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COMBINED EEG/TMS/FMRI STUDIES ASKING WHETHER PHASE MATTERS

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Introduction: The effects of TMS have been largely studied in the motor system, using motor evoked potentials (MEP) as the output. There is a large between-pulse variability in MEP's, requiring multiple pulses and averaging. One potential source of the MEP variability might be the EEG phase cycle of the motor cortex relative to the TMS pulse. We have succeeded in performing TMS in the fMRI scanner with high fidelity EEG. As the first step in understanding whether the phase of a brain region matters with respect to the effect of a TMS pulse, we have started in motor system, using local and secondary BOLD response, and assessing whether the local alpha phase influences the TMS pulse impact.

Methods: 150 TMS pulses were acquired separated by several TR's. EEG and fMRI data were recorded continuously during the experiment. BOLD images were acquired using a 3T Siemens Tim Trio MRI system and a custom 12 channel head coil (RAPID Biomedical) with a holder for the TMS coil. TMS pulses were delivered at the brain's motor region corresponding to the right thumb at 110% of the subject's motor threshold, using a Magstim Super Rapid stimulator and 70mm double figure of 8 coil. EEG was acquired using a custom MRI-compatible EEG cap with 36 bipolar electrodes (impedances reduced to less than 20K ohm) while TMS pulses were delivered. A high resolution structural T1 MPRAGE (1.3x1.3x1.3mm) was acquired, followed by the EEG-TMS-fMRI runs using a standard Siemens ep2d_bold sequence (TR 2500ms, TE 23, 3x3x3mm voxel size, 43 slices, 150 single TMS pulses total, separated by several TRs). During each BOLD sequence, EEG data was acquired continuously and single TMS pulses were fired in a 100ms gap at the end of each specified TR (to prevent MRI gradient interference).We have then analyzed the whole brain response to TMS regardless of EEG phase, as well as parsing the data into local EEG rising or falling alpha. Ongoing work involves delivering pulses prospectively either in rising or falling alpha, and performing these same experiments with the coil over dorsolateral prefrontal cortex, to assess whether local or transynaptic (rostral anterior cingulate) BOLD response depends on prefrontal alpha phase.

Results: Simultaneous EEG/TMS/fMRI in human subjects is feasible. Preliminary data suggest larger local and transynaptic (caudate) BOLD response when the TMS pulses are delivered during the rising alpha phase. The figure shows blood flow in regions of bilateral thalamus in one subject during a TMS pulse that correlate with the phase of a 10 Hz filtered EEG signal localized to the left motor cortex, suggesting the importance of the state of the EEG signal at the precise time of the TMS pulse.

Discussion: Combined TMS/EEG/fMRI may be a useful tool initially to understand the degree to which external pulses need to be coordinated with underlying brain rhythms. With further development, methods of phase synchronization may fundamentally shape the way rTMS is delivered in clinical and research applications.

Keywords: EEG, rTMS, fMRI, alpha phase