Automated Tract Based Analysis of Diffusion Properties in Amyotrophic Lateral Sclerosis

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Target Audience

Researchers and clinicians interested in amyotrophic lateral sclerosis, tractography and diffusion tensor imaging

Introduction

Amyotrophic lateral sclerosis (ALS), the most common form of motor neuron disease, is a devastating, relentlessly progressive neurodegenerative disorder that results in degeneration of lower and upper motor neurons. In contrast to conventional MRI, diffusion tensor imaging (DTI) has been demonstrated as a promising technique for assessing disease-related microstructural tissue changes.[1] Unlike deterministic approaches, global probabilistic fiber tracking is less dependent on user interaction, such as positioning of seed regions for fiber tracking.[2] Therefore, in this study, we applied a combination of a global probabilistic approach with an automated seed region positioning to examine differences in diffusion properties between ALS patients and healthy controls in major fiber tracts of the brain.

Table 1: Results between controls and ALS patients for the segmented tracts. Values are given in $*10^{-3}mm^2/s$.

	FA			MD			RD			AD		
	ALS	CON	p-val	ALS	CON	p-val	ALS	CON	p-val	ALS	CON	p-val
ATR	0.390	0.390	0.99	0.753	0.751	0.88	0.587	0.584	0.82	1.085	1.085	0.99
CAB	0.342	0.343	0.92	0.785	0.777	0.46	0.639	0.630	0.46	1.076	1.070	0.64
CCG	0.487	0.488	0.91	0.743	0.736	0.54	0.529	0.522	0.64	1.169	1.164	0.74
CST	**0.489**	**0.506**	**0.05**	0.721	0.706	0.10	**0.510**	**0.489**	**0.03**	1.142	1.138	0.79
ILF	0.454	0.454	0.95	0.792	0.811	0.11	0.579	0.592	0.31	1.219	1.248	0.05
SLFP	0.397	0.402	0.53	0.781	0.795	0.28	0.591	0.601	0.47	1.088	1.095	0.63
SLFT	0.428	0.427	0.93	0.753	0.754	0.97	0.569	0.570	0.92	1.122	1.121	0.94
UNC	0.394	0.395	0.84	0.788	0.788	0.99	0.613	0.612	0.95	1.139	1.140	0.92
FMAJOR	0.596	0.583	0.29	0.770	0.792	0.10	0.465	0.489	0.11	1.381	1.396	0.40
FMINOR	0.467	0.474	0.57	0.789	0.787	0.88	0.566	0.559	0.68	1.234	1.241	0.69

Subjects and Methods

23 ALS patients (age range 34-82 years, mean ALS functional rating scale score = 37.9) and 18 age-matched healthy controls underwent a comprehensive clinical examination and MRI at 3T (Tim Trio, Siemens Medical Systems). Structural images were acquired with an MPRAGE sequence with 1mm isotropic resolution (TR/TE/TI/FA = 1.9s/2.19ms/0.9s/9°). DTI data were collected using a two-dimensional diffusion weighted EPI sequence with 12 diffusion sensitizing directions (TR/TE/FA = 6.7s/95ms/90°) and an image resolution of $2x2x3mm^2$. Global probabilistic tractography and diffusion parameter analysis were performed using TRACULA[3], which allows to automatically identify 18 major white-matter tracts based on the high resolution structural MPRAGE scan (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). ANOVA and regression analysis served to identify tracts affected by ALS, and to investigate the relationship between diffusion properties (fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD) and axial diffusivity (AD)), disease duration and severity.

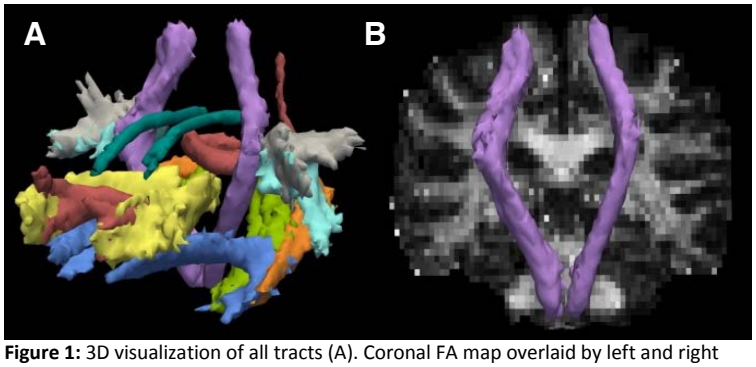

Figure 1: 3D visualization of all tracts (A). Coronal FA map overlaid by left and right corticospinal tract (B).

Results

Differences between patients and controls were observed in the corticospinal tract (CST) for FA ($p = 0.05$) and RD ($p = 0.03$). Group analysis results for FA, MD, RD, and AD for all tracts are presented in Table 1, where values from bilateral tracts have been averaged. Figure 1A illustrates a 3D visualization of all segmented tracts for a single patient. Figure 1B, however, depicts the coronal FA map overlaid by a 3D visualization of the probabilistically tracked CST.

Discussion and Conclusion

The utilization of a fully automated approach allowed the determination of all major white-matter tracts in both ALS patients and controls. This confirmed structural damage of the CST of patients with ALS, which is in line with previous studies.[1,4] The absence of demonstrable damage to other structures is in correlation with the prevailing role of the CST in ALS, but in view of more widespread histopathologic abnormalities it may also indicate a limited sensitivity of employed technique. In contrast to other group-based analysis approaches, such as TBSS or VBM, TRACULA yields tractographic measures on a subject level. This will therefore allow comparisons of microstructural changes including side to side differences of the CST with clinical severity (as assessed by motor scores) on an individual basis. Thus, TRACULA may develop into a valuable diagnostic and prognostic tool in future research.

References

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