Imaging the Cortical Myelination Pattern and Investigating its Correlation with Clinical Disability in Multiple Sclerosis

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Introduction- Cortical demyelination represents a major component of disease progression in multiple sclerosis. While extensive cortical demyelination is seen in postmortem studies, the ability to recognize and quantify grey matter demyelination in-vivo using MRI will greatly improve understanding of MS disease evolution and the origins of disability. T1/T2 has been used as a method to detect cortical myeloarchitecture in macaques, chimpanzees and humans. We hypothesize that neuroinflammatory changes to the cortical ribbon can be detected using T1/T2 signal and that these changes will correlate with clinical measures of disability in multiple sclerosis.

Methods- Five healthy volunteers (age: 45.2 ± 9.7, 2 men) and 11 MS cases (age: 46.8 ± 18.5, median Expanded Disability Status Scale or EDSS: 2, 7 men) were recruited for this study. The cortical grey matter ribbon was segmented in each subject using multi-echo MPRAGE sequence in Freesurfer. T1/T2 image was generated using the T1-weighted MPRAGE and T2-FLAIR sequences. Signal intensity from the middle 40% of the cortical ribbon (to remove CSF and WM signal contamination) was overlaid on the surface maps generated from Freesurfer. Additionally, the signal intensities from T1-weighted, uniformized T1-weighted, and quantitative T1, were studied. Signal intensities from specific Freesurfer ROIs (precentral gyrus, paracentral gyrus, postcentral gyrus, medial temporal lobe, occipital pole, superior occipital lobe, and frontal superior lobe) were compared between healthy volunteers and MS patients. Signals from these ROIs were also correlated with clinical measures of disability in MS.

Results- T1/T2 signal, mapped on to the brain surface, showed higher signal in areas that are known to have higher levels of cortical myelination in healthy volunteers. T1/T2 signal was more sensitive and reliable in detecting cortical myeloarchitecture in healthy volunteers when compared to other normalized measures, such as quantitative T1 maps. Surface map (Figure 1) shows reduced T1/T2 signal from MS case (bottom, 28 y.o. M, EDSS 6.5) when compared to a healthy volunteer (top, 61 y.o. F). Indeed, the group average T1/T2 signal intensity from all ROIs tended to be lower in MS patients compared to healthy volunteers (Figure 2). Time required to complete the 9-hole peg test with one hand was significantly negatively correlated with T1/T2 values from the precentral gyrus in the contralateral hemisphere (n=7 [14 hemispheres], r=-0.65, p=0.012) (Figure 3).

Discussion and Conclusion- T1/T2 tended to decrease in MS patients compared to healthy volunteers, and preliminary results suggest that it may be correlated to functional measures of disability. Patients with many juxtacortical lesions had significant segmentation errors in Freesurfer at the cortical boundaries. To minimize segmentation confounds, we restricted the analysis to signals from the middle-40% of the cortical ribbon. However, manual editing of errors or a lesion-aware tissue classification algorithm such as Lesion-CRUISE (MIPAV) will be explored in the future. These data represent the promising result of a pilot study to test methodologies, and additional data are being collected prospectively.

Acknowledgments- This study was supported by the Intramural Research Program of NINDS. Special thanks to the Neuroimmunology Clinic and the NINDS Summer Internship Program (Rita Devine and Tony Casco).