

# Combined Structural and Functional Connectivity Analysis in Multiple Sclerosis

Edmund W Wong<sup>1</sup>, Roxana Teodorescu<sup>2</sup>, Lazar Fleisher<sup>2</sup>, Cheuk Ying Tang<sup>1</sup>, Matilde Inglese<sup>2</sup>, and David Matthew Carpenter<sup>1</sup>

<sup>1</sup>Radiology, Mount Sinai School of Medicine, New York, New York, United States, <sup>2</sup>Neurology, Mount Sinai School of Medicine, New York, New York, United States

## Introduction

Techniques are emerging to combine fMRI and DTI in order to improve the understanding of connections in the human brain. These techniques are relatively new and how the relationship between structural and functional connectivity changes in disease is an area of active investigation. In multiple sclerosis (MS) it has been shown that patients with a higher lesion load and greater structural damage of normal-appearing brain tissue have increased and more widespread task-based activation when compared to controls suggesting that an increased recruitment of “critical” cortical networks might have a compensatory role. Here we combined the DTI and resting state fMRI to assess the relationship between white matter integrity and functional coactivation during rest in patients with relapsing-remitting MS (RR-MS) and healthy controls.

## Methods

**Subjects:** Resting state fMRI and DTI were acquired on 5 patients with RR-MS and 5 age and gender matched controls on a Philips 3T Gemini scanner.

**Image Acquisition:** High resolution T1 anatomical scans were acquired using a sequence with the parameters: TR = 2.5s, TE = 3.5ms, FOV = 22.4cm, matrix size = 224x224, 172 slices with thickness 1mm. EPI BOLD scans were acquired using a sequence with the parameters: TR = 3600ms, TE = 27ms, FOV = 22cm, matrix size = 112x112, 57 slices, 2.5mm slice thickness, no gap between slices. The resting state protocol acquired 250 measurements (15 minutes). DTI was acquired with TR = 5.7s, TE = 70ms, matrix size = 128x128, 54 slices, FOV = 21cm, b-factor = 1200s/mm<sup>2</sup>, and number of directions = 32.

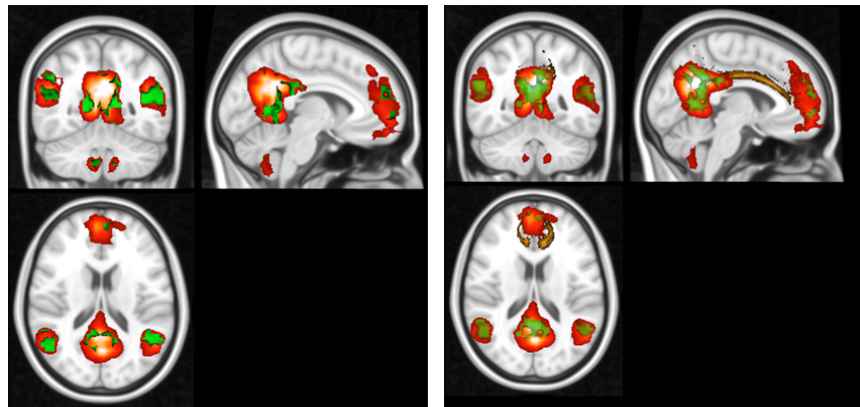
**Image Analysis:** Multi-subject independent component analysis (ICA) was used to identify 20 unique networks of resting state activity using MELODIC (Beckmann and Smith 2004) as implemented in FSL. Raw diffusion images were eddy-current corrected, diffusion tensors were calculated and FA maps were generated using FSL (Smith 2004). Mean global white matter FA was derived from the whole brain average of the white matter skeleton computed using the tract-based spatial statistics normalization and skeletonization routine (FSL). The mean FA of the cingulum bundle was calculated using a mask made by the union of the cingulum bundle of the John Hopkins University (JHU) white matter probability atlas and each individual’s white matter skeleton. The FA values were entered into dual-regression analysis to find voxels where coactivation of the default mode network correlated with global and, in a separate analysis, cingulum bundle FA. The dual regression was limited to areas designated by the ICA to be within the default mode network ( $t > 2.6$ ).

Students t test was used to compare global and cingulum FA between patients and healthy volunteers.

## Results

Global white matter FA was decreased in patients ( $t = 3.2$ ,  $p = .012$ ). Global FA was inversely correlated with coactivation of much of the default mode network. Figure 1 shows the DMN (red) and the areas that had a negative correlation between FA and coactivation (green;  $p < .05$ ). Peak significance reached  $p = .001$  in the right parietal cortex,  $p = .002$  in the left parietal cortex,  $p = .001$  in the anterior cingulate, and  $p = .001$  in the posterior cingulate cortex.

We followed up with a tract-specific FA correlation. The cingulum bundle directly connected the anterior and posterior of the cingulate cortex and is therefore highly anatomically relevant to the default mode network. FA of the cingulum bundle (Figure 2, yellow) also had negative correlations ( $p < .05$ ; Figure 2, green) within areas of the default mode network (Figure 2, red). Peak significance reached  $p = .001$  in the right parietal cortex,  $p = .001$  in the left parietal cortex,  $p = .001$  in the anterior cingulate, and  $p = .001$  in the posterior cingulate cortex. The patients had lower FA in the cingulum bundle but this did not reach significance ( $t = 1.6$ ,  $p = .148$ ).



**Figure 1:** Negative correlation of global FA (green) with coactivation in default mode network (red).

**Figure 2:** Negative correlation of cingulum FA with coactivation in default mode network (red). Cingulum bundle shown in yellow.

## Discussion

Although preliminary, our results show that white matter damage is inversely correlated with co-activations within the DMN suggesting that high temporal coherence between spatially distinct, functionally-related brain regions is affected by abnormal structural connectivity.

## References

- C.F. Beckmann, C.E. Mackay, N. Filippini, and S.M. Smith, Group comparison of resting-state fMRI data using multi-subject ICA and dual regression, *OHBM*, 2009
- C.J. Honey et al., Predicting human resting-state functional connectivity from structural connectivity, *PNAS*, 2009
- C.F. Beckmann and S.M. Smith, Probabilistic Independent Component Analysis for Functional Magnetic Resonance Imaging. *IEEE Transactions on Medical Imaging*, 2004