DTI Detects Progressive Neurodegeneration in the Brain and Cervical Spinal Cord in ALS

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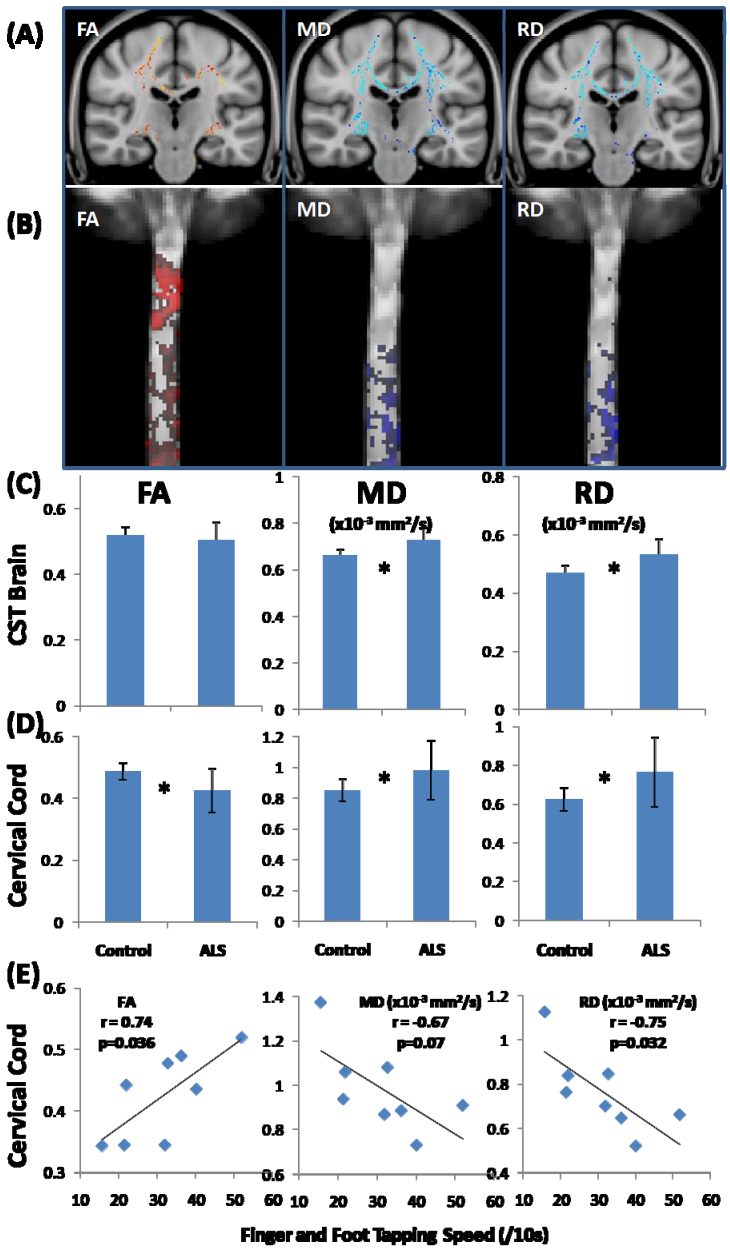
Introduction: Amyotrophic Lateral Sclerosis (ALS) is a devastating and progressive neurodegenerative disease affecting both the upper and lower motor neurons. There is a pressing need for biomarkers of disease progression that might be used to facilitate therapeutic development. We sought to detect changes in the corticospinal tract (CST) of ALS patients using DTI and to correlate these DTI measurements with clinical measures of disease progression such as finger and foot tapping speed and forced vital capacity (FVC, % predicted).

Method: Twelve patients with ALS (2 female, 56 ± 10 years age, median disease duration of 825 days) and 10 healthy control subjects (HC group, 3 females, 51 ± 12 years age) were imaged on a Siemens 3T Tim system. DTI was performed using standard single-shot EPI sequence in the brain of 10 ALS and 10 HC subjects with in-plane resolution of 1.1mm^2, slice thickness of 5mm and 2 averages, and in the cervical spine of 8 ALS and 8 HC subjects with in-plane resolution of 1.25mm^2, slice thickness of 2.5mm and 4 averages. Diffusion gradients were applied along 60 directions in the brain and 30 direction in the cord with a b-value of 1000s/mm^2. The images were corrected for eddy current and distortions, and fractional anisotropy (FA), mean diffusivity (MD), and radial diffusivity (RD) calculated using FSL (Analysis Group, FMRIB, Oxford, UK). ROIs were drawn along the CST (from white matter supporting motor cortex through to C6) and DTI parameters from these ROIs were correlated with clinical measures of ALS severity such as average tapping speed from all four limbs over 10 seconds.



Results and Discussion: The image distortions due to susceptibility changes were corrected, and the WM skeleton reliably detected using TBSS functions in FSL. Regions of decreased FA and increased MD and RD were evident along the CST in brain and cervical cord of ALS subjects (Fig. A, B; $p<0.1$), with more widespread differences seen in MD and RD. MD and RD increased by 10% and 14% in the brain and 15% and 22% in the cervical cord respectively, while FA decreased by 13% in the cervical cord (Fig. C, D; $p<0.1$). DTI measurements from some individual ROIs (cervical segments, pyramids and peduncles) significantly correlated with tapping speed and FVC (data not shown). Averaged FA, MD and RD from cervical cord (C6 through pyramids) showed significant correlation with tapping speed (Fig. E).

Conclusion: DTI reveals neurodegenerative changes in the brain and cervical cord of ALS patients and DTI measurements in the cervical cord correlate significantly with clinical measures of disease severity. The results suggest that DTI measurements may be useful imaging biomarker for disease progression in ALS.

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