Searching Further and Wider: Single Pulse TMS Still Leads to Elevated BOLD Activity in the ACC and Caudate

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Background
Interleaved TMS/fMRI presents researchers with a powerful technique that combines the causal effects of TMS pulses with the ability to record brain-wide activity changes. Our group has recently published support for TMS/fMRI, showing that active TMS leads to greater BOLD activity in areas such as the ACC and caudate, relative to well-matched control stimulation (1). This prior report, however, had a limited field of view, making it impossible to draw conclusions regarding activity in much of the brain. Here, we present data to address this concern, while also implementing acquisition techniques that improve the signal to noise ratio of interleaved TMS/fMRI (2).

Methods
We delivered 4 runs of 10 TMS pulses to participants (n=10), of which two were active stimulation with the TMS coil positioned over the left DLPFC, while the other 2 runs used 3cm of padding to preserve the sensory aspects while dramatically reducing magnetic field entry (identical to the previous methods). The order of events was counterbalanced amongst participants. Rapid whole brain fMRI data was collected using a multiband multiecho imaging sequence (MB 2, TR 1.2, TEs 11,28.8,45.56 ms; 3.7x3.7x3.7 mm). We confirmed the perceptual similarity of stimulation conditions after each session. Data underwent standard preprocessing in AFNI. Subject level modeling was performed using both a conventional double gamma hemodynamic response, as well as using AFNI's TENT functions to estimate hemodynamic responses without prior shape constraints. Mixed effects multilevel analyses methods were used for inference at the group level (3).

Results
As in our earlier work using a rapid TR with a limited slice prescription, we found that both active and control TMS led to activation in the insulae, thalamus, anterior cingulate, somatosensory regions and lateral prefrontal cortex. With the larger field of view, we are able to confirm similar activation also occurs in the inferior parietal lobule, paracentral lobule, cerebellum, and middle temporal gyrus (voxel threshold, $p<0.005$). Examining the TENT model, we find greater BOLD activity in response to active TMS relative to sham in the anterior cingulate, caudate and putamen (voxel threshold $p<0.01$).

Conclusions
This data represents a conceptual replication of our prior work, showing that interleaved TMS/fMRI activates putatively connected regions. It also bolsters the argument that interleaved TMS/fMRI requires appropriately controlling for the non-specific effects of delivering TMS within the MRI environment. Future studies may benefit from using multiband/multiecho techniques to obtain full brain coverage with better signal to noise characteristics. Furthermore, unconstrained modeling approaches may offer a better way to determine the areas that respond to active TMS, though this remains to be tested in a larger sample.

References
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