Real-time fMRI Neurofeedback Training of Amygdala in MDD Patients

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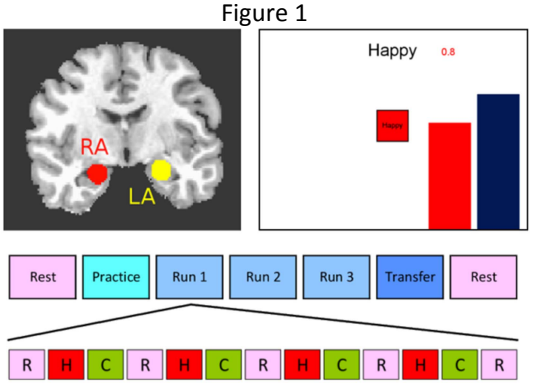
Target Audience: Researchers and clinicians employing advanced fMRI and real-time fMRI neurofeedback techniques to study human emotions and those interested in emotion regulation mechanisms and in the development of novel therapeutic approaches for neuropsychiatric disorders, particularly depression.

Purpose: Many patients with major depressive disorder (MDD) do not respond to pharmacological and psychological treatments[1]. Thus there is a need to develop novel and non-invasive treatments for MDD. MDD is associated with the dysregulation of neural circuits that mediate and modulate emotion processing. Research has shown that the hemodynamic response of the amygdala is exaggerated to negative stimuli and attenuated to positive stimuli in MDD, and that this latter response, in particular, normalizes in association with symptom remission[2]. The availability of real-time fMRI (rtfMRI) and recent advances in rtfMRI neurofeedback (rtfMRI-nf) permit, for the first time, direct targeting of this region's function with sufficiently high temporal and spatial resolution to investigate neuromodulation of the human amygdala[3]. The current study aims to determine whether individuals with MDD are able to use rtfMRI-nf to enhance the hemodynamic response of the amygdala to positive stimuli.

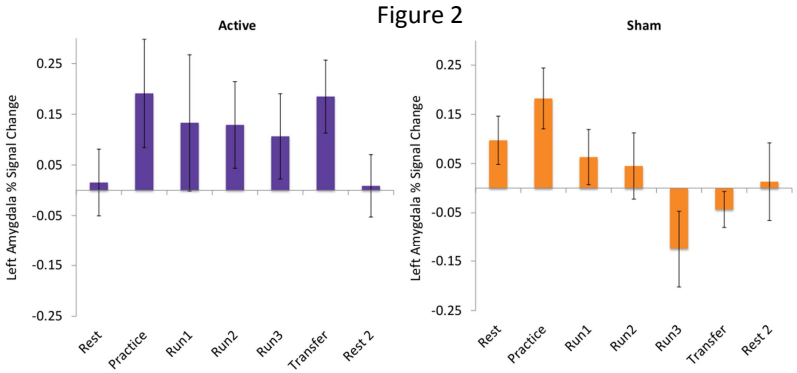
Methods: The experiments were performed using GE MR750 3T MRI scanner with the 8-channel head coil. fMRI: gradient echo EPI with FOV/slice=240/2.9mm, TR/TE=2000/30ms, SENSE=2, 96×96, flip=90°, 34 axial slices. T1-weighted MPRAGE sequence was used for anatomical reference and to define ROIs. Neurofeedback was implemented using a custom real-time fMRI system[4] utilizing AFNI[5] real-time features and a custom GUI software[4]. The study included 19 unmedicated, currently depressed participants with MDD. For each subject, three spherical ROIs (7 mm radius in Talairach space) were centered, respectively, at the left and right amygdala (Fig.1) and the left horizontal segment of intraparietal sulcus (HIPS) region. An average fMRI signal from the target ROI was presented as a red bar (Fig.1) updated every 2s. Twelve subjects took part in experiments with real rtfMRI neurofeedback (target ROI: left amygdala). For the other 7 subjects, sham neurofeedback was used (target ROI: HIPS region not involved in emotional processing). The experiment design is shown on Fig. 1. Each run (except Rest) consisted of 40 s long blocks with Rest, Happy, and Count conditions. For the Happy condition, the subject was asked to feel happy by recalling happy autobiographical memories so as to raise the level of the red bar displayed on the screen. The target level (blue bar) was raised from run to run. No neurofeedback was provided (no bars displayed) during the Rest and Count conditions or during the entire Transfer run. The fMRI data analysis was based on GLM and performed in AFNI[5].

Figure 1



Results: The fMRI activation levels for the left amygdala ROI during the Happy condition compared to the Rest condition, averaged for each run for the active and sham groups, are exhibited in Fig. 2. Steady increase in left amygdala activation during the Happy condition across all runs with the real neurofeedback was observed. The results for the right amygdala exhibit a similar trend, but the training effect is less pronounced, and no trend of increased activity over time was present in the HIPS region for either sham or active feedback conditions (not shown). Four of the MDD patients in the active rtfMRI-nf group were unable to learn to successfully regulate their amygdala (defined as LA BOLD response no different from 0 during the transfer run) and were therefore excluded from the group analysis.

Figure 2



Discussion: Our results show that by using rtfMRI-nf from the LA during recall of positive autobiographical memories, a subset of individuals with MDD can learn to self-regulate their amygdala BOLD responses. We also found an association between the ability to regulate the LA and reductions in depression ratings, as well as improvements in happiness ratings. These preliminary results suggest that rtfMRI-nf training and positive autobiographical memory recall holds potential clinical application in the treatment of MDD.

References: 1) Rush A., "Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report", American J. Psychiatry 163:1905-1917; 2) Price, J.L. (2012), 'Neural circuits underlying the pathophysiology of mood disorders', Trends in Cognitive Science, 16(1): 61-71; 3) Zotev, V. (2011), 'Self-regulation of amygdala activation using real-time fMRI neurofeedback', PloS ONE, 6(9): e24522, doi:10.1371/journal.pone.0024522; 4) Bodurka, J. (2008), 'Real time software for monitoring MRI scanner operation', Neuroimage, 41 (Supp. 1), S85. 5) Cox, R.W. (1996), 'AFNI: software for analysis and visualization of functional magnetic resonance neuroimages' Computers and Biomedical Research, 29:162-173.