Optic Radiation DTI Measures of White Matter Integrity Inversely Correlate with Visual Acuity in MS

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Background: There are generally poor correlations between lesion load measures on MRI and composite disability measures in multiple sclerosis (MS), attributed to the lack of specificity of both whole-brain MRI and clinical metrics. Restricting imaging experiments to single anatomic pathways where structure and function can be specifically quantified may provide insights into MS pathogenesis and yield outcome measures for testing neuroprotective therapies. Diffusion tensor imaging (DTI) provides one method which may provide stronger correlations between structure and function [Fox]. We applied DTI to the optic radiation (OR) in patients with MS.

Methods: 14 patients with a prior history of unilateral optic neuritis underwent DTI, optical coherence tomography (OCT), and visual acuity testing with a 2.5% contrast (gray-on-white) Sloan chart during a single study visit.

Retinal nerve fiber layer thickness (RNFLT) was quantified using Zeiss Stratus OCT by the Fast RNFL protocol.

DTI measurements were performed on a Siemens TIM Trio (Erlangen, Germany) with a standard 12-channel head coil. HARDI data were acquired with a twice-refocused spin echo [Reese] (TE/TR=102/7700msec, 128x128x48 matrix, FOV=256x256x96mm), 71 b=1000 sec/mm2 acquisitions with gradient directions selected by a coulomb repulsion algorithm [Jones], and 8 b=0 acquisitions at equally spaced intervals. Motion correction was performed using FSL [Smith]. Spherical deconvolution, with regularization optimized by generalized cross validation, was performed in each voxel to estimate fiber orientation [Sakaie].

Regions of Interest (ROI) were manually drawn on the lateral geniculate nucleus and occipital cortex using AFNI [Cox], which served as seed points and targets for OR fiber tracking. Probabilistic tracking between seed and target regions was performed, with each step determined by rejection sampling [Tournier]. The number of tracks intersecting a given voxel is used to estimate connectivity between that voxel and the seed/target regions. An anatomic mask white matter mask was applied for each individual patient.

Relationships between clinical and imaging variables were assessed using the Pearson correlation coefficient and single-sided hypothesis tests for the expected relationship.

Results: Longitudinal diffusivity (LD) and transverse diffusivity (TD) in the OR correlated inversely with visual function measured by Sloan low-contrast letter acuity eye chart (Figure 1). There was a trend but no significant correlation with fractional anisotropy. No significant correlations were observed between retinal thickness and visual acuity or retinal thickness and DTI measures.

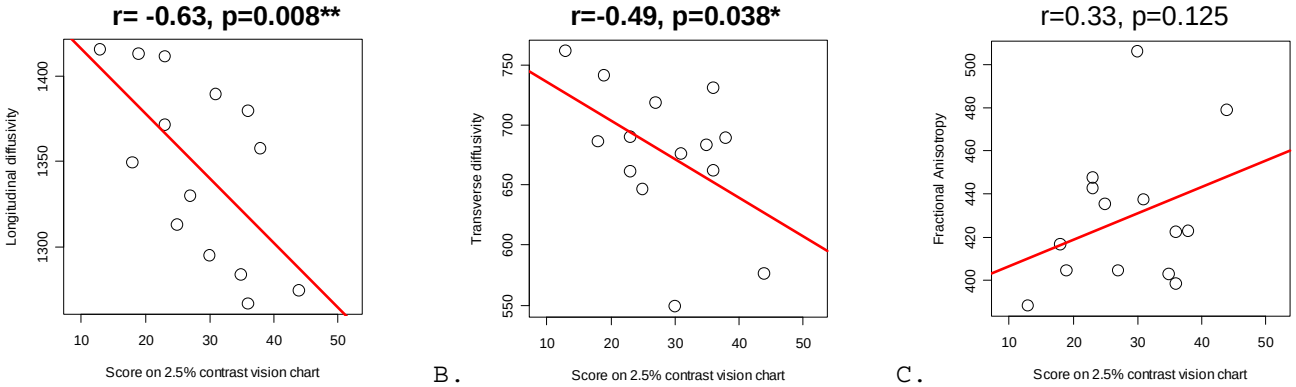

Figure 1: Scatterplots of DTI-derived longitudinal diffusivity (A), transverse diffusivity (B) and fractional anisotropy (C) versus low-contrast letter acuity. Lower score on vision chart corresponds to poorer visual acuity.

Discussion: DTI measures in the optic radiations correlate with clinical function in patients with MS and may represent a measure to quantify structural integrity in the visual system. Pathologic processes underlying these changes may include axon loss, demyelination, astrogliosis, or most likely a combination of these processes. Future studies will address whether these changes affect the visual system preferentially versus a diffuse process affecting all cerebral white matter.

References:

1. Fox RJ et al. Arch Neurol 65:1179-1184 (2008).
2. Reese TG et al Magn Reson Med 49:177-82 (2003).
3. Jones DK et al Magn Reson Med 42:515-25 (1999).
4. Smith SM et al Neuroimage 23 Suppl 1:S208-19 (2004).
5. Sakaie KE and Lowe MJ. Neuroimage 34:169-76 (2007).
6. Cox RW et al. Comp Biomed Res 29:162-173 (1996).
6. Tournier JD et al. ISMRM 13:1343 (2005).