

Reduction of Negative Attentional Bias in Depression with Decoding-based fMRI-Neurofeedback

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Introduction

A core feature of our cognition is to guide attention towards valenced stimuli in order to process them, respond adaptively, and disengage when attending is no longer beneficial. Individuals with Major Depressive Disorder (MDD) show an inflexible attentional bias towards negative stimuli and thoughts. Once they attend to negative content, they particularly struggle to disengage from those states, leading to a self-reinforcing feedback loop clinically manifested as cognitive rumination. In this double-blind, randomized controlled study, we applied a validated closed-loop neurofeedback procedure designed to reduce this bias. We hypothesized that decoding-based neurofeedback training would teach patients to disengage from negative states.

Methods

Internal attentional states were decoded in real time from functional magnetic resonance imaging (fMRI) data. Participants were shown overlaid negative face and neutral scene images with variable opacity values and were instructed to attend to the neutral scene while ignoring the negative face. When their decoded attentional state indicated a failure to attend to the scenes, the negative faces became more opaque, thus externalizing the brain's momentary attentional state. Forty-eight participants with MDD were randomly assigned to either the real neurofeedback group (N = 24) or to a sham control group who received feedback yoked to a participant in the training group (N = 24). Each participant completed three fMRI neurofeedback sessions. The main pre-registered outcome quantified the extent to which participants get "stuck" in the most negative attentional state. This occurs when they attend to the negative face and see it grow increasingly opaque but then are unable to draw their attention back to the neutral scene. We hypothesized that, relative to the sham control group, the real neurofeedback group would learn to escape the most negative attentional state more readily from before to after training.

Results

We used a Bayesian linear mixed model to estimate the time-by-group effects. Consistent with our hypothesis, real neurofeedback training reduced the probability of getting stuck in a negative state (posterior mean for group-by-time interaction = -0.223 , SD = 0.110 , 95% HDI [-0.446 , -0.014]; standardized effect distribution (estimating effect magnitude): mean = -0.955 , 95% HDI [-1.925 , -0.052], corresponding to a moderate to large effect). We then asked what consequences such training had on established neural markers of deficient emotional processing in MDD. We modelled the parametric effect of negative face opacity on the BOLD signal during neurofeedback and contrasted the late- versus early-training change between groups. We restricted our analysis to five regions of interest (ROIs) previously highlighted as exhibiting altered responses to emotional faces specifically in MDD compared to healthy controls: left amygdala, fusiform face area, ventromedial and right dorsolateral prefrontal cortices, and subgenual anterior cingulate cortex. ROI analysis revealed that the real neurofeedback group showed a decreased response to negative faces relative to sham in the ventromedial prefrontal cortex (beta = -0.8291 , $t = -2.878$, $p(\text{uncorrected}) = 0.006$, $p(\text{FDR}) = 0.0308$, Cohen's $D = -0.869$).

Conclusions

In this study, we replicate and extend prior work, demonstrating the efficacy of remediating negative attentional bias in MDD with neurofeedback from real-time fMRI. Compared with standard behavioral therapy approaches that have demonstrated relatively weak efficacy in treating this bias, our approach shows promise by targeting the underlying neural mechanisms instead of their downstream behavioral outputs. A larger-scale clinical trial is needed to estimate long-term clinical efficacy. If validated at scale, this mechanism-based approach could lead to precision, brain-based interventions for depression and related affective disorders.