## Integration of Concurrent Real-time fMRI and EEG data: Simultaneous Real-time fMRI and EEG Neurofeedback

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INTRODUCTION: Concurrent functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) measurements allow for the study of brain electrophysiological activity and neurovascular coupling, and such a multimodal approach offers multiple advantages [1-3]. However, during experiments data streams from both modalities are independent, and multimodal data fusion is performed after experiments in the data postprocessing stage. Conceptually, integration of real-time data streams from both fMRI and EEG modalities would make it possible to develop a novel class of experiments to study brain functions. In particular, such multimodal integration would allow for a real-time simultaneous fMRI and EEG multimodal neurofeedback (rtfMRI-EEG-mnf) approach, in which research participants can receive information about their cerebral electrophysiological and hemodynamic activity in what is experienced as "real-time" and then use this information to volitionally regulate subsequent neural responses. Here we describe a system design in which such multimodal fMRI and EEG data integration was achieved for the purpose of simultaneous rtfMRI-EEG neurofeedback, and which we implemented on a commercial MRI scanner with a commercial MR-compatible EEG system.

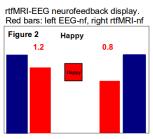
METHODS: The rtfMRI-EEG-mnf design was based on a custom-developed real-time fMRI system [4], which has made it possible to establish rtfMRI with neurofeedback (rtfMRI-nf) [5]. The overall system block design is shown on Figure 1. Control and communication programs (shown in pink) were written in Python (RTeeg, eeg client, math modules) and Perl (RTmri, RTcontrol, mGUI). All programs run on a Linux workstation with a kernel customized for high-speed inter-process communications with message queues, synchronization with semaphores, and large data exchange via shared memory. This system's modular design allowed for integration of real-time EEG data streams after MRI and cardioballistic artifacts were removed from raw EEG data in real time using Brain Products' RecView software. The system combines real-time fMRI and EEG data streams with real-time processing and analysis, and includes custom multimodal graphical user interface (mGUI) neurofeedback software where data integration takes place. The rtfMRI-EEG-mnf system was implemented to work with a General Electric Discovery MR750 3T MRI scanner and 128-channel MRcompatible EEG system (Brain Products GmbH). Experimental phantom validation: for fMRI, single-shot gradient echo EPI sequence with FOV/slice=240/2.9mm, TR/TE=2000/30ms, SENSE=2, image matrix 64×64, flip=90°, 34 axial slices, and 180 reps was used. Concurrent EEG recordings were obtained using a 32-channel sinusoidal test signal generator attached to MR-compatible BrainAmp MR Plus amplifier in 0.016-250 Hz band with 0.1 µV resolution and 5 kHz sampling bandwidth.

RESULTS and DISCUSSION: The multimodal rtfMRI-EEG neurofeedback system real-time performance was extensively tested on phantoms for multiple MRI/EEG hardware configurations (different RF coils: 8, 16, 32 channels, EPI image resolutions; EEG caps: 32, 128 channels; data samplings rates; neurofeedback signal computations/combination/averaging; etc.). For

System for simultaneous real-time fMRI and EEG neurofeedback Data Storage: HDD1 Figure 1 AFNI rt\_plugin svnc Shared Memory waveforms Msg gueue **RTcontrol** Semaphores Math1 Data CP/IP CP/IP socket Storage: Math2 eeg client HDD2 socket Control lines socket **mGUI** socket Software Data modules Merge fMRI data Visual projection EEG data Linux real-time workstation MRI host computer EEG acq. computer, Remote display RTmri main control artifacts removal LCD\_projector/screen MRI hardware EEG hardware Subject in MRI magnet sync

our implementation, and our requirement of the real-time conditions (total processing delays for each neurofeedback update no longer than single TR or 2sec) the system is limited by fMRI acquisitions/image reconstruction speed, currently excluding the use of 32ch brain arrays coils. The rtfMRI-nf neurofeedback signal is updated every TR and can be based on a preselected brain region of interest (ROI), such as the amygdala as described in [5]. The EEG-nf neurofeedback signal can be updated at much faster rate than TR (as short as 100ms). The current implementation of the EEG-nf allows for: i) selection of individual electrode and/or a combination of signals from multiple electrodes for a given, preselected time segment duration, and application of mathematical operations (addition, subtraction, ratios, etc.) on consecutive segments with or without moving window averaging; ii) real-time power spectrum analysis of each electrode signal to allow selection of single electrode or spectrum band in any combination (for example to

produce real-time measure of frontal (F3, F4 electrode) high beta (21-30 Hz) band power asymmetry, updated every 400ms from 2048ms EEG time segment data length, which is a relevant indicator in patients with depression [6]). The multimodal neurofeedback graphical user interface (mGUI) integrates fMRI and EEG real-time data streams, computes neurofeedback signals, and converts these signals into graphical representations for subject viewing. Our mGUI is a multithreaded graphics applications and supports images, graphics primitives (such as bars), and text to form a dynamic display based on the neurofeedback signals levels. The neurofeedback display used for our proof-of-concept experiments is shown on Figure 2. Both red bars are moving bars, where bar heights depend on the current neurofeedback signal levels (left red bar is EEG neurofeedback beta band asymmetry A=(P(F3)-P(F4))/(P(F3)+P(F4)), and updated every 0.4s, where P is the EEG power in a 21-30 Hz band, right red bar is fMRI neurofedback signal from arbitrarily chosen phantom ROI, and updated every 2s), whereas both blue bars are static fixed target bars. During each run, both real-time neurofeedback EEG and fMRI signal values were EEG-nf, rtfMRI-nf signals (bar heights) incrementally saved to the files and later on were compared to values obtained from corresponding fMRI and EEG updated every 0.4s, and 2s, respectively



data processed offline. We found the values obtained from real-time neurofeedback consistently match offline data analysis values, confirming that the system operates correctly and robustly.

CONCLUSION: We have developed and implemented a first-of-its-kind system for providing simultaneous real-time fMRI and EEG neurofeedback. The capability of this novel rtfMRI-EEG-mnf system suggests potential applications in the development of novel cognitive neuroscience research paradigms. In particular this system can be used in the development of novel and enhanced cognitive therapeutic approaches for major psychiatric disorders.

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