Longitudinal Evolution of MRI Parameters with Disease Progression in ALS

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Introduction: Amyotrophic lateral sclerosis (ALS) is a rapidly progressing neurodegenerative disease affecting the upper and lower motor neurons. MRI parameters such as FA, RD and T1 can detect these neurodegenerative changes in cross-sectional studies, but their ability to detect longitudinal changes during disease progression have not been compared and fully explored. This abstract describes longitudinal changes in T1 and DTI in the brain and cervical cord of subjects clinically diagnosed with ALS, and correlates these changes with clinical markers of disease.

Method: T1-weighted images were acquired twice from the brain of 10 ALS subjects (Initial age 51 ± 11 years, median disease duration 287 days, median duration between scans of 61 days, initial ALS Functional Rating Scale-Revised (FRS-R)=42±5 with change of -5±5 between scans) using MPRAGE sequence (TI=900 ms, 1 mm3 isotropic resolution). DTI was acquired twice from the brain of 5 ALS subjects (Initial age 47 ± 12 years, median disease duration 286 days, median duration between scans of 60 days, initial ALSFRS-R=41±4 with change of -4±4 between scans) using double spin echo EPI sequence (b=0, 1000 s/mm2, 2 mm3 isotropic resolution, 2 averages). DTI was acquired twice from cervical cord of 10 ALS subjects (Initial age 46 ± 12 years, median disease duration 286 days, median duration between scans of 61 days, initial ALSFRS-R=41±4 with change of -4±3 between scans) using double spin echo EPI sequence (b=0, 1000 s/mm2, 1.25x1.25x2.5 mm resolution, 4 averages). Clinical parameters such as FVC (forced vital capacity) and average tapping speed from all 4 limbs over 10 seconds were recorded immediately prior to each imaging session. T1 images were segmented in to GM and WM, coregistered and modulated by the Jacobian of the warp field to account for volumetric changes in FSL (FMRIB, Oxford, UK). DTI data were corrected for distortions, FA and radial diffusivity (RD) maps reconstructed. Each map was transformed into common space. T1, FA and RD changes between the sessions from various ROIs along the corticospinal tract were determined for each subject and correlated with changes in clinical parameters.

Results and Discussion: A decrease in signal with progression of disease, as expected in FA and T1, would manifest as a significant negative correlation with duration between scans and positive correlation with ALSFRS-R, FVC and tapping speed. Several MRI parameters showed the expected longitudinal changes with clinical measures of disease progression, such as a decrease in modulated T1 signal from the premotor cortex with decrease in ALSFRS-R (Fig. A), decrease in FA from the CST (average bilateral) with a decrease in average tapping speed from all 4 limbs (Fig. B), and decrease in FA from the WM of the C-spine with decrease in FVC (Fig. C). A summary of MRI changes with ALS progression is shown in Table D. Higher correlations were observed between GM (T1 brain) and clinical parameters, compared to WM changes detected using DTI. However a direct comparison of the correlation across various MRI methods was not possible due to differences in subject samples and progression rates. Surprisingly, several subjects showed significant improvement in some clinical measures of ALS progression, such as tapping speed and FVC. Similar improvements were seen in MRI parameters, such as FA in ipsilateral CST etc, both of which could be due to the effects of therapeutic drugs (such as Rilutek and Arimoclomol). A larger cohort of subjects, including age-matched healthy controls, are currently being evaluated using longitudinal MRI and clinical techniques to confirm these trends, as well as to remove confounding factors such as the effect of therapeutic drugs.

Conclusion: Here we present preliminary data showing a correlation between MRI measures of GM and WM in the brain and cervical cord and clinical markers of disease progression. A larger study with longer duration of follow-up is needed (and currently underway) to further explore the potential of MRI as a biomarker of disease progression in ALS.

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