A voxel based diffusion tensor image analysis on cognitive decline in mildly and moderately impaired multiple sclerosis patients

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Introduction: The aim of this study was to examine differences diffusion tensor imaging (DTI) measures between healthy subjects on the one hand and mildly and moderately affected Multiple Sclerosis (MS) patients on the other hand. In addition, the relationship between the Paced Auditory Serial Addition Test (PASAT) tests of cognitive decline and micro-structural white matter breakdown, as assessed by DTI measures, was studied in an automated whole brain analysis. To this end, an optimized voxel based analysis approach, in terms of coregistration, atlas construction, and smoothing, was used to compare the diffusion properties of all subjects in every brain voxel and to correlate them with PASAT scores.

Methods: Twenty patients with definite multiple sclerosis according to the recently revised McDonald criteria were included. Ten patients with an expanded disability status scale (EDSS) between 0 and 3.5, inclusive (MS group 1), and ten patients with an EDSS score between 4 and 7, inclusive (MS group 2), were selected. A control group of ten healthy volunteers was matched to the patient groups for age, gender and educational level. A population specific DTI atlas was constructed from all the data sets [1]. Thereafter, the DT images were coregistered to this atlas using a viscous fluid model and mutual information, including all DT information in the coregistration procedure [2]. The fractional anisotropy (FA), $\lambda_{||}$, $\lambda_{\perp}$, and mean diffusivity (MD) maps were calculated for all data sets and smoothed with an adaptive, anisotropic smoothing kernel (FWHM = 3 mm). In each voxel, all diffusion parameters were compared between the three groups with an Kruskall-Wallis test. A Mann-Whitney U-test was then used to identify group differences. In addition, Spearman correlation tests were performed in each voxel to quantify the relation between the different diffusion properties and the PASAT scores. A correction for multiple comparisons based on the false discovery rate (q-value of 0.05) was applied.

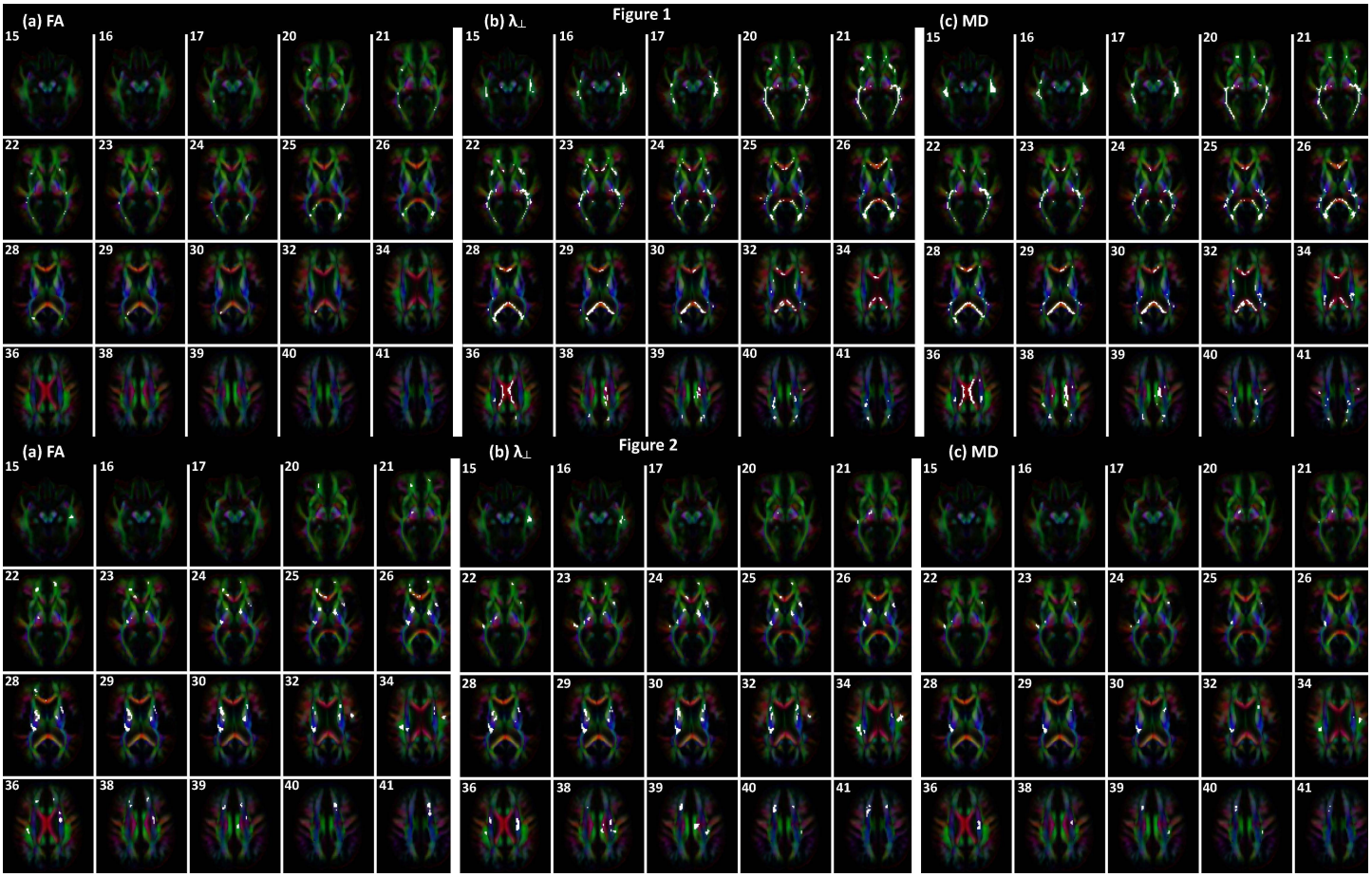

Figure 1

Figure 2

Results: The Kruskall-Wallis group analysis results are shown in Fig. 1. Differences in $\lambda_{\perp}$ and MD between the three groups were found in the genu, body, and splenium of the corpus callosum, the inferior longitudinal fasciculus, capseula externa, optic radiation, capsula interna, forceps major, and corico spinal tracts. Mann-Whitney U tests revealed that these differences were especially present between the control group and MS group 2 (results not shown). The FA measure is correlated with the PASAT score in the left inferior longitudinal fasciculus, forceps minor, anterior and posterior part of the capsula interna, capsula externa, cingulum, corona radiata, and cortico spinal tracts (see Fig. 2). Most of these regions also show correlations between $\lambda_{\perp}$ and the PASAT score. Less significant correlations are found for the MD and no correlations are observed for the $\lambda_{||}$.

Conclusions: In this work, we have demonstrated that the $\lambda_{\perp}$ and MD diffusion measures are most sensitive to detect differences between a control group and mild and moderate MS patients. As expected, differences were most significant between the control group and the MS patient group with highest EDSS scores. On the other hand, FA, $\lambda_{\perp}$, and MD values were significantly correlated with the PASAT score in different WM regions involving executive function, memory, attention, and general cognitive processing. Most of these results are in agreement with the known literature [3-9].

References: [1] Van Hecke et al. (2008) NeuroImage; [2] Van Hecke et al. (2007) IEEE TMI; [3] Bammer et al. (2000) Magn Reson Med; [4] Cicarelli et al. (2003) J Neurol; [5] Dineen et al. (2008) Brain; [6] Ge et al. (2004) J Magn Reson Imag; [7] Griffin et al. (2001) Mult Scler; [8] Hasan et al. (2005) J Magn Reson Imag; [9] Pagani et al. (2005) NeuroImage