Simultaneous Real-time fMRI and EEG Neurofeedback for Self-Regulation of Human Brain Activity

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INTRODUCTION: The integration of real-time functional magnetic resonance imaging (rtfMRI) [1] and electroencephalography (EEG) makes it possible to develop novel, simultaneous rtfMRI-EEG multimodal neurofeedback approaches, in which participants can receive information about their cerebral hemodynamic and electrophysiological activity in what is experienced as real time, and use this information to volitionally regulate subsequent neural responses. The current study utilized such an approach to enable subjects to regulate their frontal EEG asymmetry, which previously has been shown to reflect and influence emotional processing [2]. Specifically, the regulation of asymmetric electrophysiological activity in either alpha (8−13 Hz) or high-beta (21−30 Hz) band by means of EEG neurofeedback has been associated with changes in emotional state [3,4]. The frontal high-beta asymmetry is particularly relevant in patients with major depression, who exhibit excessive high-beta power in right frontal regions [4,5]. Here we report the first proof-of-concept simultaneous multimodal rtfMRI-EEG neurofeedback experiments for regulation of both BOLD-fMRI activation of left amygdala and frontal high-beta EEG asymmetry. We demonstrate the feasibility of this multimodal neurofeedback approach in healthy volunteers performing a positive-mood induction task [6].

METHODS: Three healthy subjects (one female) participated in the study. The experiments were performed on a General Electric Discovery MR750 3T MRI scanner with an 8-channel receive-only head coil array. A single-shot gradient echo EPI sequence with FOV/slice=240/2.9mm, *TR/TE*=2000/30ms, SENSE=2, image matrix 64x64, flip=90°, 34 axial slices, was employed for fMRI. Concurrent EEG recordings were performed using a 32-channel MR-compatible EEG system (Brain Products GmbH), in 0.016−250 Hz band with 0.1 μV resolution and 5 kS/s sampling rate. MRI and cardioballistic artifacts were removed from raw EEG data in real time using Brain Products' RecView software. Multimodal rtfMRI-EEG neurofeedback was implemented using a custom developed real-time system that combined real-time fMRI and EEG data streams with real-time processing and analysis, and included a custom neurofeedback GUI software (Fig. 1a). The rtfMRI neurofeedback was based on fMRI activation in a left amygdala ROI (Fig. 1d) as in [6]. The fMRI bar height (red bar on the right in Fig. 1a) was updated every 2 s. EEG signals from F3 and F4 frontal electrodes (Fig. 1c) with FCz reference were used to generate the EEG neurofeedback. The EEG power spectrum was computed every 400 ms for a moving data interval lasting 2048 ms using a Hanning window. The asymmetry was defined as $A=(P(\mathrm{F3})-P(\mathrm{F4}))/(P(\mathrm{F3})+P(\mathrm{F4}))$, where P is the EEG power in a given frequency band. The difference in A values from the high-beta band (beta3, 21-30 Hz) between the task and the rest baseline (multiplied by10) was calculated and updated every 0.4 s, and used to generate the neurofeedback visual representation, expressed as the height of the EEG bar (red bar on the left in Fig. 1a). The experimental protocol included seven runs, and each run (except Rest) consisted of 40 s long blocks of **R**est, **H**appy Memories, and **C**ount conditions (Fig. 1b), as described in [6]. For each Happy Memories condition, the subject was instructed to feel happy by evoking positive autobiographical memories, while trying to raise the levels of both red bars (EEG left and fMRI right) on the screen. No bars were displayed during the Rest and Count conditions, and during the entire Rest and Transfer runs.

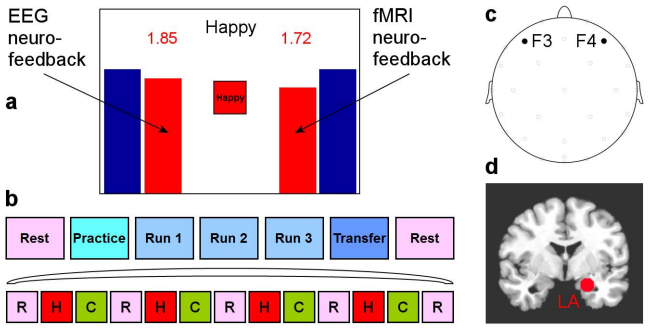

Fig. 1. a) GUI screen with neurofeedback bars (red) and target bars (blue); b) experimental protocol; c) EEG electrodes used to provide EEG neurofeedback; d) left amygdala ROI for rtfMRI neurofeedback.

RESULTS: Fig. 2a exhibits an average change in frontal high-beta (21−30 Hz) EEG asymmetry during the Happy Memories conditions compared to the Rest conditions for each run across three subjects (mean±s.e.m.). The results are based on offline EEG data analysis with careful removal of artifacts. The corresponding average left amygdala activation levels, based on offline GLM analysis as in [6], are shown in Fig. 2b. Both quantities increased during the neurofeedback runs – Practice (PR), Run 1 (R1), Run 2 (R2), Run 3 (R3) − and the training effects persisted during the Transfer run (TR). Notably, the EEG results exhibited less inter-subject variability than the fMRI results.

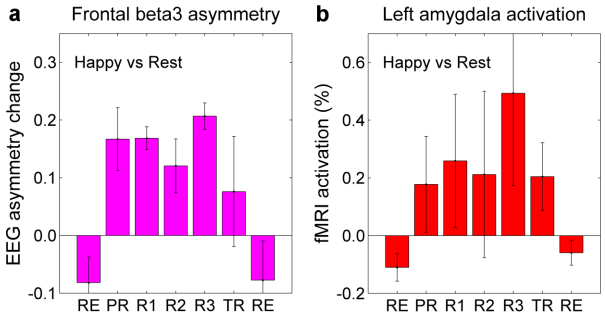

Fig. 2. Effects of EEG-fMRI neurofeedback training: a) changes in frontal EEG asymmetry in 21−30 Hz band; b) fMRI activation of left amygdala.

CONCLUSION: These proof-of-concept results demonstrate, for the first time, that healthy participants can learn to simultaneously regulate their frontal high-beta EEG asymmetry and left amygdala fMRI activation using retrieval of positive autobiographical memories along with rtfMRI-EEG neurofeedback. Conceivably, the combined use of rtfMRI and EEG during neurofeedback training may prove more efficient than either EEG or rtfMRI neurofeedback techniques applied separately. Our data further suggest potential applications of rtfMRI-EEG neurofeedback in the development of cognitive neuroscience research paradigms and enhanced cognitive therapeutic approaches for major neuropsychiatric disorders, particularly depression.

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