DIFFUSION TENSOR IMAGING OF OPTIC NEURITIS AND ITS RECOVERY

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INTRODUCTION

Optic Neuritis (ON) is a retrobulbar, inflammatory injury to the optic nerve, and is strongly associated with multiple sclerosis (MS). ON patients present with eye pain, subacute onset vision loss, and/or dyschromatopsia (color vision loss); however, symptoms typically resolve over a period of about six weeks, and may continue up to one year. Diffusion tensor imaging (DTI) has emerged as a tool to provide in vivo assessment of the pathology of the optic nerve as well as multiple sclerosis lesions [1]. Increases in the mean diffusivity (MD) or apparent diffusion coefficient (ADC) as well as a reduction in fractional anisotropy (FA) have been demonstrated in MS patients and may represent axonal disruption [1-3]. Recently, DTI has been used to characterize the shape of the optic nerve and the presence of lesions [4-6], suggesting that optic nerve DTI may provide an indication of its structural integrity. Because of the inherent spatial distortion in DTI images of the optic nerve due to the close proximity of the fontal sinuses, DTI measures are susceptible to high variability. Hence, the appropriate DTI measures to characterize the presence and severity of ON as well as evaluate its recovery have not been established. As a result, in this study we hypothesized that the optic nerve experiencing ON may not actually exhibit significantly different FA or ADC from that of the unaffected eye or over the course of recovery. Instead, we predicted that ON is characterized by a greater distribution of FA and ADC (i.e., greater standard deviation), suggesting that acute ON is associated with more heterogeneous diffusion within the optic nerve.

METHODS

Nine patients (mean age 33 years) with unilateral ON as a clinically isolated syndrome or in the presence of MS participated in this study, which was approved by the research ethics board governing the institution. Patients underwent two imaging sessions, one at symptom presentation (baseline) and one at 6 months post ON onset. Image acquisition was conducted using a 3 Tesla MR scanner (Signa VHI; GE Healthcare, Waukesha, WI), equipped with an eight-channel phased-array radiofrequency head coil. DTI images were acquired in a coronal plane perpendicular to the optic nerve (11 directions, 2 averages, b = 850 s/mm^2, TR/TE = 8000/84.3 ms, FOV = 240x240 mm, 24 slices, 3-mm thick, matrix 128 x 128). FA and ADC images were reconstructed using *Functool* (GE Healthcare). Using the drawing tool of FSL (FMRIB, Oxford University), the optic nerve of each eye was manually segmented by computer mouse with the aid of the b_0 image of the DTI data set. The mean and standard deviation of FA and ADC were obtained for each nerve, for each patient and scan. These mean and standard deviation values of ADC and FA were each entered into an analysis of variance with eye and scan session as within-subject factors. Post-hoc tests were conducted by paired Student's *t*-tests.

RESULTS

There were no significant effects of eye or scan session for mean FA. For the standard deviation of FA, there was a trend to significance for eye ($F(1,8)=5.03$, $p=0.055$). Follow-up tests revealed a significant difference between eyes at baseline (Table 1). For mean ADC, there was a significant effect of scan session ($F(1,8)=9.32$, $p=0.02$), but no effect of eye. Follow-up tests (Table 2) revealed that mean ADC increased significantly over scan sessions for the ON eye, and approached significance for the unaffected eye. For the standard deviation of ADC, there were significant effects of scan session ($F(1,8)=15.2$, $p=0.005$) and eye ($F(1,8)=5.96$, $p=0.04$). Follow-up tests revealed a significant difference between the eyes at baseline (Table 1) and significant differences across scan sessions for both eyes (Table 2).

Table 1. DTI comparisons between affected and unaffected optic nerves at symptom onset (baseline). ADC values are reported as x1000 mm^2/s.

Eye	Mean FA	SD FA	Mean ADC	SD ADC
Affected	0.40 (0.05)	**0.16 (0.1)**	1.22 (0.10)	**0.48 (0.04)**
Unaffected	0.39 (0.04)	**0.15 (0.2)**	1.24 (0.16)	**0.40 (0.07)**
p value	0.75	***0.04***	0.69	***0.01***

Table 2. DTI comparisons across scan sessions for the affected and unaffected optic nerves. ADC values are reported as x1000 mm^2/s.

	Affected Eye				Unaffected Eye			
	Mean FA	SD FA	Mean ADC	SD ADC	Mean FA	SD FA	Mean ADC	SD ADC
baseline	0.40 (0.05)	0.16 (0.1)	**1.22 (0.10)**	**0.48 (0.04)**	0.39 (0.04)	0.15 (0.2)	1.24 (0.16)	**0.40 (0.07)**
6 months	0.38 (0.04)	0.17 (0.2)	**1.51 (0.18)**	**0.60 (0.10)**	0.40 (0.04)	0.16 (0.2)	1.44 (0.16)	**0.54 (0.05)**
p value	0.49	0.60	***0.009***	***0.03***	0.61	0.16	0.062	***0.002***

CONCLUSION

Our results to date suggest the standard deviation of the ADC and FA, and not their means, may be sensitive indicators of the presence of ON at symptom onset. That is, there may be increased variability in water diffusion in the optic nerve in the presence of ON due to inflammation or swelling. Mean ADC does, however, increase during recovery, as inflammation and swelling resolve. The standard deviation of FA within the optic nerve does not change over the course of recovery. This may be due to the limited dynamic range of FA itself, thus limiting its sensitivity over repeated sessions. Why the standard deviation of ADC within the optic nerve of both eyes increases over 6 months is unclear at this time unclear. The response of the unaffected eye may be compensatory in nature at baseline, with standard deviation equalizing to that of the ON nerve by the end of recovery. Further studies are warranted to investigate this issue. In summary, the variability of DTI measures, rather than their means, may be more sensitive indicators of the presence of ON and its subsequent recovery.

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