# Self-Regulation of Amygdala Activation with Real-Time fMRI Neurofeedback in Combat-Related PTSD

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Target Audience: Researchers and clinicians interested in emotion regulation, novel PTSD treatments, and real-time fMRI.

Purpose: Post-traumatic stress disorder (PTSD) is a chronic and disabling psychiatric condition. Individuals with PTSD suffer from the dysregulation of several types of emotion including fear, anxiety, anger, and depression. Neurocircuit models of PTSD emphasize the role of the amygdala.[1] We utilize recent advances in real-time functional magnetic resonance imaging neurofeedback (rtfMRI-nf) to directly target and modulate amygdala activity. This technique measures neuronal activity with sufficiently high temporal resolution so that information from the amygdala is immediately available to form a feedback loop. Previous research has shown that healthy individuals can learn to use rtfMRI-nf to regulate the left amygdala.[2] The current study aimed to determine whether veterans with PTSD are also able to use rtfMRI-nf to enhance the control of the hemodynamic response of the amygdala.
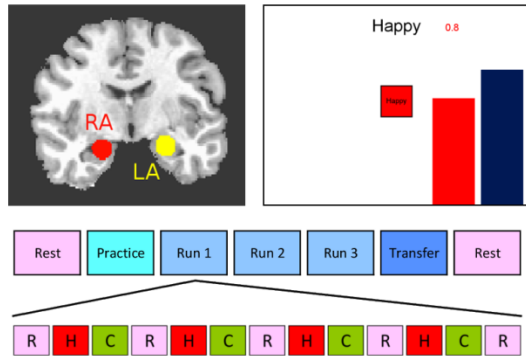
Methods: Experiments were performed using a GE MR750 3T MRI scanner with the 8-channel receive-only head coil. BOLD fMRI parameters were: gradient echo EPI with FOV/slice=240/2.9mm, TR/TE=2000/30ms, SENSE=2, 96×96, flip=90°, 34 axial slices. T1-weighted MPRAGE sequence was used for anatomical reference and to define regions of interest (ROIs). Neurofeedback was implemented using a custom real-time fMRI system[3] utilizing AFNI[4] real-time features and a custom GUI software. The study included 6 unmedicated male veterans with a current combat-related PTSD diagnosis. 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 horizontal segment of intraparietal sulcus (HIPS, a region putatively not involved in emotion processing). An average fMRI signal from the target ROI (the left amygdala), was presented as a red bar, updated every 2s (Fig.1). Each run (except Rest) consisted of 40 s long blocks with Rest, Happy, and Count conditions. For Happy condition, subjects were 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 adjusted and raised from run to run. No neurofeedback was provided (no bars displayed) during Rest and Count conditions or during Transfer run. The fMRI data analysis performed in AFNI was based on GLM.
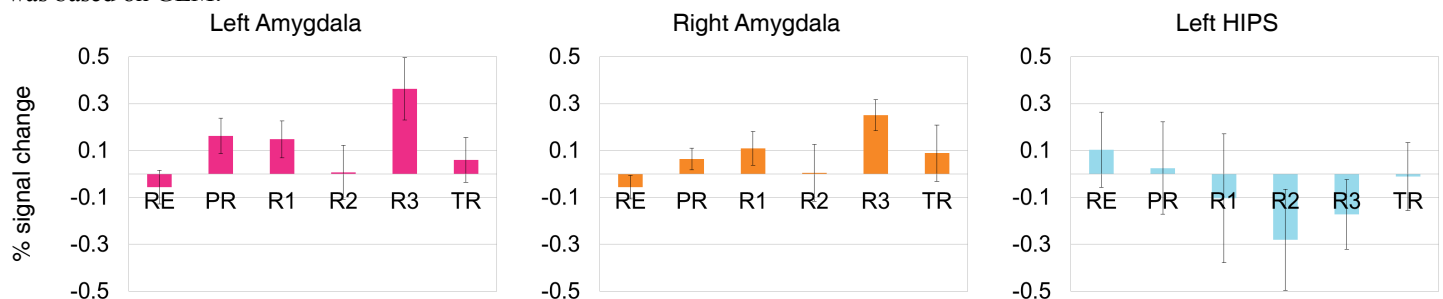
Results: The fMRI activation levels for the left amygdala ROI during the Happy condition compared to the Rest condition, averaged for each run for the three ROIs, are exhibited in Fig. 2. By the third neurofeedback run, significant upregulation was observed in both the left ($t(5)$=2.729, $p = 0.041$) and right amygdala ($t(5)$=3.774, p=0.013). No significant upregulation of the HIPS was observed during any of the runs. Symptom ratings and assessments taken before and after the neurofeedback session revealed a significant decrease in the Profile of Mood States (POMS) depression subscale ($t(5)$= -4.108, $p = 0.009$).

Discussion and Conclusions: Our results demonstrated, for the first time, that individuals with PTSD can learn to self-regulate their amygdala BOLD responses during recall of positive autobiographical memories. Notably real time fMRI neurofeedback training of the left amygdala also significantly reduced ratings of depression. Our preliminary results suggest feasibility of rtfMRI-nf training combined with positive autobiographical memory recall in research of novel treatment of PTSD.

References: 1) Rauch, S. L., Shin, L. M. & Phelps, E. A. Neurocircuitry models of posttraumatic stress disorder and extinction: human neuroimaging research--past, present, and future. Biol Psychiatry 60, 376-82 (2006). 2) Zotev, V. (2011), 'Self-regulation of amygdala activation using real-time fMRI neurofeedback', PloS ONE, vol. 6, no. 9, e24522, doi:10.1371/journal.pone.0024522. 3) Bodurka, J. (2008), 'Real time software for monitoring MRI scanner operation', Neuroimage, 41 (Supp. 1), pp. S85. 4) Cox, R.W. (1996), 'AFNI: software for analysis and visualization of functional magnetic resonance neuroimages' Computers and Biomedical Research, Vol. 29, pp. 162-173.