Strength of connectivity to the anterior cingulate predicts processing speed in Multiple Sclerosis

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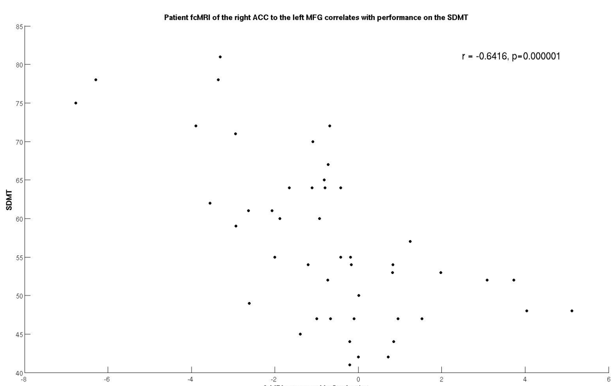
Introduction: A common symptom in the demyelinating disorder Multiple Sclerosis (MS) is loss of cognitive abilities, affecting more than 40% of patients [1]. Although no specific pattern of cognitive impairment has been identified, some studies have suggested that particular domains are preferentially affected. Information processing speed, memory, and verbal fluency are the most frequently cited deficits, mediated by disease duration and disease course [2]. Though macroscopic lesions are the most obvious marker of MS, they are not well-correlated with cognitive measures. Diagnosis and prognosis of MS patients could be improved with advanced measures of functional imaging that correlate with cognitive decline [3].

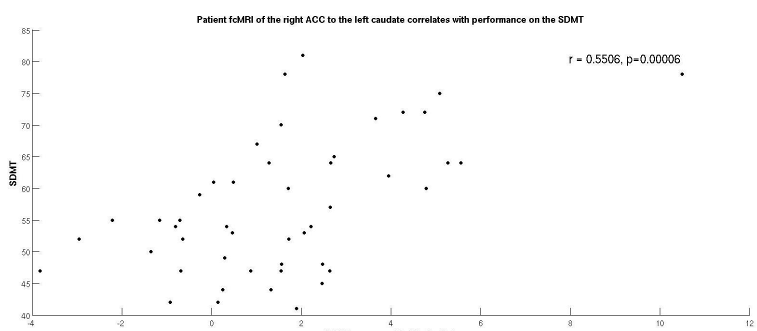
Recently, several studies have shown that functional connectivity MRI (fcMRI) in MS shows correlation with cognitive decline and with measures of structural connectivity such as DTI [4,5]. fcMRI is a measure of the strength of connection between anatomically distinct regions of the brain, and can provide insight into the mechanisms of cognitive decline and reorganization in MS. The current study presents results from a group study comparing resting state fcMRI of the right dorsal anterior cingulate (ACC) in MS and controls. We find significant differences in patterns of connectivity between the two groups, and different regions of the brain related to performance on a cognitive task.

Methods: 47 MS patients (mean age 43.13 (9.16), mean EDSS 2.45, 13 male) and 24 healthy controls (mean age 40 (9.11), 9 male) were scanned in an IRB-approved protocol at 3T using a bitebar to reduce head motion, in a 12-ch receive head coil. Scans included T1-MPRAGE and a resting connectivity fcMRI scan at 2x2x4mm voxels, 1954 Hz/pix BW, 31 axial slices, TR/TE/FA=2800/29/80. A subset of 10 MS subjects and 10 controls performed a verbal memory retrieval task corrected as described in [6] and the fMRI student's t-maps from the correct retrieval condition were coregistered to the connectivity scans. All individual maps were then transferred to MNI space. A one-way ANOVA between the patient and control coregistered student's t-maps revealed a difference in activation in the anterior cingulate (Figure 1). A nine-voxel in-plane ROI was drawn around the ACC voxel that showed the most significant difference between the groups and was used to calculate individual whole-brain seed-based correlation fcMRI maps as described in [6]. Correlation of low-pass filtered reference timeseries were converted to t-scores, which represent our fcMRI connectivity metric. In patients, correlation between performance on the SDMT, a measure of information processing speed commonly used in MS, and functional connectivity was calculated, voxel-by-voxel. Additionally, fcMRI maps of a subset of the highest (n=20) and lowest (n=20) performing patients were entered into an ANOVA to probe differences in connectivity between cognitively impaired and cognitively intact patients. The same analysis was performed on a subset of high (n=10) and low (n=10) performing controls.

Figure 2. fcMRI from the right ACC to the L MFG and L caudate correlates with SDMT performance in patients.



Results and Discussion: In patients, performance on the SDMT was significantly correlated with right ACC connectivity to the left caudate (r = 0.55, p=0.00006, corrected) and inversely correlated with right ACC connectivity to the left medial frontal gyrus (r = -.64, p=0.000001, corrected). Controls showed no significant correlations between task performance and connectivity measures. This suggests that different patterns of functional connectivity influence cognitive performance in MS.



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