Improved results of voxel-based DTI analyses by using non-rigid coregistration and a population-based DTI atlas

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Introduction

Voxel-based analyses (VBA) are increasingly being used to detect white matter (WM) abnormalities with diffusion tensor imaging (DTI) in different types of pathologies. The validity, specificity and sensitivity of statistical inferences of group differences depend to a large extent on the quality of the spatial normalization of the DTI images and on other post-processing parameters such as the choice of the reference system. The coregistration quality may be improved by using high-dimensional non-rigid coregistration techniques that are able to align both the spatial and orientational diffusion information and by incorporating appropriate templates that contain this complete DT information. In this study, we use a coregistration algorithm that was optimized for coregistration of DTI data and a population-based DTI atlas to validate our previously published VBA, which compared the fractional anisotropy (FA) and mean diffusivity (MD) maps of patients with amyotrophic lateral sclerosis (ALS) to those of healthy controls.

Materials and Methods

DTI data of 28 ALS patients and 26 healthy age- and sex-matched controls were acquired using a 3T scanner (Intera, Philips, Best, the Netherlands). For both the original and the new analysis, motion and eddy current correction was applied. Additionally, we performed a b-matrix rotation in order to compensate for the rotational component of the motion correction (Leemans and Jones, in press). In our original approach, we registered the subject's high-resolution anatomical T1-weighted image to the T1-weighted Montreal Neurological Institute template (MNI) (Figure 1A). The parameters of this transformation were subsequently applied to the FA and MD maps to bring these into MNI space. For our new analysis, we built a population-based DTI atlas from the DTI data of all subjects included in the study according to the method described by Van Hecke et al (2008) (Figure 1B). As this atlas contains the complete diffusion information, this information can be used to drive the coregistration process. The individual DTI datasets were non-rigidly coregistered to this DTI atlas using an algorithm based on a viscous fluid model that was optimized for coregistration of DTI images by Van Hecke et al (2007). In order to evaluate whether this new coregistration algorithm could outperform our original approach, we compared the coefficient of variance (COV) of the FA and MD between both approaches. These COV maps were computed for each approach by dividing the standard deviation map by the mean map of all spatially normalized FA or MD maps.
Non-parametric statistics were used to compare the FA maps between ALS patients and controls for both analyses using the SnPM toolbox, whereas for MD, parametric 2 sample t-tests were performed in SPM2. Statistical threshold for significance was set at $p<0.05$, corrected for multiple comparisons.

Results

The COV was significantly smaller when using the new approach compared to the original approach. The COV was especially lowered in the periventricular WM, both for FA and MD (Figure 2).

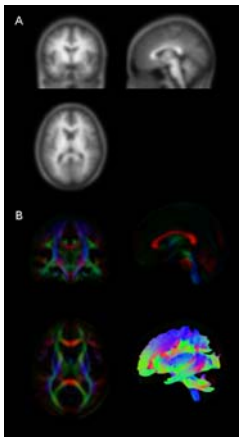

Figure 1: For spatial normalization, the MNI T1-weighted template (A) was used for the original approach, whereas for the new approach, a population-based DTI atlas was generated.

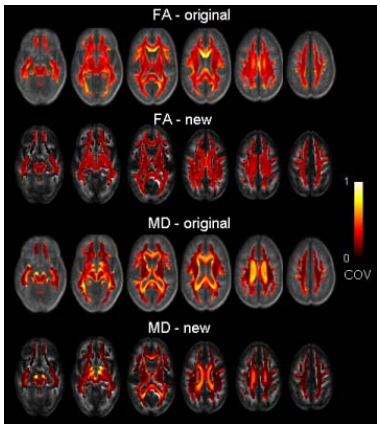

Figure 2: Maps of the coefficient of variance (COV) for FA and MD for the original and new analysis, in which the color-coded COV values within the applied WM mask were overlaid on axial and slices of the mean FA map for the old analysis (row 1 and 3) and on the FA map of the DTI atlas for the new analysis (row 2 and 4).

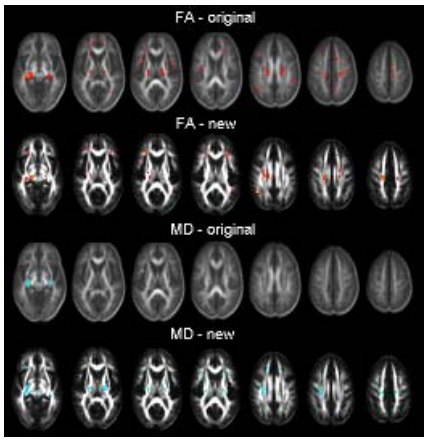

Figure 3: Results of the VBA of FA and MD for the original and new analysis. WM regions showing significant decrease of FA in ALS patients are shown in red and WM regions showing significant increase of MD are shown in blue. Results were overlaid on axial and slices of the mean FA map for the old analysis (row 1 and 3) and on the FA map of the DTI atlas for the new analysis (row 2 and 4).

Using our original approach, we found a pattern of reductions of FA in ALS patients throughout the entire WM, including the CST, the WM underneath the premotor cortex and supplementary motor area and also extramotor WM areas, such as the (pre)frontal WM, the orbitofrontal WM, the insula and the hippocampal formations (Figure 3, row 1). In the new approach, a similar pattern of FA reductions in ALS patients compared to controls was observed (Figure 3, row 2).
In our original analysis, a significant increase of MD in ALS patients was restricted to the hippocampal formations, the right insula and the pons (Figure 3, row 3). Using our new approach, a more extensive pattern of MD elevation can be observed. Compared to our original analysis, we found large clusters of an increase of MD within the CST, the insula, the hippocampal formations and the (pre)frontal WM (Figure 3, row 4), yielding a more widespread pattern of MD changes in ALS patients compared to controls.

Conclusion

In conclusion, we demonstrate that by using improved coregistration and a population-based DTI atlas for the post-processing of DTI data, the reliability of VBA can be improved. This is especially the case for MD, as the effect of improved coregistration will have a larger effect on the COV of MD compared to the COV of FA. As we find both FA and MD changes throughout the brain WM of ALS patients, this study supports the notion of ALS being a multisystem disease.

References

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