Characterization of Functional Homotopy in Multiple Sclerosis using Resting-state functional MRI

L. Tang[1], X. Zuo[2,3], C. Kelly[2,3], Y. Zhou[1], H. Jaggi[1], J. Herbert[1], R. I. Grossman[1], M. Milham[2,3], and Y. Ge[1]

[1]Radiology, Center for Biomedical Imaging of New York University, New York, NY, United States, [2]Phyllis Green and Randolph Cowen Institute for Pediatric Neuroscience, [3]New York University Child Study Center, New York, NY, United States

Introduction:

Functional homotopy, the high degree of synchrony in spontaneous activity between geometrically corresponding inter-hemispheric regions, is a fundamental characteristic of the brain's intrinsic functional architecture [1, 2]. A key feature of multiple sclerosis (MS) is extensive axonal degeneration within the corpus callosum (CC), the white matter tract connecting the cerebral hemispheres. Decrements in the integrity of the CC may be expected to affect functional interactions between the hemispheres The aim of this study was to determine whether homotopic resting state functional connectivity (RSFC) is altered in patients with MS using a recently developed voxel-wise analysis [2] of resting-state functional MRI (RS-fMRI) data, named voxel-mirrored homotopic connectivity (VMHC).

Methods:

Six patients with clinically definite relapsing-remitting (RR) MS (females, mean age = 33 years, mean EDSS score = 1.72) and six sex/age matched health volunteers were recruited. The patients had a varied degree of symptoms with mean disease duration of 5.6 years, five patients showed lesions on the CC or mild atrophy. RS-fMRI was performed at 3T using a gradient echo EPI sequence (TR/TE = 2sec / 30msec, flip angle = 75^{o}, FOV = 220 x 220 mm^2 and acquisition matrix size = 128x128). 20 slices were collected parallel to a line passing through the anterior-posterior commissure (AC-PC line) with 5 mm slice thickness and 1mm gap and positioned to cover the entire cerebrum. In addition, sagittal MPRAGE scans were also performed to acquire high resolution 3d anatomical images.

Data were preprocessed using both FSL and AFNI (scripts containing the processing procedures are available via The 1000 Functional Connectomes Project: http://www.nitrc.org/projects/fcon_1000). Preprocessing steps included spatial smoothing with FWHM=6mm, band pass temporal filtering 0.01-0.1Hz, removal of nuisance signals (motion parameters, the global signal, and signals derived from CSF and white matter), and transformation to MNI152 space (2x2x2mm^3). VMHC, the Pearson's correlation between the preprocessed time series of each pair of symetrical inter-hemispheric voxels, was computed according to the procedures outlined in [2]. The resultant values were z-transformed (using Fisher's r-to-z transform) and were used for subsequent group-level analysis. We compared VMHC between the patient group and normal control group using a student two sample *t*-test.

Results:

As demonstrated in Figure 1a, robust whole brain VMHC (Z>2.3, cluster level p<0.05, corrected) was detected in both groups. Healthy controls exhibited the strongest VMHC within visual, motor and somatosensory cortex, whereas relatively weaker VMHC was observed between homotopic prefrontal and temporoparietal association areas, particularly dorsolateral and ventrolateral regions which are known to demonstrate lateralization of function related to language, attention and cognitive control (Figure 1). These findings are consistent with previously reported results [1, 2].

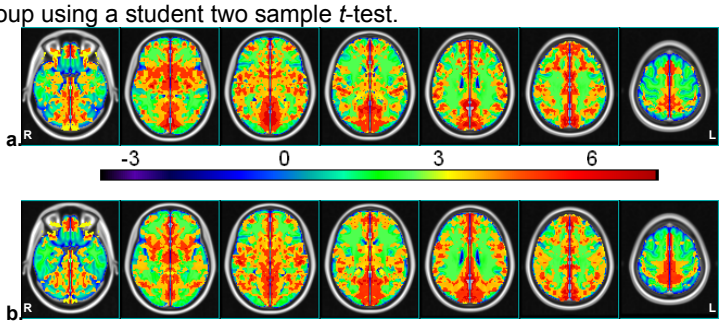

Figure 1. Rendered group results of whole brain homotopic RSFC patterns (red colors represent higher strength). **a.** normal controls, **b.** MS patients.

Figure 1b exhibits multi slices view of whole brain homotopic RSFC pattern of MS patients. The results of direct comparisons of VMHC (P<0.05) are shown in Figure 2. Relative to controls, MS patients exhibited weaker VMHC within many higher-order cognitive regions, including frontal, temporal and occipital lobes (e.g. cingulate gyrus, lingual gyrus, precuneus; shown in blue in Figure 2). As shown in red in Figure 2, relative to healthy controls, MS patients also exhibited increased VMHC in regions associated with sensory processing and motor control, including the parietal lobes (e.g. supramarginal gyus, angula gyrus) and motor cortex. Such increases in VMHC may reflect compensatory increases in interhemispheric coordination in MS.

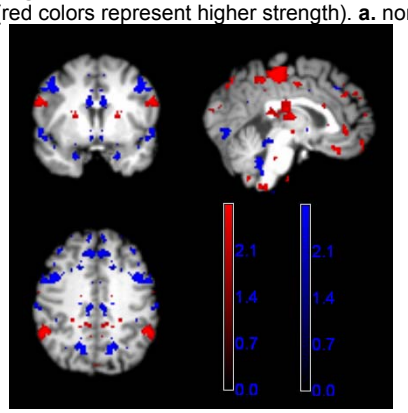

Figure 2. Comparison map, p<0.05. In contrast to group of normal controls, regions showing increased homotopic RSFC in MS are in red blobs; regions showing reduced homotopic RSFC in MS are in blue blobs.

Discussion:

Our data provide preliminary evidence of the potential utilty of VMHC analyses for the detection of abnormalities of inter-hemispheric coordination in MS. We demonstrated that whole brain homotopic RSFC patterns were altered in patients with MS, with reduced interhemispheric coordination in many higher-order cognitive regions and increased interhemispheric functional connectivity between primary sensorimotor regions. We suggest that these alterations in the brain's intrinsic functional architecture changes may reflect underlying degeneration of the CC. Further studies in a large population investigating region-specific changes of VMHC in individual MS patients with different segmental pathological involvement of CC are warranted.

References:

[1] Stark, DE et. al, J Neurosci, 2008.

[2] Zuo, X, et. al, J Neurosci, 2010.