Alterations of Water Diffusion and Magnetization Transfer Metrics in the Brains of Amyotrophic Lateral Sclerosis Patients

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Target Audience

Scientists and clinicians interested in studying microstructural cerebral tissue changes in amyotrophic lateral sclerosis.

Introduction

Amyotrophic lateral sclerosis (ALS) is a rapidly progressive, invariably fatal neurological disorder, which results in the degeneration of the motor neuron system. Diffusion tensor imaging (DTI) has revealed microstructural tissue changes in the corticospinal tract (CST) of ALS patients,[1] but previous findings and their relation to clinical function have been conflicting. Here, we aimed at investigating radial (RD) and axial diffusivity (AD) and their corresponding scalars along major fiber tracts in more detail, and how these metrics relate to disease duration and disability. In addition, we analyzed the magnetization transfer ratio (MTR) as a complementary measure for microstructural tissue changes in all white matter tracts.

Subjects and Methods

33 ALS patients (age range 32–82 years, mean ALS functional rating scale score (ALSFRS) = 37.7) and 35 age-matched healthy controls (HCs) underwent an extensive clinical examination and MRI of the brain at 3T (Tim Trio, Siemens Medical Systems). Structural scans were acquired with an MPRAGE sequence with 1 mm isotropic resolution and whole brain coverage. DTI data were acquired using a 2D diffusion-weighted EPI sequence with 12 diffusion directions, two b-values (b = 0 and 1000 smm^{-2}), and an image resolution of 2x2x3 mm^3. TRACULA[2] was used to perform global probabilistic tractography and diffusion parameter analysis. It allowed for automatic identification of 18 major white-matter tracts (anterior thalamic radiation, cingulum angular bundle, cingulum cingulate gyrus, corticospinal tract, inferior fasciculus, parietal and temporal superior longitudinal fasciculus, uncinate fasciculus, forceps major and minor) based on the high resolution structural MPRAGE scans. MTR was calculated from a subset of the ALS patients (n = 18) and controls (n = 29) based on a spoiled 3D gradient-echo sequence, which was performed with and without a Gaussian-shaped saturation pulse with an image resolution of 0.9x0.9x3 mm^3 (TR/TE/FA = 40 ms/7.38 ms/15°). To compare the MTR and diffusion properties, tracts were registered linearly from the diffusion into the magnetization transfer space. Group and regression analyses were performed to investigate the relationship between diffusion properties (fractional anisotropy (FA), mean diffusivity (MD), RD and AD), MTR, disease duration and the ALSFRS. Statistics were done globally for all tracts and along the CST.

Results

In ALS, statistically significant microstructural tissue changes were found only in the CST, while all other tract properties did not differ from HCs. RD was increased, but AD remained unchanged. Consequently, this resulted in a decreased FA and an increased MD. When looking at the profile along the CST, we found that these tissue changes were global. The corresponding profiles are shown in Figure 1, where FA average and standard deviation for ALS patients are depicted in blue and those of HCs in red. Sample points, marked with an asterisk, showed significant differences in a local t-test. MTR findings were closely related to FA changes. No correlation was found between microstructural tissue changes and ALSFRS, or disease duration.

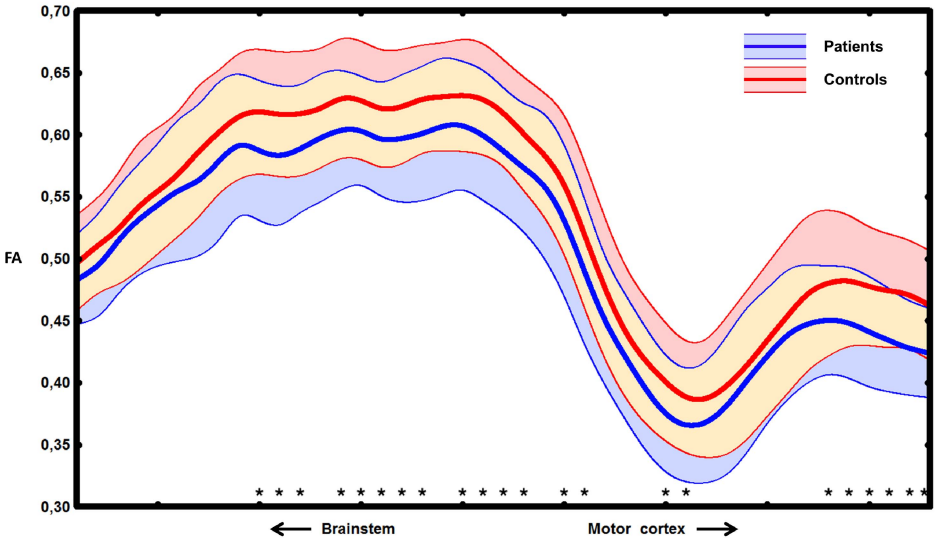

Figure 1: Profile of the FA in the CST of ALS patients and controls. Statistically significant differences between ALS patients and controls are marked with an asterisk.

Discussion and Conclusion

In line with previous studies, we found microstructural damage of the CST in patients with ALS.[1, 3] The observation that the radial, but not the axial diffusivity, is increased suggests damage to the myelin, which is also in agreement with global MTR reductions. While there were no significant correlations between clinical measures and these findings, our results indicate that a tract-based analysis of the CST on an individual level might allow for a sensitive and reliable quantitative assessment of microstructural tissue changes in ALS, which in turn might stimulate future studies in that direction.

References

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