REDUCING THE NEGATIVE ATTENTIONAL BIAS IN DEPRESSION WITH CLOSED-LOOP REAL-TIME fMRI NEUROFEEDBACK TRAINING

Anne C. Mennen[1], Nicholas B. Turk-Browne[2], Darsol Seok[3], Megan T. deBettencourt[4], Kenneth A. Norman[1,5], Yvette I. Sheline[3]

[1]Princeton Neuroscience Institute, Princeton University, [2]Department of Psychology, Yale University, [3]Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, [4]Institute for Mind and Biology, University of Chicago, [5]Department of Psychology, Princeton University

Introduction

Depressed individuals are biased to attend to negative stimuli [1,2], which has inspired attention training research aimed at improving depressive symptoms. However, meta-analyses of behavioral training paradigms reveal mixed efficacies [3-5]. More recently, research has suggested that the negative bias in depression is caused by a problem with disinhibiting negative information [6].To address this issue, we use a closed-loop real-time fMRI task [7] to train sustained attention by forcing subjects to pull themselves out of negative states. Additional tasks were administered before and after neurofeedback to understand how changes in neurofeedback related to other clinical, neural, and behavioral measures.

What differences do we see between depressed and control subjects before neurofeedback?

Can we improve depression severity by training depressed subjects to get themselves out of negative states?

Do the improvements in neurofeedback relate to improvements in other domains?

Study design

GROUP 1: healthy control (HC) n=11

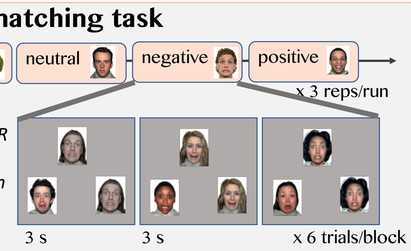
GROUP 2: depressed (MDD) n=14

Task	Clinical assessments	Gaze task [8]	Go/no go attention task [7]	fMRI – resting state	fMRI – Face-matching [9]	fMRI – real-time neurofeedback [7,10]
Symbol	✍	👀	🛑	💭	👧	📈

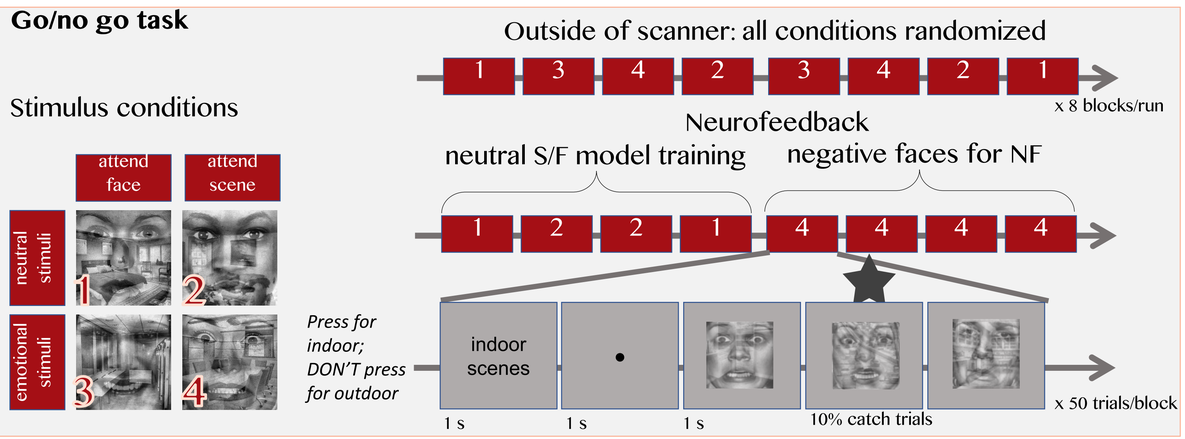
VISIT 1: Pre NF ✍👀🛑 → VISIT 2: NF 1 💭👧📈 → VISIT 3: NF 2 👀🛑📈 → VISIT 4: NF 3 📈👧💭 → VISIT 5: Post NF ✍👀🛑 → VISIT 6: 1M FU ✍👀🛑 → VISIT 7: 3M FU ✍

Gaze task

Face-matching task



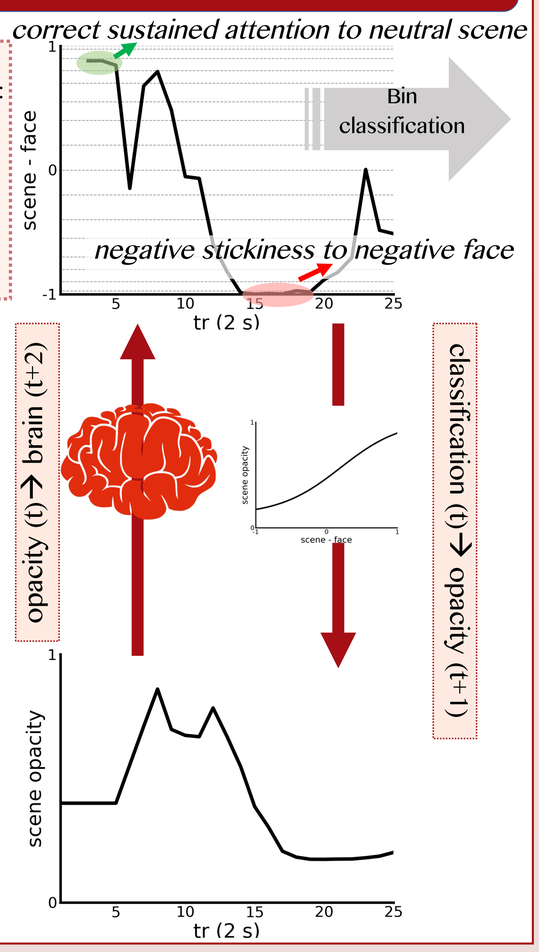
Go/no go task



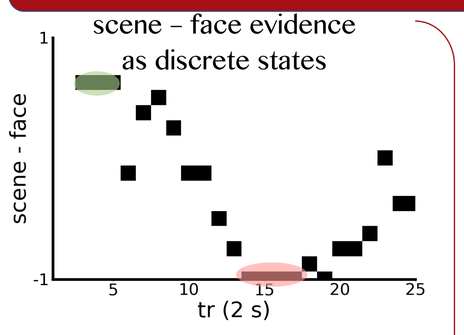
Closed-loop neurofeedback

Example neurofeedback:

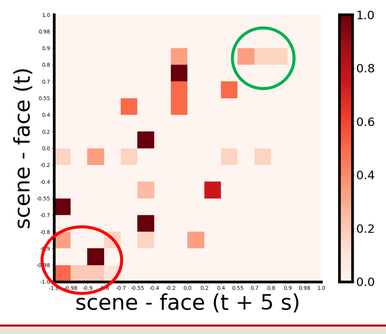
scene – face decoded classification



Quantifying neurofeedback performance

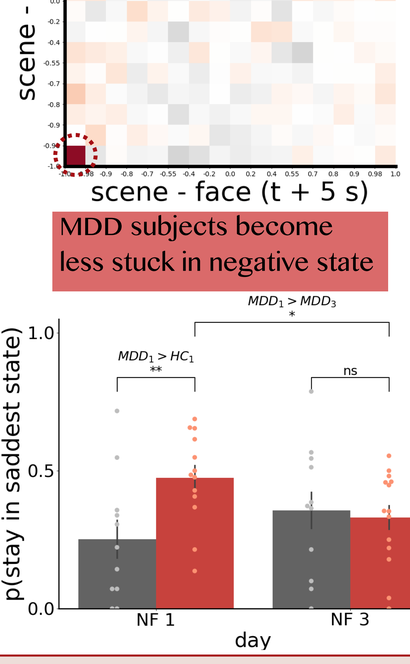


conditional probability: given the classification state at *t*, what is the state 5 s later?



Combine across runs & subjects to compare groups over time

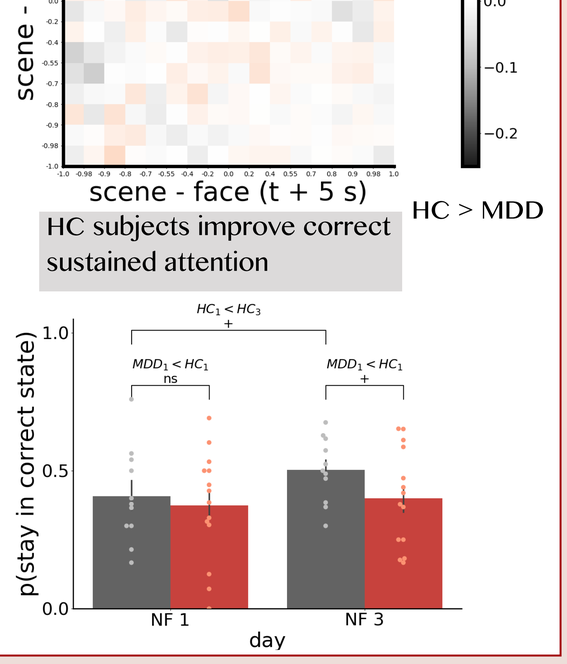
NF 1: largest difference is in most negative state



MDD subjects become less stuck in negative state

NF 3: largest difference is in most correct state

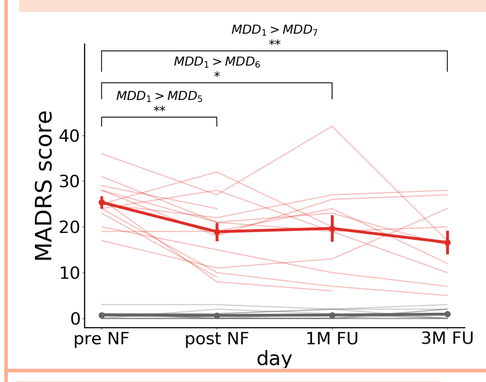
MDD > HC



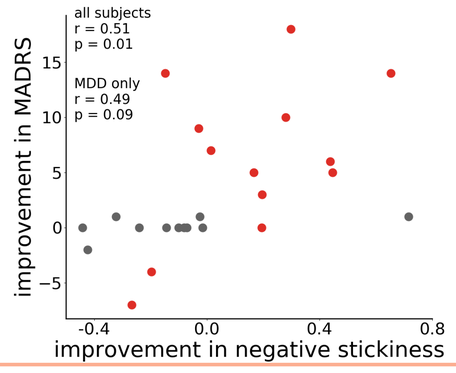
HC subjects improve correct sustained attention

Preliminary results: NF transfer to other measures

Depression severity decreases over time

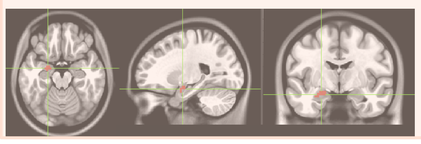


Improvement in NF negative stickiness is positively related to improvement in depression



How does neurofeedback performance relate to response to negative faces in MDD and HC?

Face-matching task: group differences in amygdala reactivity to negative faces



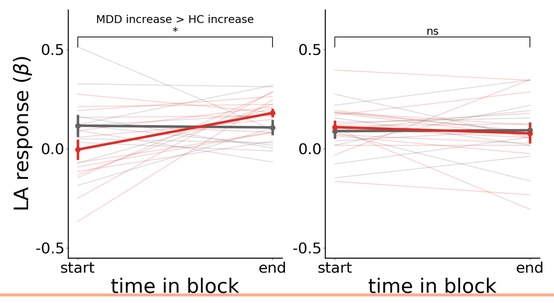
Data preprocessed with fMRIPrep, FreeSurfer, & AFNI

ROI: left amygdala (LA)

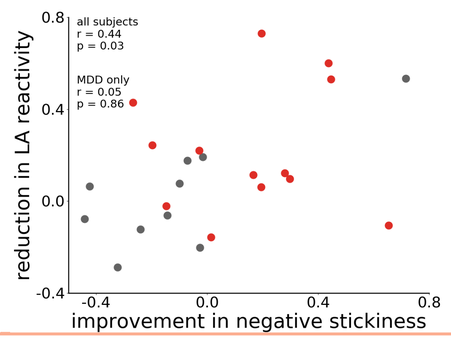
Measurement: beta values during negative face blocks

Pre NF: MDD shows increased reaction to negative faces over block

Post NF: no group difference



Improvement in neurofeedback is related to change in amygdala reactivity



Conclusions and future directions

Over the course of training, depressed subjects improved in terms of depression severity, amygdala reactivity to negative faces, and negative stickiness during neurofeedback. Additionally, the improvement during neurofeedback was related to the improvement in depression and amygdala reactivity.

Future analyses will focus on other behavioral and neural estimates (e.g., resting state, eye-tracking etc.), and analyzing potential links to NF and severity improvement.

Data collection is still ongoing, as we aim to collect 16 subjects per group.

References: **[1]** Gotlib, Ian H., et al. 2004. "Attentional Biases for Negative Interpersonal Stimuli in Clinical Depression." *Journal of Abnormal Psychology* 113 (1): 127–35. **[2]** Mogg, Karin, and Brendan P. Bradley. 2005. "Attentional Bias in Generalized Anxiety Disorder Versus Depressive Disorder." *Cognitive Therapy and Research* 29 (1): 29–45. **[3]** Cristea, Ioana A., et al. 2015. "Efficacy of Cognitive Bias Modification Interventions in Anxiety and Depression: Meta-Analysis." *The British Journal of Psychiatry: The Journal of Mental Science* 206 (1): 7–16. **[4]** Hallion, Lauren S., and Ayelet Meron Ruscio. 2011. "A Meta-Analysis of the Effect of Cognitive Bias Modification on Anxiety and Depression." *Psychological Bulletin* 137 (6): 940–58. **[5]** Jones, Emma B., and Louise Sharpe. 2017. "Cognitive Bias Modification: A Review of Meta-Analyses." *Journal of Affective Disorders* 223 (December): 175–83. **[6]** Mennen, A. C., et al. 2019. "Attentional bias in depression: understanding mechanisms to improve training and treatment." *Current Opinion in Psychology* 29: 266-273. **[7]** deBettencourt, Megan T., et al. 2015. "Closed-Loop Training of Attention with Real-Time Brain Imaging." *Nature Neuroscience* 18 (3): 1–9. **[8]** Kellough, Jennifer L., et al. 2008. "Time Course of Selective Attention in Clinically Depressed Young Adults: An Eye Tracking Study." *Behaviour Research and Therapy* 46: 1238–43. **[9]** Chai, Xiaoqian J., et al. 2015. "Functional and Structural Brain Correlates of Risk for Major Depression in Children with Familial Depression." *NeuroImage Clinical* 8 (May): 398–407. **[10]** Schnyer, David M., et al. 2012. "Neurocognitive Therapeutics: From Concept to Application in the Treatment of Negative Attention Bias." *Biology of Mood & Anxiety Disorders* 5 (1). https://doi.org/10.1186/s13587-015-0016-y.

Funded by NIH Training Grant T32MH065214 to A.C.M., Intel Corporation, & University of Pennsylvania Endowment

Contact: amennen@princeton.edu

Poster #41