CONTINUOUS THETA-BURST STIMULATION INDUCES CHANGES IN FUNCTIONAL CONNECTIVITY DURING REST

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TARGET AUDIENCE: Neuroscientists with an interest in brain connectivity measures, and in the combination of MRI and electrophysiology.

PURPOSE

Continuous theta-burst repetitive stimulation (cTBS) results in long-lasting decreases in indices of cortical excitability (1). Recently it has been showed that connectivity between distant brain areas can change after anodal stimulation over the primary motor cortex (2). In this study, we combined cTBS and resting state functional magnetic resonance imaging (RS-fMRI) approaches to investigate changes of functional connections (FC) induced by cTBS at rest.

MATERIAL AND METHODS

Eighteen healthy subjects (M/F=9/9; mean (SD) age=27,1 (4.18)) underwent an MRI scan at 3.0 T before and after cTBS stimulation within the same day. The acquisition protocol included: 1) MPRAGE (TR=1338 ms, TE=2.4 ms) 2) T2-weighted EPI sensitized-to-BOLD (TR=2080 ms, TE=30 ms, 32 axial slices, 220 volumes), acquired during rest. A MagStim Super Rapid magnetic stimulator was used to deliver cTBS. Three-pulse bursts at 50 Hz repeated every 200 ms for 40s were delivered over the right prefrontal cortex (F4 electrode International 10-20 system) at intensity of 80% of active motor threshold (AMT) (3). Each subject underwent the same paradigm replacing cTBS with a sham stimulation on a separate session. The RS-fMRI data were preprocessed in SPM8 (motion correction, slice timing correction, normalisation), and data were band-pass filtered to remove high frequency variations. Seed-based RS-fMRI analysis of the pre-stimulation datasets was performed to identify the cortical areas functionally connected with prefrontal cortex region. The seed ROI was extracted from Harvard Oxford atlas (4). The resulting regions were then used as a reference to define a network of 29 spherical nodes from which mean time courses were extracted to estimate a connectivity matrix for each subject. The Network Based Statistics (NBS) toolbox (5) was used to compare the connectivity between each node of the network before and after cTBS, using a paired T-test design. The same analysis was repeated with the data collected before and after sham stimulation. False discovery rate (FDR) procedure was used to adjust for multiple comparisons. Results were considered significant for $p<0.05$.

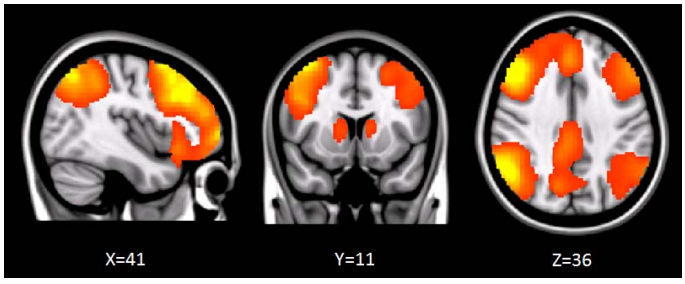

Figure 1. *Brain areas functionally correlated to the prefrontal cortex used as seed in seed-based analysis*

RESULTS

Seed based analysis revealed a specific pattern of correlation between right prefrontal cortex and several brain regions: left prefrontal, parietal, temporal corteces, precuneus, posterior cingulated cortex, thalamus and caudate nuclei (Fig. 1). Based on these results, we identified 29 nodes, and we created 29 spheres (Fig. 2) to extract the main time courses. The connectivity matrices before and after cTBS were compared using NBS. A decrease of correlation between the right prefrontal cortex and right parietal cortex (Brodmann areas 10 and 40 respectively) was detected (Fig 3). No significant change was found for sham stimulation.

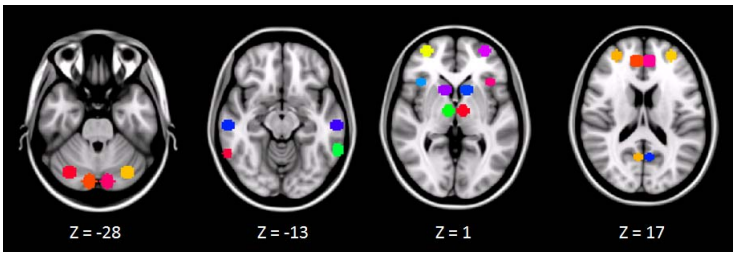

Figure 2. *Spherical ROIs defining the nodes of the network investigated before and after cTBS*

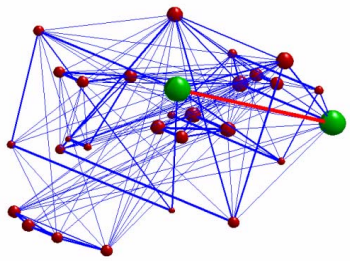

Figure 3. *3D graph representing the investigated network. The green nodes indicate the ROIs whose connectivity was decreased after stimulation*

DISCUSSION

To our knowledge this is the first study that demonstrates within-subject changes in FC induced by cTBS applied on the prefrontal area. Moreover, these findings are supported by unchanged correlation after sham stimulation. The possibility to induce selective changes in a specific region without interfering with functionally correlated area could have several implications for the study of functional properties of the brain, and for the emerging therapeutic strategies based on transcranial stimulation.

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