Comparative analysis of neuronal tracts DTI metrics and physical disability in multiple sclerosis

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Target audience

Researchers interested in clinically relevant applications of Diffusion MRI to Multiple Sclerosis (MS) and other neurologic diseases.

Purpose

It has been noticed that DTI metrics on certain white matter (WM) tracts, such as optic radiation, correlate better with MS physical disability scores than other WM tracts, in particular corticospinal tract[1] (CST). This is interesting because one of the criticisms of the Expanded Disability Status Scale[2] (EDSS) is its emphasis on ability to walk. It has been suggested[1] that anatomy of the CST (which is very susceptible to registration issues), could be causing lower correlations. On the other hand, it has long been hypothesized that neurodegeneration in MS is a tract-specific process[3], with different disease progression among tracts.

We compared correlation between EDSS and DTI metrics on CST obtained by two different methods: (1) Region-of-Interest (ROI) based method[4] and (2) recently developed tractography method where neuronal tracts are reconstructed directly on patient data[5]. Further, we investigated age related differences in EDSS and DTI metrics and used 3 longitudinal EDSS scores on the same cohort of patients, which lead to propose that observed differences in correlation with physical disability occur because changes in certain WM tracts are due to primary MS pathology, while differences in other tracts are mostly due to secondary atrophic degeneration.

Methods

Patient cohort: The patient cohort consisted of 69 MS patients (all female, ages 24-76, average 40.2 years) with 3 EDSS scores: one approximately 1 year before the scan, one within 7 days of the MRI scan and one approx. 1 year after the scan; median EDSS at the time of the scan was 2, range 0-7.

Data acquisition: MRI scans were obtained on a 3TGE scanner, with 33 direction echo-planar diffusion weighted whole-brain scans at b=1000 s/mm^2 and one at b≈0s/mm^2. Voxel size was 1.8x1.8x2.5mm^3.

Table 1. EDSS correlation with MD (averaged over two cerebral hemispheres were applicable)

	1yr before the scan		at the time of the scan		1yr after the scan	
	R^2	*p*	R^2	*p*	R^2	*p*
Posterior thalamic radiation (including optic radiation)	0.17	<0.005	0.19	<0.005	0.15	<0.005
Genu of Corpus Callosum	0.1	<0.005	0.13	<0.005	0.1	0.01
Splenium of Corpus Callosum	0.11	0.01	0.12	0.007	0.1	0.02
Corticospinal Tract(ROI based)	0.02	0.3	0.02	0.39	0.01	0.42
Corticospinal Tract (Tracula)	0.01	0.3	0.01	0.3	0.01	0.35

Data processing: ROI-based results were obtained by non-linear coregistration of the low diffusion weighted ("b_0") images to White Matter Parcellation Map consisting of 48 tract specific ROIs[4]. DTI indices were averaged across entire ROIs. We also applied the recent tractography method (Tracula) for direct reconstruction of neuronal tracts[5] which may have advantages over earlier methods since it constrains only tract trajectory relative to the surrounding anatomical structures.

Statistical processing: Stepwise method for multilinear regression was used to probe relationship of EDSS with age and mean diffusivity as predictive terms. The same analysis was performed with other standard DTI statistics coupled with age as predictors: age and axial diffusivity (AD), age and radial diffusivity, age and FA.

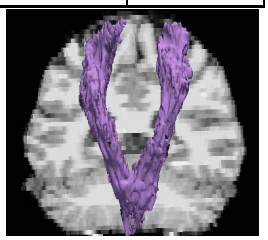

Figure 1. CST tract reconstructed by Tracula.

Results

For the ROI-based method, stepwise regression revealed the best correspondence between EDSS and MD on the ROI that includes posterior thalamic and optic radiations, followed by the ROIs in corpus callosum (Table 1). These correlations are statistically significant and independent from age. Correlations were always the best with the EDSS scores at the time of the MRI scan and ROIs with the best correlation at the time of the scan were also the best predictors of future EDSS. We did not observe significant differences between left and right brain hemisphere.

Tractography based method did not yield improvement in correlation between CST and EDSS (Table 1). However, CST (fig.1.) was the only among the tracts delineated by direct tractography that had negative correlation between age and axial diffusivity (R=-0.37, p=0.0064). ROI-based method confirmed this finding: among 48 ROIs in the atlas, only 13 had negative AD age dependence. These ROIs are spatially contiguous and symmetric (fig. 2).

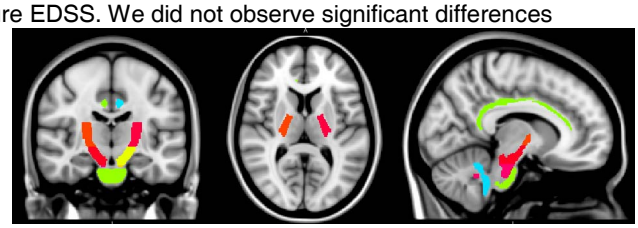

Figure 2. Regions exhibiting negative AD age-dependence with ROI-based method.

Discussion

Our analysis first confirmed essential findings from the recent study[1], although we used somewhat different ROI-based method[4] and a different patient cohort. Further, the results indicate that correlation between DTI indices and EDSS scores is robust with respect to time, with tracts that correlate the best at present time also having the best (short-term) prognostic value. The modest (but statistically significant) correlation stipulates need to include gray matter metrics as predictors.

Methodologically very different tractography method[5] did not improve correspondence between CST and EDSS. Age-dependence analysis revealed negative trend in AD and decrease in AD is associated with secondary, atrophic axonal loss[6]. These facts lead us to put forward a possibility that poor correlation of MRI metrics on CST with physical disability is because observed changes on CST are dominated by secondary atrophic degeneration and not primary MS pathology.

Conclusion

MS is a life changing diagnosis and prognosis on disease progression is one of the most important questions for patients. Determining the most predictive MRI biomarkers and clarifying technical questions, such as whether certain observations are due to methodological imperfections or due to MS pathophisiology is very important. Our results confirm previously observed predictive value of the optic and thalamic radiations with a somewhat different DTI methods and offer a possible explanation for the low predictive value of the DTI statistics on the corticospinal tract. Further work will include analysis of spine MRI data and longitudinal MRI scans.

References

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