Multimodality Voxel-Based MRI Study: Possible Tool for Disease Diagnosis and Monitoring in ALS

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Introduction:

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease that destroys the motor neurons responsible for voluntary muscle control. Currently, no non-invasive method to identify and evaluate pathological changes in the brain in ALS exists. Clinically MRI has been used for ALS studies primarily as a tool to exclude other potentially identifiable neurological pathologies. To enhance the sensitivity and specificity to identify ALS with MRI, we conducted a multimodality MRI study on ALS with simultaneous DTI and T_2 mappings. Comparisons of ALS with age-matched normal control subjects using voxel-based statistical methods revealed significant change in ALS in the subthalamic region by both modalities. This new finding is important for diagnosis and understanding the pathological process of ALS.

Method:

Five ALS patients (3 male 2 female), mean age 44.4 ± 7.2 years, were studied. Mean disease duration was 31.7 ± 17.7 months and the average ALS FRS/RFRS was 24.4 ± 0.2/30.4 ± 11.8. For each subject DTI and multi spin-echo images were acquired on a 3.0 T system (Intera, Philips Medical). The DTI images were acquired with single-shot spin-echo EPI, SENSE factor 2.5 and diffusion gradients applied in 32 non-collinear directions with b = 1000 s/mm^2. The voxel size was 0.9 x 0.9 x 2.5 mm. FA was calculated from the DTI dataset using DTI Studio [1]. Whole brain multi spin-echo images were acquired axially with 11 echoes, 8 ms echo spacing, 3s TR, SENSE factor 2, and 0.9 x 0.9 x 4.0 mm voxel size. The T_2 images were calculated using linear regression with in-house software. The ALS subjects were compared with 6 normal age-matched controls (3 male, 3 female, mean age 45.7± 8.0 yrs) using SPM2 [2].

Results:

The SPM results in Fig. 1 show significant bilateral focal FA reduction ($p \leq 0.005$) in the corticospinal tract (CST) at the level of the cerebral peduncle. Medial and superior to this abnormality in FA in the CST, T_2 ($p \leq 0.005$) in Fig. 2 reveals significant increases in the subthalamic regions in the ALS group. The SPM results are overlaid on the corresponding parametric maps. The involvement of subthalamic/thalamic region in ALS has not been previously reported. These findings could be important for understanding the pathological foundation of the disease.

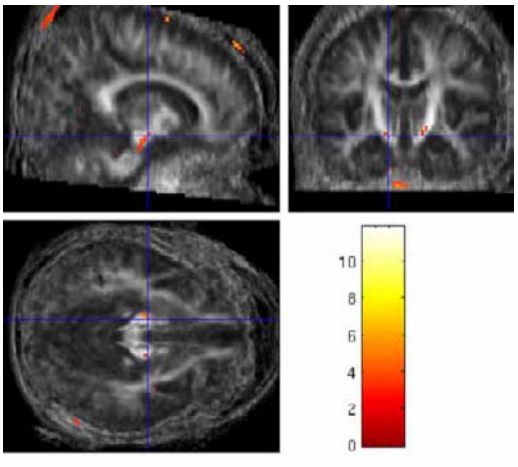

Figure 1. Areas of statistically decreased DTI FA overlaid on the normalized DTI FA image of a young male control subject.

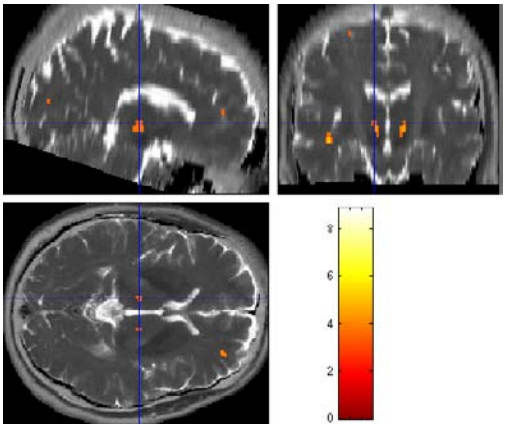

Figure 2. Areas of statistically increased T_2 overlaid on the normalized T_2 image of a young male control subject.

Conclusion:

DTI studies have shown a reduction of FA at multiple levels of CST in ALS subjects [3-6]. The changes in FA in CST are believed to be an indication of degeneration of axon myelination. The T_2 increases in the brain are generally associated with inflammatory lesions. The FA abnormality in CST was observed in the area near the subthalamic region with significant increases of T_2 in our study cohort. It is likely that these abnormalities detected by the different MRI modalities reflect the focal pathological changes of different brain tissue in very close brain regions. These results indicate that by using multiple MRI modalities it might be possible to characterize damages specific to the gray matter or white matter from the same lesioned brain area. This would provide greater specificity in detection and monitoring of ALS than using a single modality alone. Further work, both longitudinally and between groups coupled with histological analysis must be conducted in order to better characterize the extent and magnitude of the changes that occur in DTI FA and T_2 images in ALS.

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