Diffusion Tensor Imaging in Pediatric Multiple Sclerosis: Studying Hemispheric White Matter

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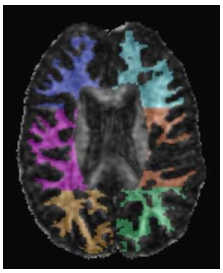
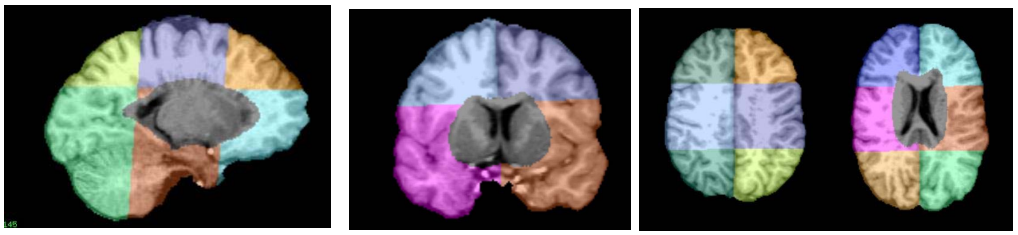
Introduction and purpose: Diffusion tensor imaging (DTI) provides a measure of white matter (WM) integrity in adults with MS. Studying DTI in children with MS provides an ideal patient population to explore whether disruption of myelin pathways occurs as a component of early MS pathology. Little is known about the applications of DTI in this unique population. The goal of this study was to explore hemispheric white matter changes in pediatric onset multiple sclerosis using DTI.

Subjects and Methods: Sixteen children with clinically diagnosed MS (mean age 15.0, range 10-17 years) and 16 healthy children (mean age 11.7, range 6-17 years) participated in the study. Diffusion data were acquired with a GE LX 1.5T MRI scanner using a single shot spin echo DTI sequence with an EPI readout (25 directions, TE/TR=0-79/8300 ms, 28 contiguous axial slices, 3 mm thick, 128 x 128 matrix, FOV = 26 cm, rbw = 125 kHz). Hemispheric regions were defined on a T1 anatomical SPGR image. Acquisition of a PD/T2 interleaved sequence facilitated co-registration of images to DTI space. Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) were calculated for six bilateral hemispheric regions including left and right occipital (LO, RO), parietal-occipital (LPO, RPO), temporal (LT, RT), frontal-parietal (LFP, RFP), inferior frontal (LIF, RIF) and frontal (LF, RF) regions (Figures 1 & 2). Group differences in FA and ADC were calculated across all regions of white matter using multivariate analyses to control for Type I error.

Figure 1: FA with segmented WM. **Figure 2**: T1 anatomical scan with hemispheric regions shown in three planes.





Results: Based on multivariate analysis, FA values for MS patients were significantly reduced relative to controls across all hemispheric regions ($p<0.001$). Specific group effects were evident for each region (Table 1). An extreme example of the difference in anisotropy was a 42% reduction in the right frontal lobe FA for MS patients versus that of controls (mean FA = 0.31 versus 0.53) ($p<0.001$). In addition, mean ADC values were 55% larger in MS patients relative to controls across hemispheric regions ($p<0.001$) (Table 1).

Table 1: Mean FA and ADC within hemispheric regions (p<.001)

Hemispheric Region (R=Right, L=Left)	Mean FA		Mean ADC	
	Controls	MS Patients	Controls	MS Patients
R Inferior Frontal	0.48	0.33	0.000804	0.001886
L Inferior Frontal	0.48	0.33	0.000791	0.001892
R Frontal	0.53	0.31	0.000779	0.001807
L Frontal	0.52	0.32	0.000779	0.001824
R Temporal	0.51	0.33	0.000758	0.001840
L Temporal	0.51	0.34	0.000752	0.001807
R Frontal-Parietal	0.53	0.33	0.000706	0.001883
L Frontal-Parietal	0.52	0.34	0.000711	0.001915
R Occipital	0.49	0.30	0.000734	0.001853
L Occipital	0.49	0.31	0.000729	0.001838
R Parietal-Occipital	0.49	0.29	0.000708	0.001859
L Parietal-Occipital	0.48	0.29	0.000710	0.001838

Conclusions: We present a unique DTI study focused on WM integrity in pediatric MS. Dramatic differences in FA and ADC strongly suggest profound losses of the integrity of WM in affected children. Reduced FA values indicate less directional water diffusion occurring in MS patients, possibly suggesting demyelination or axonal membrane damage [(1)]. Similarly, increased ADC or diffusivity could indicate microstructural tissue damage in WM. Segmentation of lesional and non-lesional WM is now underway, and will provide further insight to the relative contribution of MS lesions towards the observed DTI findings. Lesional analysis will indicate how the disease differentially impacts normal appearing WM relative to lesion tissue.

1) Mabbott, D.M., Noseworthy, M.D., Bouffet, E., Rockel, C., and Laughlin, S. (2006). Diffusion tensor imaging of white matter after cranial radiation in children for medulloblastoma. Correlation with IQ. *Neuro-Oncology*. July, 244-251.