

## Structural differences in OCB-/+ patients with clinically isolated syndrome suggestive of MS

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### Introduction

Clinically isolated syndrome describes a first neurological episode that is consistent with acute onset of inflammatory or demyelinating syndrome in the central nervous system (CNS). Interestingly, 90% of MS patients manifest themselves as CIS patients during initial clinical visits and more than 80% of CIS patients with MRI lesions will eventually develop MS. Furthermore, 95% of MS patients are oligoclonal immunoglobulin G bands (OCB) positive in CSF (OCB+) in the western countries. Therefore, one could hypothesize that OCB+ CIS patients may be more vulnerable to evolve to MS. In this study, we directly compared the OCB-/- CIS patients for structural differences using both diffusion tensor imaging (DTI) parametric maps and tissue density maps.

### Materials and Methods

This is an IRB approved study. T1 weighted (1mm<sup>3</sup> in voxel size) and DTI images (6 different encoding directions and 2mm<sup>3</sup> in voxel size) were collected from 10 OCB-(3M, 7F 42.1±14.1 years old) and 11 OCB+(0M, 11F, 35.3±11.5 years old) CIS patients. All of the images were acquired with a Siemens 3T head only scanner. Written consents were obtained from all subjects prior to image acquisition. Four parameters were evaluated, including fractional anisotropy (FA), mean (MD), axial (AD) and radial diffusivities (RD) from DTI. All of the T1 images were registered towards a pre-segmented template (not a subject from this study) using an elastic registration approach, HAMMER [3]. After registration, a series of pre-defined ROIs in the template space (including frontal, parietal, temporal, occipital white matter, corpus callosum, internal capsules, thalamus and basal ganglia) were mapped towards each individual subject's original frame to compute the medians of the four DTI parameters (FA, MD, AD and RD) for the t-tests between OCB-/- groups. Besides ROI based analysis, we further compared the DTI parametric maps and tissue density maps based upon T1 segmentation between the two groups with a voxel based analysis approach.

### Results

Using ROI analysis, OCB+ group demonstrated significantly decreased FA, increased MD and RD in the corpus callosum, and significantly increased AD within the frontal white matter compared to the OCB- group (Fig. 1). In voxel based comparisons, significant regions were identified in the medial left frontal lobe with an elevated axial diffusivity in OCB+ patients (indicated with red arrows, top panel, Fig. 2).

Additionally, in T1 based tissue density comparisons, OCB+ patients demonstrated two large regions with white matter tissue loss compared to OCB- patients. The two regions included the left splenium of corpus callosum (red arrows, middle panel, Fig. 2) and the right frontal lobe (green arrows, middle panel, Fig. 2). In order to confirm this finding, we further compared the tissue density maps from OCB+ patients with a large group of healthy controls (35 volunteers). Similar regions were observed with the exception that the abnormal volumes were larger and an additional region in left frontal (blue arrow, bottom panel, Fig. 2) was observed for the comparison between OCB+ and controls (bottom panel, Fig. 2). No such white matter tissue loss was observed in OCB- patients when compared with healthy control.

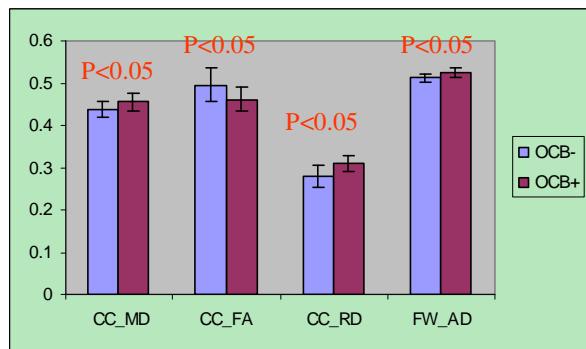


Fig.1. OCB+ patients have significantly elevated MD, reduced FA, elevated RD in corpus callosum, and significantly elevated AD in frontal white matter.

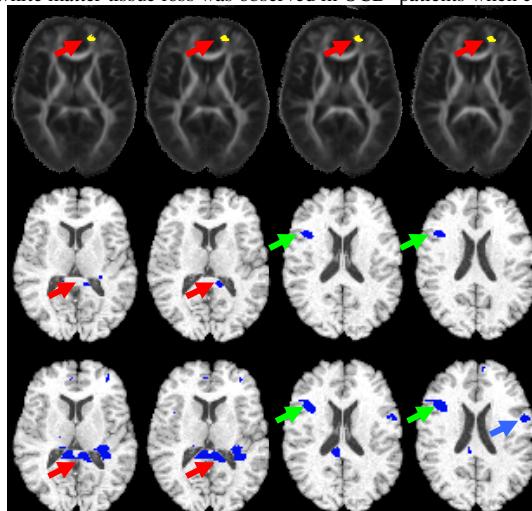


Fig.2. OCB+ patients have significantly elevated AD (top panel), reduced white matter density (mid panel) compared to OCB- patients. OCB+ patients also demonstrated similar abnormal regions with white matter tissue density loss compared to healthy control (bottom panel).

### Discussion

Structural differences between the OCB+ and OCB- CIS patients are observed using both DTI and T1-weighted images. Specifically, corpus callosum and frontal white matter were identified with significant differences between these two groups in both ROI based and voxel based analyses. Both these two regions have been identified in MS patients. Using a voxel based analysis with FA and MD, frontal white matter was found abnormal in relapsing remitting MS patients when compared to healthy control [4], while corpus callosum is one of the common areas for white matter degeneration in MS [5]. Both of these regions are not likely to be evident with clinical testing/EDSS since neither area controls major motor or sensory functions. Thus, our results suggest that OCB+ patients exhibited more severe structural abnormality and the identified regions were similar to those observed in MS patients.

### References

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