Group analysis of threshold-free cluster enhancement score with application to normal ageing white matter study by diffusion spectrum imaging

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Introduction

Diffusion MRI is a powerful tool to probe the microstructural integrity of the white matter. To estimate the normal ageing effect, the white matter of the human brain has been segmented into major fiber tracts based on the diffusion tensor imaging (DTI) data [1][2]. Previous studies suggested that the development and degradation rates of the white matter tracts varied in the brain [1], and that the degeneration pattern of the normal ageing white matter tracts was more severe in the frontal part of the brain [2]. Threshold-Free Cluster Weighted Analysis (TFCW) has been developed to enhance the statistical power of clustering in the curve profiles of the white matter property. This study used template-based diffusion spectrum imaging (DSI) tractography to analyze the microstructural integrity of 74 fiber tracts over the whole brain, and applied TFCW to evaluate the age effect on the tract integrity.

Materials and Methods

Subjects The subjects included 63 young healthy right-handed adults (mean ages 27 yrs) and 49 healthy elderly right-handed adults (mean ages 68 yrs). ***Image Acquisition*** MR scanning was performed on a 3T MRI system (Siemens) with a 32 channel head coil. DSI was acquired using diffusion echo planar imaging (EPI) sequence, TR/TE=9600/130ms, FOV 200 mm, image matrix size 80 x 80, and 2.5 mm slice thick. A total of 102 diffusion encoding gradients with the maximum diffusion sensitivity bmax=4000 s/mm² were sampled on the grid points in a half sphere of the 3D q-space with $|q| \leq 3.6$ units. ***DSI template-based antumatic analysis (TBAA)*** The TBAA method entails 2 pieces of information, a high quality DSI template and a whole brain white matter tract atlas. The DSI template was constructed by coregistering 122 healthy participants' DSI datasets (male: femlale=63:59) to the Montreal Neurobiology Institute (MNI) space using the Large Deformation Diffeomorphic Metric Mapping (LDDMM) method. Whole brain white matter tracts were reconstructed on the DSI template using multiple regions of interest (ROIs) and whole brain seeding. A total of 74 tracts were reconstructed from 60 ROIs defined in the Automatic Anatomical Labeling system. Each reconstructed tract was subdivided into multiple steps with even spacing and the step coordinates along tract bundles were saved as sampling coordinates. The procedures of TBAA method were described as follow: 1) Study subjects (normal young & elderly groups) were coregistered to create a study specific template (SST) using LDDMM. 2) The SST was coregistered to the DSI template. 3) Sampling tract coordinates were transformed from the DSI template to individual DSI datasets via the transformation matrix between DSI template and SST and the matrix between SST and individual DSI. 4) The generalized fractional anisotropy (GFA) values were sampled in the native DSI space using the transformed sampling coordinates. ***Generalized fractional anisotropy (GFA) profiles analysis*** A threshold free cluster weighted (TFCW) method was used following Smith's approach [3] to estimate weighted scores ($S_{(p)} = \sum_{h=h_0}^{h_d} e_p(h)$, where e_p is the cluster extent level which survives at the given threshold h at step p) of the effect size at each step. The 98%, 95%, 90% and 85% cut-points of the histogram of TFCW scores were estimated to determine the most different clusters between these two groups.

Results

Table 1 shows the results of the TFCW with threshold 98%, 95%, 90% and 85%. With the decreasing level of the threshold, more tracts with significant ageing effects appear. Figure 1 displays the 4 tracts such as dorsolateral prefrontal cortex part of commissure fibers (CC_DLPFC), Anterior Commissure (AC), left and right Fornix of the Association fibers (Fx_L, Fx_R), which are the tracts with most severe degeneration.

Conclusion

Detailed investigation of the fiber tracts shows that the patterns of the white matter degeneration are heterogeneous. Our findings suggest that the core part of the normal ageing patterns are the bilateral fornices and the anterior part of the commissure fibers. The age-related white matter degeneration increases gradually from the tracts connecting limbic and temporal lobes to the anterior part of the brain. The degeneration of the commissure and projection fibers is most pronounced in the anterior part of the brain. The corticospinal tract of the projection fibers did not display significant ageing effect. Our study supports some previous DTI literature that the microstructural integrity of the ageing brain decreases with age and the frontal part of the brain is the most severe region. In conclusion, our study provides detailed degenerative patterns of the white matter tracts in normal ageing which can serve as a useful reference for neurodegenerative diseases.

85%	90%	95%	98%	System	Subgroup	Name
			↓	Association		Left fornix
				Association		Right fornix
				Commissure		Anterior commissure
				Commissure	Corpus callosum	Dorsolateral prefrontal segment
			↓	Association		Right uncinate fasciculus
				Commissure	Corpus callosum	Hippocampal segment
				Association		Left cingulum: hippocampal segment
				Association		Left uncinate fasciculus
				Projection	Frontostriatal	Left orbitofrontal segment
				Projection	Frontostriatal	Right orbitofrontal segment
				Commissure		Posterior commissure
				Commissure	Corpus callosum	Supplementary motor area segment
				Commissure	Corpus callosum	Temporal pole segment
				Association		Left cingulum: main body segment
				Association		Left superior longitudinal fasciculus II
				Projection	Frontostriatal	Left ventrolateral prefrontal segment
				Projection	Thalamocortical	Left ventral anterior frontal segment
				Projection	Thalamocortical	Left anterior precentral segment
				Projection	Thalamocortical	Right anterior precentral segment
				Projection	Thalamocortical	Right superior postcentral segment
				Projection	Thalamocortical	Left optic tract
				Projection	Thalamocortical	Left dorsoanterior segment
				Commissure	Corpus callosum	Genu
			↓	Commissure	Corpus callosum	Amygdala segment

Table. 1 The TFCW result of the GFA profiles of 24 tracts with the significant segments under ageing effects.

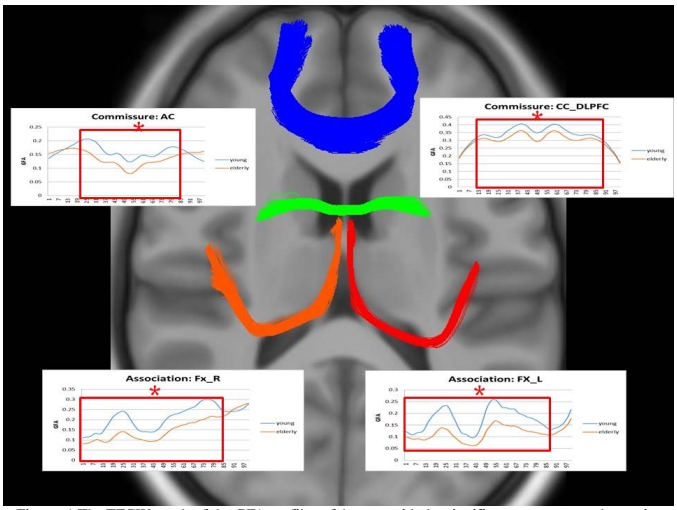

Figure. 1 The TFCW result of the GFA profiles of 4 tracts with the significant segments under ageing effects (Effect Size 0.98). The 4 fibers are dorsolateral prefrontal cortex part of commissure fibers (CC_DLPFC), Anterior Commissure (AC), left and right Fornix of the association fibers (Fx_L, Fx_R)

References

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