Optic Nerve Injury Increases Water Diffusivity

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Introduction

The lack of correlation between neurological disability and conventional magnetic resonance imaging (MRI) injury markers presents a conundrum in the care of multiples sclerosis (MS) patients. Diffusion tensor imaging (DTI) has been widely applied to MS patients for a better assessment of the underlying pathology. To evaluate if DTI parameters correlate with the neurological disability in MS, the optic nerve was chosen to study because it is often affected in MS patients. The optic nerve provides a CNS white matter tract with relatively simple architecture (no gray matter or neurons). Furthermore, optic nerve function can be quantified *in vivo* using standard, acceptable measures that can be readily analyzed statistically. Thus, it is an ideal model tissue to determine whether DTI indices correlate with neurological disability. In this study, DTI was performed on nine healthy volunteers and three chronic optic neuritis patients. Increased apparent diffusion coefficient (ADC) and decreased relative diffusion anisotropy were observed in the patients' affected eyes.

Methods

In vivo DTI data was acquired using a 4-element phased array "optic nerve" coil on a 3-tesla Allegra scanner (Siemens AG, Erlangen, Germany). A fat saturation-suppression spin echo EPI diffusion sequence was employed with parallel imaging (GRAPPA, acceleration factor 2, and 24 reference lines). Diffusion weighted images were acquired trans-axially (field of view = 168 × 168 mm^2, 128 × 128 data matrix , and partial Fourier factor 6/8) resulting in an isotropic voxel of 1.3 mm^3. Sixty-four magnitude images were acquired with TR/TE = 3000/76 ms and *b* values = 0 and 800 s/mm^2 and averaged off-line after correction for motion and eddy currents. Six icosahedral diffusion gradient directions were employed to minimize noise propagation during tensor calculation [1].

Results and Discussions

The ADC value for the optic nerve in healthy volunteer (Fig. 1A) was 0.71 ± 0.11 $\mu m^2/ms$ (n = 9) compared to an elevated value of 1.27 ± 0.10 $\mu m^2/ms$ (n = 3, $p < 0.001$) in the patients' affected nerve (left box, Fig. 2A). The axial ($\lambda_{\parallel}$) and radial ($\lambda_{\perp}$) diffusivity, which characterizes the water diffusion parallel and perpendicular to the nerve fiber, correspondingly increased from 0.95 ± 0.18 $\mu m^2/ms$ and 0.59 ± 0.09 $\mu m^2/ms$, to 1.39 ± 0.10 $\mu m^2/ms$ and 1.20 ± 0.10 $\mu m^2/ms$, respectively. The anterior-posterior orientation of the nerve fiber is reflected as green (red: left-right; blue: superior-inferior) in the color coded anisotropy map (Fig. 1B). The dimmer green in the patient's affected nerve (left box, Fig. 2B) indicates lower diffusion anisotropy. A whisker plot representing the projection of the principal eigenvector in each voxel overlaying the scaled relative anisotropy (sRA) map (Fig. 1C and 3C) can also show the fiber coherence in the optic nerve. The whiskers in the optic nerve were assigned as red in contrast to yellow of the non-nerve tissues. The sRA was measured to be 0.06 ± 0.01 (n = 3) in the patients' affected eyes (left box, Fig. 3C), a three-fold decrease from 0.19 ± 0.04 for the healthy volunteers. In addition to the color coded anisotropy map and the whisker plot, diffusion ellipsoids may be used to characterize the diffusion property in each voxel (Fig. 1D). The enlarged and more spherical diffusion ellipsoids reflecting the increased ADC in patient's affected nerve (left box, Fig. 2D) is consistent with the decreased sRA and loss of the fiber coherence (left box, Fig 2C).

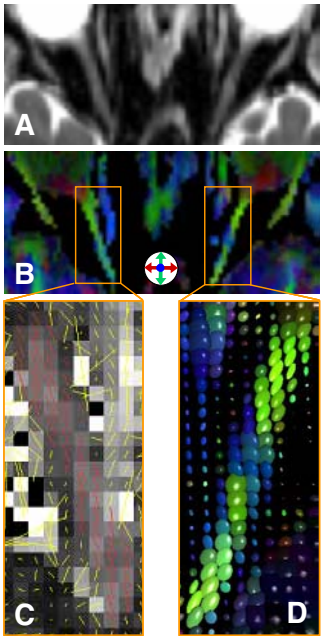

Figure 1. Healthy optic nerve. (A) ADC map, (B) color coded anisotropy map, (C) whisker plot overlaid onto sRA map, and (D) diffusion ellipsoid map.

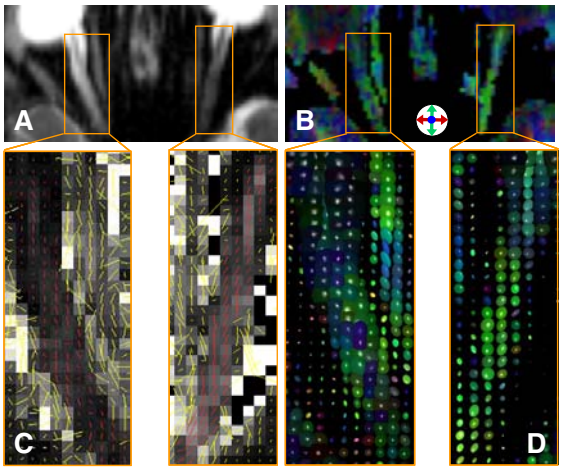

Figure 2. Diffusion tensor imaging parameter maps of the optic nerve from a chronic optic neuritis patient with one eye blind (left panels): (A) ADC map, (B) color coded anisotropy map, (C) whisker plot overlaid onto sRA map, and (D) diffusion ellipsoid map.

The limited patient population examined to date prohibits a meaningful statistical comparison between affected and unaffected eyes within the patients. However, the reduced ADC, $\lambda_{\parallel}$, and $\lambda_{\perp}$ of the presumably unaffected optic nerve from one of the patients (right panels, Fig. 2) may suggest a possible ongoing degeneration of the optic nerve in the unaffected eye. The optic nerve diffusion measurements are distinct from those reported recently [2-4] due to use of different pulse sequence, image resolution, and ROI definition. Nevertheless, the trend of diffusion changes between healthy and chronically injured eyes appears consistent with a recent report by Trip et al. [2].

Conclusion

Dramatic changes in water diffusion property were observed in the affected optic nerve of chronic optic neuritis patients. The damage so detected may involve both demyelination and the loss of ordered nerve fiber structure as reflected by the increased ADC and reduced sRA in the optic nerve from the affected eye.

Reference

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