

Diffusion tensor MRI of the lumbar spinal cord in G93A-SOD1 mice

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Background

Amyotrophic lateral sclerosis (ALS) is the most common form of motor neuron disease (MND) in humans, characterised by selective degeneration of motor neurons. Currently, clinical diagnosis relies largely on behavioural tests or histological methods to directly count neurons in affected areas. Diffusion tensor imaging (DTI) can provide information on axonal organization and has been previously used to detect both axonal and myelin spinal cord damage. Here we examine the utility of DTI to measure degeneration in the lumbar spinal cord of the G93A-SOD1 transgenic mouse model of ALS.

Methods

Spinal cord imaging of both affected SOD1 mice and wildtype littermates was performed using a 16.4 T spectrometer. Animals were imaged at ~40, 75, 100, 125 and 145 days of age (n=3), with a resolution of 70 μ m x 70 μ m. Fractional anisotropy (FA) values were obtained from regions of interest within the white matter of each lumbar spinal cord. Grip strength testing of hind limbs was used to monitor disease progression. Damage to the motor neurons were confirmed using electron microscopy.

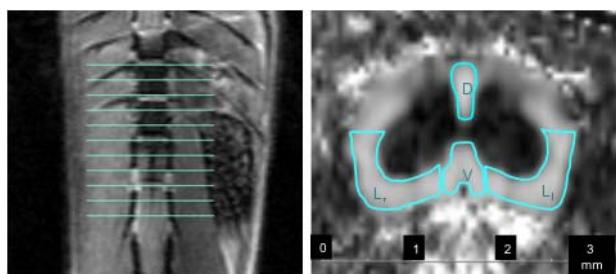


Figure 1. (left) Pilot *in vivo* T_1 -weighted images of coronal sections across the lumbar spinal cord in a WT C57Bl6 mouse. The bottom rib was used as a landmark to acquire 2D-DTI across 10 axial slices covering the lumbar enlargement, each 1 mm thick.

(right) Representative FA map calculated from an axial section within the lumbar region.

Results

The FA values were reduced in the ventrolateral white matter of the lumbar spinal cord of ALS affected SOD1 mice compared to wildtype littermates, which became more pronounced with disease progression. In contrast, there was no difference in FA in the dorsal white matter of ALS affected SOD1 mice compared to wildtype littermates. This finding is consistent with the degradation in the lumbosacral region as observed by electron microscopy.

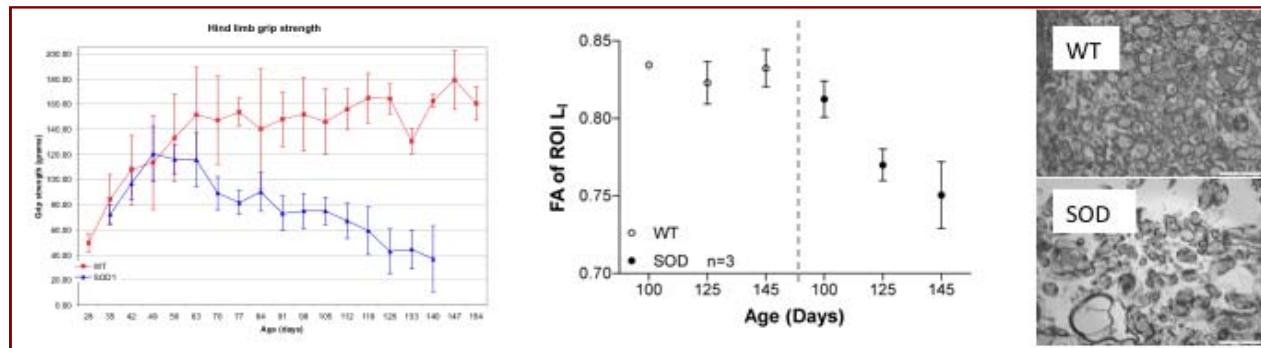


Figure 2. (left) SOD1 animals have progressive decline in the hind limb grip strength at the age of 8-10 weeks, compared to WT. (right) The decrease in FA in all ventral white matter regions became more pronounced in the older SOD1 mice (age > 100 days), as the disease progressed over time.

Conclusion

DTI may provide a useful non-invasive method to monitor the progression of ALS, allowing earlier or more accurate diagnosis of the disease. This MRI detection method could provide new way for assessing the efficacy of pilot MND treatments.