the reciprocal inhibition model. Importantly, this dimension characterized not only stable differences across individuals but also temporal fluctuations within individuals over time. Distinct psychotherapies, including Cognitive Processing Therapy and Eye Movement Desensitization and Reprocessing, induced differential shifts along this dimension. At the neural level, uPC2 was associated not with functional connectivity, but specifically with the balance of effective connectivity between the amygdala and vmPFC, and this relationship was independently replicated in a separate cohort.

Conclusions

These findings suggest that clinically meaningful psychiatric states may be represented within a low-dimensional symptom state space linked to specific circuit-level dynamics. More broadly, our results highlight a central challenge for future psychiatric neurofeedback: effective intervention may require identifying latent brain-state variables that reflect dynamically changing symptom states, rather than targeting static diagnostic categories or conventional trait-like biomarkers. This framework may provide a foundation for future state-dependent intervention in psychiatry.

References

Chiba T, Ide K, Taylor JE, Boku S, Toda H, Kanazawa T, Kato S, Horiuchi Y, Hishimoto A, Maruyama T, Yamamoto T, Sora I, Kawato M, Koizumi A. A reciprocal inhibition model of alternations between under/overemotional modulatory states in patients with PTSD, *Molecular Psychiatry* (2021), 26 : 5023–5039