

Correlation between DTI and Visual Evoked Potential in Mice with Optic Neuritis

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Introduction

Optic neuritis is usually the first symptom of Multiple Sclerosis. It starts with recurrent inflammation leading to demyelination and eventually axonal and neuronal loss. These pathologies are closely involved in clinical complaints regarding the vision blurring or the loss of vision. While magnetic resonance diffusion tensor imaging (DTI) has been demonstrated to be a sensitive tool to characterize structural changes caused by optic neuritis (1), there was no reported study to correlate DTI to neural functional outcomes in subjects with optic neuritis. In this study, we used an animal model of optic neuritis, the experimental autoimmune encephalomyelitis (EAE) induced by MOG (1), and recorded visual evoked potential (VEP) to assess changes in visual function in EAE mice. High resolution *in vivo* DTI was collected from each animal before VEP recording. The degree of correlation between DTI and VEP was assessed.

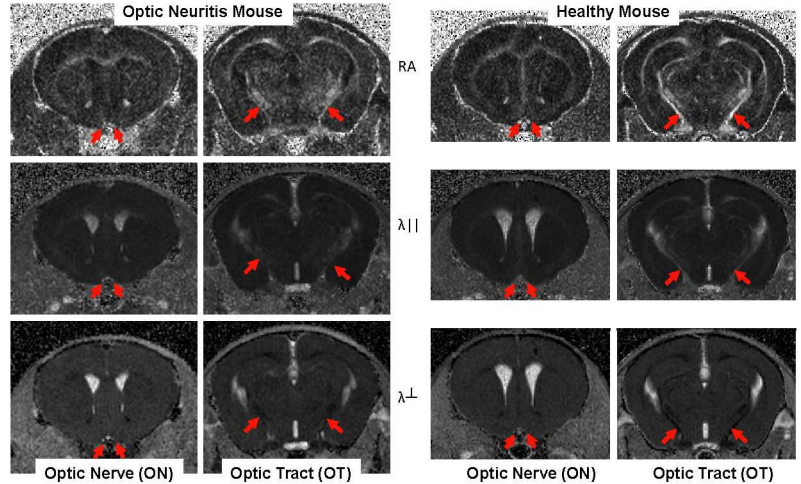


Figure 1. DTI maps of healthy and optic neuritis mice

Materials and Methods

Female, 8-week-old, C57BL/6 mice were used. Eight weeks after EAE induction (n=5) or age-matched healthy controls (n=5), DTI was collected using a Bruker 4.7T BioSpec small animal MRI instrument with slice thickness 0.5 mm, FOV of 1.5 cm x 1.5 cm and matrix 128 x 128 (zero filling to 256 x 256), TR 2.5 s, TE 29 ms, Δ 20 ms, δ 3 ms, and six-direction diffusion scheme with b-values of 0 and 0.85 ms/ μ m². Using software written in Matlab (MathWorks, Natick, MA, USA), the eigenvalues derived from diffusion tensor were used to calculate $\lambda||$, $\lambda\perp$, and RA. For VEP recording, animals were anesthetized with a mixture of oxygen and Isoflurane. Light stimulation was applied to the eye contralateral to the VEP recording site. VEPs were recorded using a glass microelectrode filled with 1M sodium acetate and inserted in the visual cortex (400 μ m below beneath the cortical surface).

Results

In EAE mice, significant damages to the optic nerves and optic tracts were suggested by the reduced RA, decreased $\lambda||$ and increased $\lambda\perp$ as compared to the healthy controls (Fig. 1 and 2). EAE mice also showed visual deficits indicated by a 30% increase of VEP latency and a 60% decrease of VEP amplitude. The correlation between VEP and DTI is summarized in Fig. 3. VEP amplitude showed significant correlations with all DTI indices, except the $\lambda||$ of the optic nerve. VEP latency, on the other hand, showed a significant correlation only with the $\lambda\perp$ of the optic tract.

Discussion

This is the first study to correlate DTI and neural functional outcomes for optic neuritis. This study demonstrates the possibility of using DTI to predict the neural functional performance. Correlation analysis showed that VEP amplitudes were significantly correlated with DTI indices of the optic nerves and optic tracts, providing the evidence that microstructural changes detected by DTI are associated with functional alteration.

References (1) Sun et al, Neurobiology of Disease 2007; 28: 30-38.

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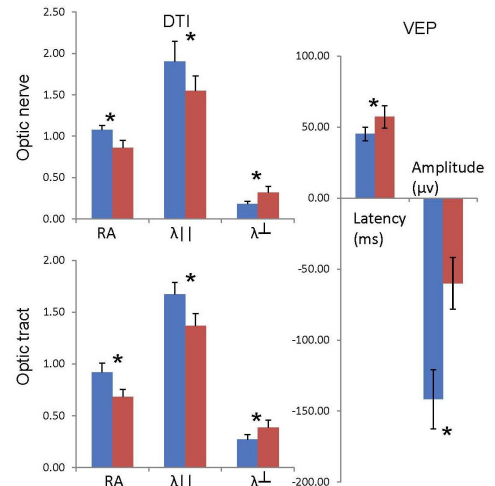


Figure 2. Mean and standard deviation of DTI and VEP quantifications of healthy (blue) and optic neuritis (red) mice.

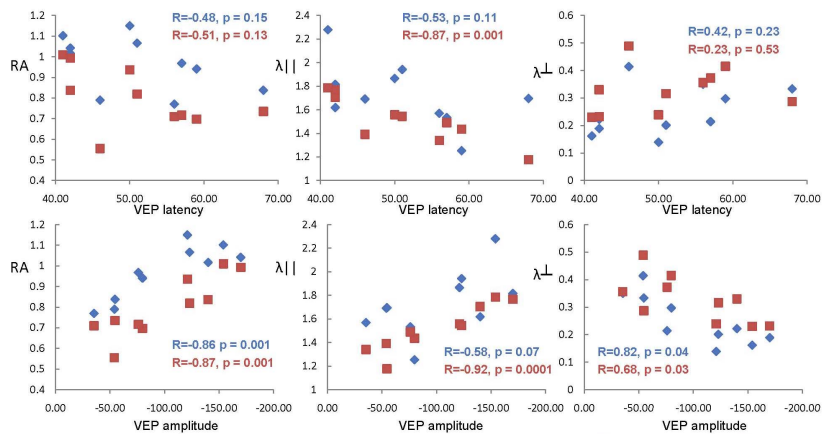


Figure 3. Scatter plots correlate VEP and DTI measured from optic nerves (blue) and optic tracts (red).