Structure-specific white matter analysis of amyotrophic lateral sclerosis

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Introduction: Amyotrophic lateral sclerosis (ALS) is a degenerative disease of motor neurons. The diagnosis of ALS requires evidence of both upper and lower motor neuron dysfunction. Currently, upper motor neuron (UMN) disease is assessed primarily by physical examination, because no objective quantitative test is widely available for clinical use. Several groups have reported the efficacy of diffusion tensor imaging (DTI) to evaluate the white matter (WM) tracts in the brain as a surrogate marker of UMN disease, specifically finding reduced fractional anisotropy (FA) in the corticospinal tracts. In this study, we evaluated the use of a structure-specific WM analysis (SSWMA) framework to detect the location and magnitude of FA changes in patients with ALS.

Materials/Methods: Eight ALS patients along with eight age-matched healthy controls were recruited. Magnetic resonance imaging was performed on a 3.0-T Siemens Trio scanner. For each subject, diffusion tensor imaging was performed using a single-shot, spin-echo, diffusion-weighted echo-planar imaging (EPI) sequence. The diffusion sampling scheme was as follows: one image without diffusion gradients (b = 0 s/mm^2), followed by twelve images measured with twelve non-collinear and non-coplanar diffusion encoding directions isotropically distributed in space (b = 1000 s/mm^2). Additional imaging parameters for the diffusion-weighted sequence were: TR = 6500 ms, TE = 99 ms, 90^o flip angle, number of averages = 6, matrix size = 128 × 128, slice thickness = 3.0 mm, spacing between slices = 3.0 mm, 40 axial slices with in-plane resolution of 1.72 × 1.72 mm^2.

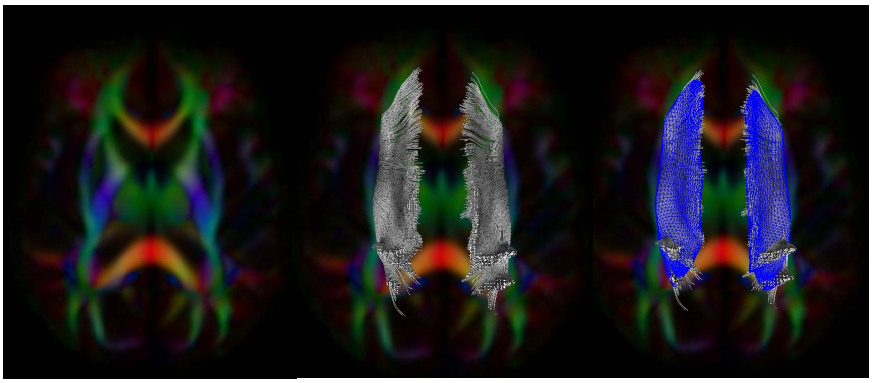

Figure 1. DT atlas (left) and the atlas overlaid with the extracted corticospinal tracts (center) and the boundary mesh of the cm-rep model fitted to the tracts. (right).

The SSWMA framework described in detail elsewhere (See Abstract 5653) is summarized briefly below. It involves: 1) Spatially normalizing all DT images to a common DT atlas derived from the images themselves using a novel high-dimensional tensor-based registration algorithm to explicitly optimize tensor orientation [1]. 2) Segmenting the corticospinal tracts in the DT atlas using an established protocol based on fiber tracking [2]. 3D segmentations of the tracts were generated by labeling voxels in the DT atlas through which at least one fiber passed. 3) Geometric modeling of the binary segmentations using the continuous medial representation (cm-rep) [3]. The models derived describe the skeletons and the boundaries of the corticospinal tracts. In this case, the skeleton of each corticospinal tract is a single surface patch. 4) Statistical mapping of WM differences on the skeletons. The cm-rep model enables the dimensionality reduction by projecting diffusion data of a given tract, a 3D object, onto its skeleton, a 2D surface patch. Following the procedure of dimensionality reduction, WM changes in the ALS population were then examined along the corresponding surface patches by quantifying its FA changes relative to the healthy controls. Permutation-based non-parametric suprathreshold cluster analysis is applied with the cluster-defining threshold set at uncorrected p-value = 0.01 and the clusters with FWE-corrected p-value < 0.05 are considered significant.

Results: The common DT atlas generated from the 16 subjects is shown in **Figure 1** along with the extracted corticospinal tract and the boundary mesh of the cm-rep model fitted to the tracts. Note the excellent fit of the model to the tracts. The Dice overlap between the fitted models and the underlying tracts are over 95%. Significant FA reductions in the ALS population were identified. **Figure 2** shows the three significant clusters identified overlaid on the mesh of the skeletons.

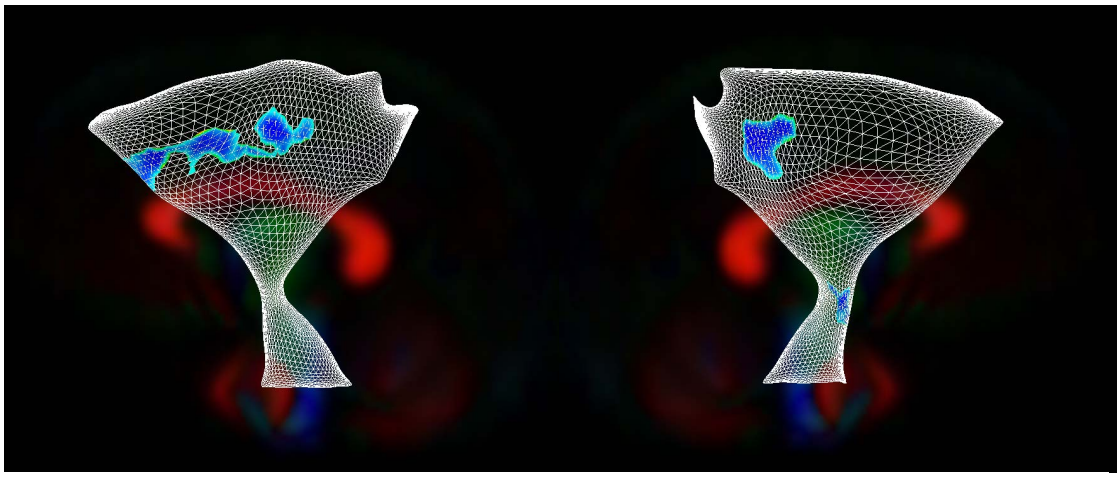

Figure 2. Significant clusters of FA changes detected on the skeletons of the corticospinal tracts. The midsagittal slice of the atlas is shown for anatomical guidance.

Discussion: In this study, we demonstrate the efficacy of using the SSWMA framework for investigating WM changes in ALS. Compared to the traditional voxel-based analysis, this framework enables us to carry out a structure-specific analysis of the corticospinal tracts and the dimensionality reduction capability can potentially improve the sensitivity of the statistical inferences.

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References:

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