Modulation of functional connectivity during finger tapping and resting state in patients with MS

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Target Audience: Functional connectivity researchers. Modulation of motor connectivity in MS.

Purpose: Resting state functional connectivity MRI (rs-fcMRI) captures intrinsic functional networks in the human brain [1]. However, much of human life does not take place at rest. Measurements of functional connectivity (*fc*) during rest are different from those measured while the subject is performing a task, and this depends on the specific task [2]. Continuous task-modulated or non resting-state connectivity MRI (nrs-fcMRI) is necessary to extend the study of brain function beyond the resting state. We investigated the modulation of motor connectivity in patients with multiple sclerosis (MS) and healthy controls by acquiring *fc* in 3 conditions (rest, 2 Hz paced finger tapping and self-paced complex finger tapping).

Methods: 14 patients with MS and 14 healthy controls matched by age, sex, and education were scanned using an IRB-approved protocol at 3T TIM Trio scanner (Siemens Medical Solutions, Erlangen). Scans: T1-MPRAGE, a complex tapping BOLD fMRI scan and 3 continuous state whole-brain fcMRI scans (where the state for each entire scan was rest, 2Hz or complex tapping, scans in random order) in a previously-described study [3]. The fMRI scan was used to localize a seed in the motor cortex (M1), coregistered to the 3 connectivity scans, and then creates whole-brain correlation fcMRI maps [3]. fcMRI maps were compared using a 2 × 3 ANOVA to probe differences in connectivity among rest and 2 tasks, and to assess whether disease status and activation condition affected the strength of M1 *fc*.

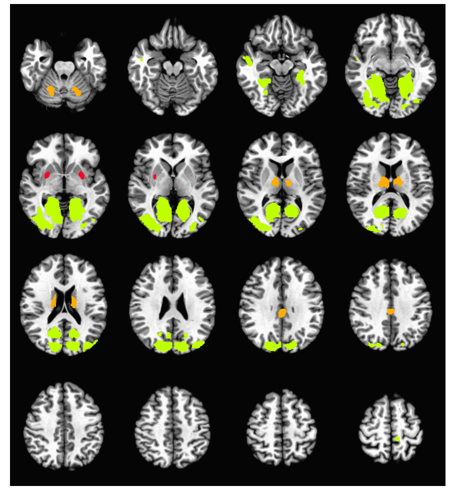

Fig. 1. Map of differences between resting, 2Hz tapping and complex tapping. Green shows increased, orange shows decreased motor connectivity during rest versus both tasks. Red shows increase during complex tapping versus 2hz and rest.

Table. 1. Summary of significant differences in *fc*

ROIs	pattern
right parahippocampal gyrus	rest >2Hz> complex
left parahippocampal gyrus	rest >complex>2Hz
inferior/middle occipital gyrus	rest >complex>2Hz
right cuneus	rest >2Hz>complex
left cuneus	rest >2Hz>complex
left paracentral lobule	rest >complex>2Hz
left middle occipital gyrus	rest >complex>2Hz
left middle temporal gyrus	rest >2Hz>complex
right middle temporal gyrus	rest >2Hz>complex
left superior cerebellum	2Hz>complex>rest
right superior cerebellum	2Hz>complex>rest
left thalamus	complex>2Hz>rest
right thalamus	2Hz>complex>rest
midline cingulate gyrus	2Hz>complex>rest
left putamen	complex>2Hz>rest
right putamen	complex>2Hz>rest

Results: The colors of 16 significant regions correspond with the pattern of significant difference among the 3 conditions in the M1 connectivity maps (Fig.1, Table 1, $p<1.9e-5$). Green indicates locations where the rest condition showed higher *fc* than both the 2Hz and complex conditions. Most of these regions are in the posterior cingulate and occipital lobe. Orange indicates lower *fc* in rest than both the 2Hz and complex tapping states. Red indicates stronger *fc* in the complex tapping condition than the 2Hz and rest conditions. For the group comparsion, patients showed significantly weaker *fc* than controls under all 3 conditions in the left postcentral gyrus, right angular gyrus, right middle frontal gyrus, left posterior cingulate, left fusiform gyrus, left superior temporal gyrus and culmen. The condition×group comparison showed that patients have weaker *fc* than controls under the resting condition in the right inferior parietal lobule ($p=0.0007$) and right precentral gyrus ($p=0.0008$).

Discussion: BOLD acquired during different conditions produced significantly different M1 connectivity, in a differential pattern. This suggests that the *fc* network related to motor function of the human brain is dynamic and can be modulated in different brain activities. The continuous performance of motor tasks disrupts resting state visuo-motor connectivity. Motor tasks also increased thalamic, cerebellar and motor cingulum connectivity, components of the canonical motor circuit [4, 5]. The self-paced complex tapping increased M1 connectivity to the motor segment of the putamen, while the 2Hz paced tapping task did not. Conversely, cerebellum *fc* was increased most by the paced tapping, and cerebellum plays a role in timing of motor control [5, 6]. We observed weaker IPL and primary motor resting *fc* in patients with MS, which may be associated with increased lesion load in periventricular regions [7]. But this effect was only seen during rest. This suggests that task performance somehow compensates for intrinsically lower connectivity in MS patients. If this is the case, resting state studies may be more effective at detecting MS-related population differences than task-related fMRI.

Conclusion: Significant fc changes in some brain regions during 2 motor tasks from rs were exhibited, showing the fc network can be modulated under different states in controls and patients with MS. There was decreased fc in certain regions of patients compared with controls. The observation that more group differences were observed in the resting state suggests that this may be the most effective way of studying functional impairment in MS.

References

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