T_1-weighted Images Detect Motor Neuron Degeneration in ALS

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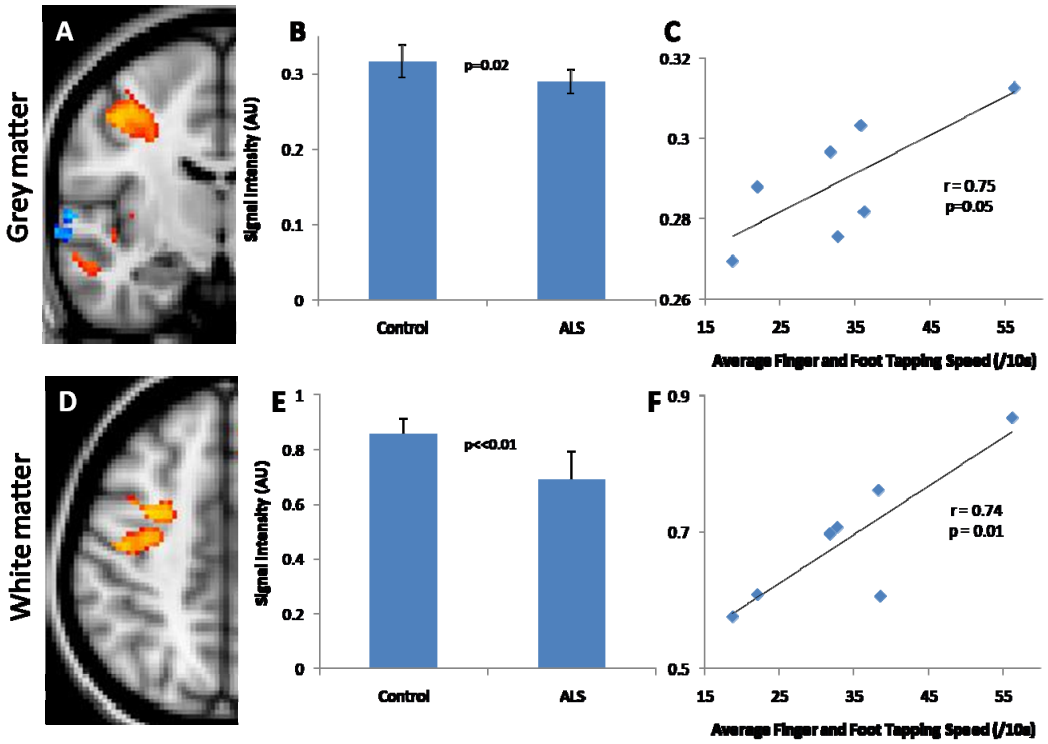
Introduction: Amyotrophic Lateral Sclerosis (ALS) is a rapidly progressive neurodegenerative disease affecting motor neurons. We sought to detect changes in the grey and white matter in the brain of ALS patients using Voxel Based Morphometry (VBM) as well as signal intensity changes on T_1-weighted images and to correlate these changes with clinical measures of disease progression such as average finger and foot tapping speed and forced vital capacity.

Method: Seven patients with ALS (57 ± 9 years age, 1 left hander, median disease duration of 991 days) and 7 healthy control subjects (HC group, 54 ± 9 years age, 2 left handed) were imaged on a Siemens 3T Tim system. T_1-weighted images were acquired in the brain using a 3D-MPRAGE sequence and a TR=2600ms, TE=3ms, TI= 900ms, flip angle =8deg, 1 slab with 192 sagittal slices, FOV = 256×256×192mm^3, isotropic resolution of 1mm^3, and 1 average. Images were segmented into GM and WM, and coregistered between all subjects. Analysis was performed using both VBM subroutines in FSL (FMRIB Software Library, Analysis Group, Oxford, UK) and an ROI analysis in which ROIs were drawn on anatomical landmarks guided by the atlas tool in FSL, and signal intensities compared between groups and correlated with clinical measures of disease severity in the ALS group. $p < 0.05$ was considered to be statistically significant.

Results and Discussion: VBM analysis of the GM revealed changes in motor cortex (Fig. A), thalamus, caudate nucleus, and parts of the middle temporal gyrus of ALS compared to HC. However, significant signal intensity reduction was observed only from the ROI drawn on the motor cortex, with the ALS group showing a 7% decrease in signal intensity (Fig. B). Furthermore, the signal intensity in the motor cortex correlated significantly with UMN dysfunction (average tapping speed, Fig C). Similarly, VBM analysis of WM revealed significant changes in the WM supporting the motor cortex (Fig. D), corpus callosum, brainstem and cerebellum. However, significant signal intensity changes were observed only from ROI drawn on the WM supporting the primary and secondary motor cortex, exhibiting a 20% decrease in ALS subjects compared to HC (Fig. E); signal intensity correlated significantly with average finger and foot tapping speed (Fig. F). A decrease in signal intensity observed in the motor cortex and underlying white matter in ALS could be due to an increase in T_1 through a loss of tissue and partial voluming with CSF as expected in neurodegeneration.



Conclusion: Neurodegenerative changes in the ALS brain could be detected using VBM. Furthermore, ROI analysis revealed a significant decrease in signal intensity from the motor cortex and WM supporting the motor cortex.

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