# Is the rate of change in fractional anisotropy with age constant within white matter tracts? A study of two segments of the Cingulum bundle

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**Introduction**

Knowledge of the normal ageing pattern in cerebral white matter (WM) is valuable for improved understanding of underlying WM pathologies in neurodegenerative diseases and neurological conditions. WM maturation and degeneration can be investigated using diffusion tensor imaging (DTI) and the fractional anisotropy (FA), which shows that an increase during childhood and adolescence flattens out around middle age and decreases during ageing. However, this process is subject to spatial variations. The retrogenesis hypothesis postulates that late-myelinated WM tracts are more vulnerable to age-related degeneration, and that breakdown of late-myelinated WM tracts mediates age-associated cognitive decline[1,2,3]. Previous studies have observed an antero-posterior gradient of age-related FA decline[3], which may appear as a consequence of later myelination of WM tracts in the anterior than in the posterior parts of the brain[4]. In this work, we compare the changes in FA within segments of the cingulum bundle, which is a late-myelinated WM tract. We divide it into anterior and posterior segments, in order to investigate the patterns of age-related WM changes. The purpose of this study is to investigate whether there are segmental differences in age-related changes within the superior part of the cingulum bundle in healthy volunteers and if an antero-posterior gradient in the rate of ageing is present.

**Methods**

MRI was performed on 80 healthy volunteers (age 30-83 years, 55% females) at two sites using Philips Achieva 3T scanners with identical DTI, distributed in across various age groups as follows: 32 aged 30-39y, 9 aged 40-49y, 10 aged 50-59y and 29 aged 60-83. Diffusion weighted images was acquired along 48 non-linear diffusion encoding directions with a single-shot spin echo sequence with echo-planar imaging (EPI), 60 contiguous slices, voxel size 2x2x2mm$^3$, TE/TR of 77/6626 ms and a diffusion-weighting factor of $b$ = 1000 s/mm$^2$. Motion and eddy current correction of the data was performed using ElastiX and diffusion parameters maps were calculated using an in-house developed software (Matlab). By using a semi-automated tracking method based on the in-house developed software, the superior part of the cingulum bundle was delineated by four regions of interest (ROI). The superior part of the cingulum was further divided into anterior and posterior segments. FA was averaged within the segments for each subject and analysed as functions of age.

**Results**

The anterior and posterior segments of the cingulum were well extracted in all subjects, with an example shown in Fig. 1. In both segments, at both left and right sides, the FA decreased with age (Fig. 2). Age-related changes in FA appeared larger in the anterior cingulum when compared to the posterior cingulum. When averaged across the left and right cingulum bundle, FA of the anterior segment of the cingulum decreased 18% between the age of 30 and 83, while FA of the posterior part of the cingulum decreased 8.3% in the same age span. Investigated in the two sides separately, the FA reduction in the left and right was 19% and 16%, respectively, in the anterior segment, compared to 11% and 9.1% in the posterior segment. The correlation with age was significant in both the anterior and the posterior left cingulum ($p<0.05$) but not in the anterior part of the right cingulum.

**Discussion**

Our results indicate that an antero-posterior gradient exists not only between different regions of the whole brain, but also between different portions within the cingulum bundle. The retrogenesis hypothesis postulates that later-myelinated WM tracts would undergo greater age-related differences than earlier-myelinated WM tracts. Age-related changes along WM tracts with a fronto-occipital course, such as the cingulum, may be partly explained by this hypothesis in case if the tract is composed of separate fiber bundles as suggested by Jones et al (2013)[5]. This also agrees with the notion that commissural and projection tracts mature in sequence from anterior to posterior[1]. Future studies should investigate whether an antero-posterior gradient exists also within other WM tracts and longitudinal studies are needed to get a better over-all clarification of the human brain WM changes over the lifespan. In conclusion, we have found indications of a spatially varying pattern of the ageing process within the cingulum, which may be in agreement with earlier findings of the composition of the cingulum and further investigations are therefore motivated with a larger number of healthy controls included in order to explore the cingulum tract and the ageing process within it.

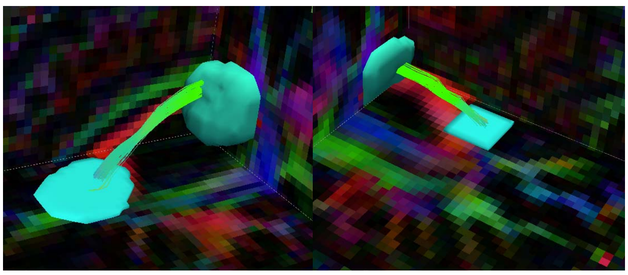

**Fig. 1.** To the left: the anterior segment of the cingulum with the anterior and the superior region of interest. To the right: the posterior segment of the cingulum with the superior and the posterior region of interest. The tractography is visualised on a FA colour map.

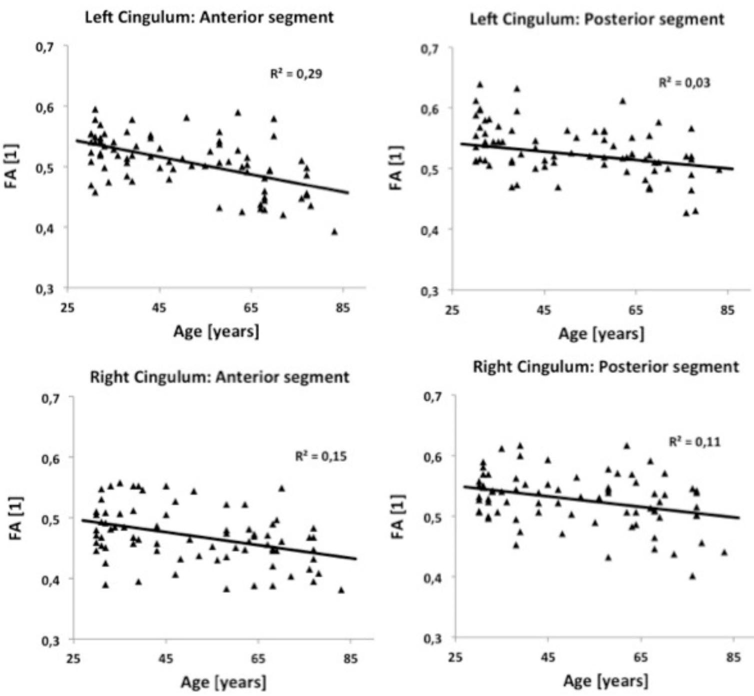


**Fig. 2.** The diagrams on the upper row show the FA values as functions of age along the anterior and posterior segments of the left cingulum. The diagrams on the lower row show the FA values as functions of age along the anterior and the posterior segments of the right cingulum.

**References:**

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