In vivo Detection of Axonal Degeneration in Cervical Spine from a Mouse Model of Amyotrophic Lateral Sclerosis

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Introduction

Transgenic mice carrying the G93A-SOD1 mutation have been used as an animal model of Amyotrophic lateral sclerosis (ALS), a neurodegenerative disease involving the selective loss of motor neurons in the cortex, brain stem, and spinal cord. Recent work suggests that *in vivo* MR-diffusion measurements can detect disease in the brain (1,2). However, there is a lack of accurate in vivo observation for cervical spinal cord, which degenerative lesion may reach chronically. In the current study, we present diffusion indices (relative anisotropy (RA), axial (λII) and radial (λ⊥) diffusivity, and trace (Tr(D)) derived by *in vivo* diffusion tensor imaging (DTI) to evaluate the progressive degeneration of nucleus and axons in brain stem and cervical spinal cord in G93A -SOD1 mice.

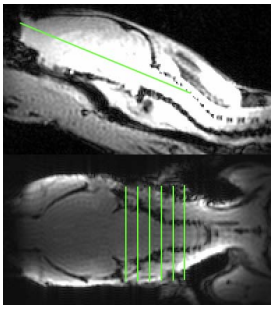

Figure 1. Transverse MR images plan is shown on sagittal and coronal view.

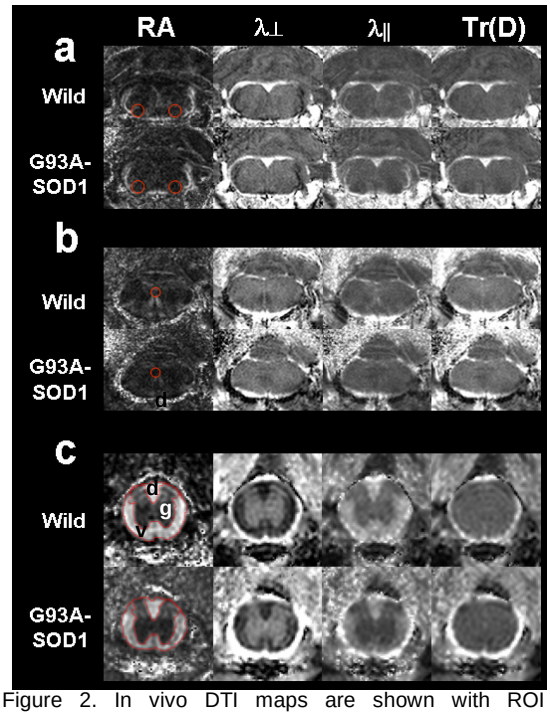

Figure 2. In vivo DTI maps are shown with ROI specifying Nc. VII (panel a), Nc XII (panel b), and cervical spinal cord (panel c). The d, g, and v in panel c represent dorsal white matter, gray matter and ventrolateral white matter.

Methods

Five 4-month-old wild type mice and five age matched G93A-SOD1 transgenic mice underwent *in vivo* DTI evaluation at brain stem and cervical spinal cord. DTI data were acquired using the set up as described previously (3). A spin-echo diffusion-weighted sequence was modified to acquire 6 transverse images with respiratory gating (Fig. 1). All images were obtained with acquisition parameters of TR 1.2 sec (gated acquisition), TE 38 msec, Δ 21 msec, δ 6 msec, slice thickness 0.5 mm, 1.0 mm gap, field-of-view 1.5 × 1.5 cm^2, data matrix 128 × 256 (zero filled to 256 × 256), total data acquisition time ~ 1.0 hrs. (Gx,Gy,Gz) = (1,1,0), (1,0,1), (0,1,1), (-1,1,0), (0,-1,1), and (1,0,-1), and b = 0 and 1.014 ms/μm^2. Image resolution was 117 × 58 × 500 μm^3.

Results and Discussion

In vivo DTI maps provide excellent contrast between gray and white matter. Thus, the region of interest (ROI) could be readily delineated in both wildtype and transgenic mice (Fig. 2). The difference between the WT and ALS mice can be seen qualitatively in the displayed λII and Tr (D) maps at Nc. VII, Nc, XII and ventrolateral white matter of cervical cord (Fig. 2). The quantitative DTI parameters at five different regions of brain stem and cervical cord are summarized in figure 3. The decrease of Tr (D) and λII is seen in the Nc. VII, Nc. XII and ventrolateral white matter with statistically significant differences, suggestive of significant neurodegeneration. Dorsal white matter and gray matter values remained unchanged. These findings are consistent with the selective loss of motor axon fibers in the ventrolateral cord in ALS. The current results suggest that *in vivo* DTI may be used to monitor the progression of neurodegenerative diseases such as ALS at cervical spinal cord.

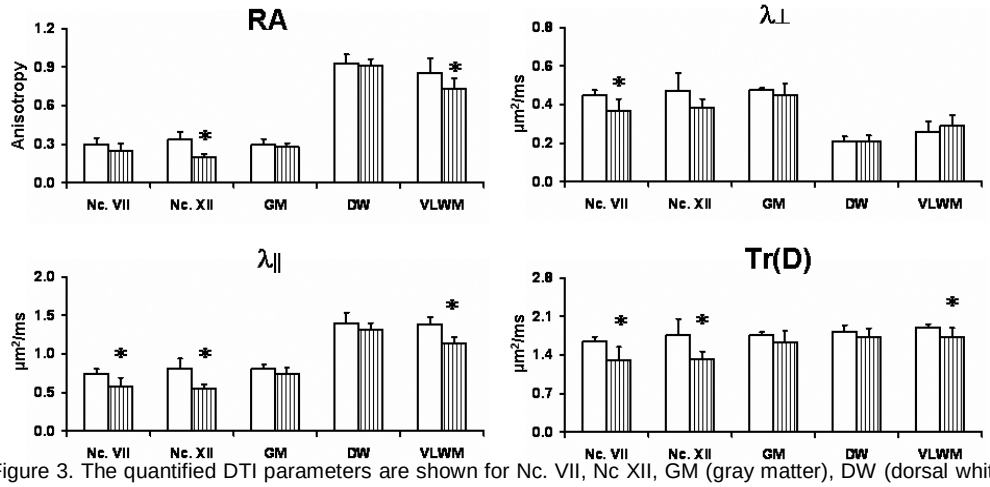

Figure 3. The quantified DTI parameters are shown for Nc. VII, Nc XII, GM (gray matter), DW (dorsal white matter), and VLWM (ventroalteral white matter); empty - control and vertical bar - G93!-SOD1. The asterisk represents that $p < 0.05$.

References

1. Niessen *et al.*, Exp. Neurol., 2006. 2. Wang *et al.*, Ann. N.Y. Acad. SCI., 2005. 3. Kim *et al.,* Neurobiol. Dis., 2006.

Acknowledgements

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