Spatial analysis of diffusion tensor tractography depicts local white matter changes

J. Mårtensson[1,2], M. Nilsson[2], C. Elfgren[3], M. Landqvist[3], F. Ståhlberg[2,4], C. Nilsson[3], D. V. Westen[1,4], and J. Lätt[1]

[1]Center for Medical Imaging and Physiology, Lund University Hospital, Lund, Skane, Sweden, [2]Department of Medical Radiation Physics, Lund University Hospital, Lund, Skane, Sweden, [3]Geriatric Psychiatry, Department of Clinical Sciences, Lund University Hospital, Lund, Skane, Sweden, [4]Department of Diagnostic Radiology, Lund University Hospital, Lund, Skane, Sweden

Introduction

Diffusion tensor tractography (DTT) is often used qualitatively, i.e. the extent and the shape of track bundles are investigated visually for depicting changes in cerebral white matter (WM) structures. Quantitative analysis of DTT, when performed, is often done only by determining global mean values of the parameter of interest within the investigated track bundles [1]. This hampers the possibility to recognize small regional differences. In this study, we present a method for pinpointing differences in specific regions of track bundles between groups of patients and healthy controls. As a proof of concept, we performed a group comparison between semantic dementia patients and healthy controls with respect to the inferior fronto-occipital fasciculus (IFO), a nerve track of importance for frontal lobe function and therefore of clinical interest in frontotemporal brain disorders.

Theory

The track bundles obtained in diffusion tensor tractography (DTT) can be approximated by a single mean track. Each position of the mean track corresponds to the centre of mass of all individual track positions within a plane normal to the mean track. To facilitate comparisons of WM pathways between different groups, anatomical landmarks can be placed along the WM pathway. Since the positioning follows anatomical definitions, these anatomical landmarks allow for co-registration of mean tracks from different patients.

Semantic dementia is one of three prototypical syndromes that results from frontotemporal lobar degeneration. Patients with this progressive neurodegenerative disorder suffer from loss of semantic memory. The IFO is assumed to be important for this function and is therefore of interest to compare between this patient group and healthy controls.

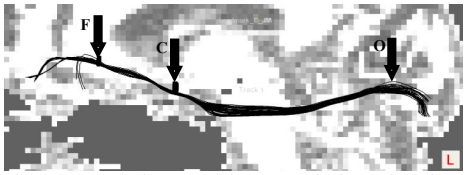

Figure 1. A typical IFO track in a semantic dementia patient. Three single voxel ROI:s were used as landmarks, showed in the figure as the black arrows in the frontal (F), central (C) and occipital (O) part of the IFO.

Method

Four patients, diagnosed with semantic dementia, and seven clinically healthy controls were examined. Measurements were performed at a Philips 3T Achieva scanner. Additional to the clinical protocols, DTT measurements were performed in 48 diffusion encoding directions with b = 0 and 1000 s/mm^2 and image resolution 2x2x2 mm^3. The diffusion images were realigned using the FSL toolkit. DTT analysis was performed using Diffusion Toolkit and Trackvis [2]. The IFO was extracted according to anatomical descriptions by Catani *et al*. [3], using one transversal and three coronal ROIs. In addition, three landmarks were placed in the same slices, following the same anatomical descriptions as the coronal ROI for DTT, in the voxel showing the highest FA value within the track bundle. The landmarks were denoted F, C and O for the frontal, central and occipital part of the IFO (Fig 1). The subsequent analysis was performed in MATLAB. The IFO tracks were co-registered according to its landmarks. The DTI parameters were projected onto the mean track and the average parameter values for each group (semantic dementia and healthy controls) were plotted in Fig 2. Investigated parameters were fractional anisotropy (FA), mean diffusivity (MD) and the largest and smallest eigenvalues of the diffusion tensor, i.e. λ_1 and λ_3, respectively. For comparison, a conventional analysis of the data was performed in Trackvis by calculating the global mean values of each group. Differences between the groups were statistically tested with a Wilcoxon rank sum non-parametric test.

Results

The mean values of the calculated parameters, as functions of the spatial position, are shown for the semantic dementia patients (red solid lines) and for the healthy controls (blue solid lines) in Fig. 2. The shaded areas represent the 95% confidence interval of the mean within each group. The black solid lines in the bottom of the graphs show areas where significant differences between the groups were found. The global mean values (standard deviation) in the IFO for the semantic dementia patient / healthy control group were calculated in Trackvis as FA = 0.44 (0.02) / 0.48 (0.03) with p = 0.07, MD = 0.97 (0.02) / 0.85 (0.04) μm^2/ms with p = 0.01, λ_1 =1.48 (0.03) / 1.39 (0.11) μm^2/ms with p = 0.11 and λ_3 = 0.60 (0.01) / 0.55 (0.08) μm^2/ms with p = 0.07, where the statistical testing for difference in median value between the groups was performed using the Wilcoxon rank sum test.

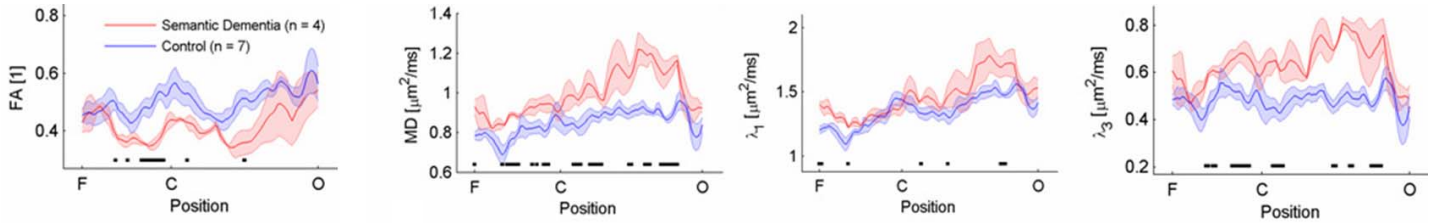

Figure 2. The plots show, from left to right, FA, MD, λ_1 and λ_3 as functions of position of the IFO. The F, C and O mark the frontal, central and occipital part of the IFO. The shaded areas represent the 95% confidence interval of the mean value within the groups. Significant differences between the two groups (p < 0.05) are marked by thick black lines slightly above the horizontal axis. In the patient group, the FA was statistically lower in the frontal lobe and MD higher in several positions along the IFO, compared to the controls. MD increased gradually between the position of the central landmark and the position of the occipital lobe. Moreover, λ_1 was significantly different between the groups in only a few regions while λ_3 was significantly different in some regions in the frontal and occipital lobe.

Discussion and conclusion

We present a method for spatial evaluation of tractography data, based on co-registration of tracks using anatomical landmarks. The feasibility of the method was tested in a patient group suffering from semantic dementia. Previous results of reduced FA and increased MD of the IFO in semantic dementia patients were reproduced [4]. The proposed method is based on user-defined anatomical landmarks, which is a possible source of error that was not addressed in the present study. The analysis pinpointed specific areas of degeneration in the WM pathways which may be of high importance in group comparisons where small regional differences are expected. The spatial analysis revealed locally significant differences for all parameters analysed, whereas with use of global mean values, only MD differed significantly between the two groups.

References

[1] Nilsson C. *et al*. Neuroradiology 2007; 49: 111–119

[2] Wang R. *et al*. Proc. Intl. Soc. Mag. Reson. Med. 2007; 15: 3720

[3] Catani M. *et al*. Cortex 2008; 2-32

[4] Landqvist *et al*. Proc. International Conference on FTD, IA, 2010