State and Trait Interoceptive Factors Influencing Therapeutic Transcranial Magnetic Stimulation Response

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1 Introduction

Repetitive transcranial magnetic stimulation (rTMS) is an emerging treatment for anorexia nervosa (AN), but clinical response is highly variable and poorly predicted by trait-level patient characteristics (Dalton et al., 2021). One factor that has received less attention is brain state at the moment of stimulation, which strongly modulates the brain's response to TMS (Grosshagauer et al., 2024). This raises the possibility that pre-stimulation state could itself be optimised to improve outcomes. AN involves persistent disturbances in cardiac interoception that remain even after weight restoration (Garfinkel et al., 2015). Under predictive-coding accounts, such disturbances may amplify emotional reactivity to food cues, making AN a suitable population in which to test whether interoceptive state can be experimentally shifted. This study examines whether brief cardiac interoceptive priming modulates autonomic state and TMS-evoked brain responses in individuals with AN compared to matched controls.

2 Methods

Forty participants (20 with DSM-5 AN, 20 age- and sex-matched healthy controls; ethical approval obtained) complete a two-session protocol. In Session 1, baseline assessment includes the heartbeat counting task, the Multidimensional Assessment of Interoceptive Awareness (MAIA-2), and the Eating Disorder Examination Questionnaire (EDE-Q). Resting-state fMRI is then used to identify each participant's left dorsolateral prefrontal cortex (DLPFC) target: the site with maximal anti-correlation to the subgenual anterior cingulate cortex (sgACC). DLPFC stimulation at this site modulates the sgACC, a hub for autonomic-affective integration, in a state-dependent manner (Grosshagauer et al., 2024). In Session 2, participants first complete a brief cardiac interoceptive priming protocol: guided audio is synchronised to their ECG signal and directs attention to bodily sensations of the heartbeat. This is followed by chronometric interleaved TMS-fMRI, with stimulation timed to food-cue events. Continuous ECG enables computation of heart-rate variability (RMSSD). Primary outcomes are TMS-evoked BOLD response in the sgACC and DLPFC, with RMSSD as an additional autonomic state marker. Linear mixed-effects models test Group $\times$ State interactions on BOLD response, with interoceptive accuracy, EDE-Q score, subjective food-cue reactivity, and priming-induced RMSSD shift as moderators.

3 Results

Data collection is upcoming. We predict that cardiac priming will increase RMSSD across participants, with attenuated increases in the AN group, reflecting well-documented interoceptive disturbances in AN. We further predict that priming will enhance the sgACC response to TMS – direct evidence of state-dependent target engagement – and that this effect will be attenuated in participants with lower interoceptive accuracy or higher EDE-Q scores. Effect-size estimates from these comparisons will inform the design of subsequent therapeutic trials.

4 Discussion

This study tests whether a brief interoceptive priming intervention can shift the brain state in which TMS is delivered, providing a mechanistic foundation for state-aware stimulation protocols in AN. A weaker state shift in the AN group would implicate a candidate physiological mechanism for the variable response to rTMS in this population. Cardiac entrainment and focused attention to bodily sensations represent two potential mechanisms underlying the priming effect; disentangling these will require dedicated control conditions in subsequent studies. The two-session design isolates state effects on circuit engagement and provides effect-size estimates for subsequent therapeutic trials.

References

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