1. Introduction

Diffusion tensor imaging (DTI) can be used to study microstructural development related to maturation and normal aging of cerebral white matter (WM) across the life-span. Parameters quantified by DTI are fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD), all of which reflect the state of the microstructure. Changes in these parameters during the life-span have often been characterized by three phases: a rapid change during early development, followed by a plateau during middle age, and an aging-associated change after approximately the sixth decade of life [1–6]. There is considerable variation between the WM tracts regarding the age at which DTI parameters reach their extreme values. For example, the tract that reaches its peak FA and minimum MD values earliest is the fornix, before 20 years of age, while the cingulate bundle (CB) is the latest to reach its peak FA and minimum MD, which occurs after the age of 40 [7].

Most studies of white matter that use tractography analyse the effects of aging by averaging DTI metrics over entire tracts. However, there is considerable heterogeneity in FA and MD along the tracts [8–10]. Subdivision of tracts into segments may thus allow for improved specificity and could help to understand whether maturation and aging affect entire tracts uniformly or there are spatial variations within tracts. Here, we investigated the hypothesis that age-related effects on DTI parameters are heterogeneous within tracts, by studying a large number of healthy individuals. We focused on the importance of...
taking the heterogeneity in age-related effects into account in analysed methods. Also, we focused on the represented method for analysing tracts in segments. The method can be applied to any WM tract where heterogeneity may be present, but in this specific work we chose two representative tracts to be analysed: the CB and the inferior fronto-occipital fasciculus (IFO). These tracts are both known to be sensitive to different aging trajectories [7]. The CB contains a mixture of long and short fibers; the latter are so-called U fibers, which connect multiple regions within the anterior cingulate cortex and between the anterior cingulate cortex and adjacent cortical gyri [11–13]. The composition of fibers in the CB is quite complex, with an apparent continuity of fibers, as well as numerous short association fibers [14–15]. The IFO is an association tract that connects the frontal, temporal, and occipital lobes and runs in an antero-posterior direction. The middle part of the tract is compressed and has a small cross section compared to its anterior and posterior parts [8].

The aim of the present study was to test for differences in age-related effects on DTI parameters between segments of the CB and the IFO. For this purpose, the superior part of the CB, which has an antero-posterior course, was divided into two segments, while the inferior part of the CB, i.e. the para hippocampal part, was analysed as one segment. The IFO was divided into three segments: the anterior part, the middle part, and the posterior part. By comparing segments within the IFO, and then also within the CB, we tested the hypothesis that the pattern of age-related changes differs between segments of these tracts.

2. Materials and methods

2.1. Participants

In total, 257 healthy individuals (104 males and 153 females), between 13 and 84 years of age (mean age ± standard deviation: 34.8 ± 19.4) and with no self-reported history of neurological or psychiatric disease or brain injury, were included in this study. They had been enrolled as controls in previous clinical DTI studies at two university hospitals. Informed consent had been obtained from all participants aged 15 or older, and from the parents for individuals younger than 15 years. This multicenter study with retrospective analysis of previous cohorts was approved by the ethical committee in Uppsala, Sweden.

2.2. Image acquisition

Morphological and diffusion MRI of the brain was performed at two sites using similar 3 T MRI scanners (Philips Achieva, Best, the Netherlands). DTI was performed with identical protocols at both sites, using a single-shot spin echo sequence with echo-planar imaging (EPI), 60 contiguous slices, voxel size $2 \times 2 \times 2$ mm$^3$, TE/TR of 77/6626 ms/ms, a diffusion-weighting factor $b = 1000$ s/mm$^2$ and diffusion encoding along 48 directions. Motion and eddy current correction of the data was performed using ElastiX [16], and diffusion parameter maps were calculated using in-house developed software (Matlab). The tensor fitting procedure utilized linear least squares fitting and corrected for the heteroscedasticity resulting from the log transform. Morphological MRI scans of all participants were evaluated visually by an experienced neuroradiologist. Due to pathologic or artifactual information in any of the images, ten subjects were excluded from the study. The presence of WM lesions was quantified by scoring T2-weighted fluid attenuated inversion recovery (FLAIR) images using the Fazekas scale [17]. The Fazekas scale ranges from 0 to 3, where 0 equals normal, 1 is assigned to punctate lesions and 3 is assigned to the most extreme cases where extensive and confluent lesions are present. Two subjects with WM lesions graduated as Fazekas score 3, located in the vicinity of the investigated tracts, were excluded in order to avoid confounding on DTI measurements. The subsequent analyses were performed on the remaining 257 subjects.

2.3. Fiber tracking diffusion measurements

A semi-automated method was used for the whole process leading to calculated tractography and extraction of two major WM tracts in each subject. Steps in the first part of the process, i.e. corrections for motions and eddy current effects and the deterministic tractography calculation, were performed using in-house developed software. Steps in the latter part of the process were performed using the FMRIB Software Library (FSL). Regions of interest (ROIs) were drawn in MNI (Montreal Neurological Institute) template space and projected back to the native space in which the data were acquired using the FMRIB’s nonlinear image registration tool (FNIRT) tool in the FSL software. The back-projected ROIs were then manually checked and, if necessary, corrected in each individual. The back projection used the warp fields produced by registering the FMRIB58 FA template to the FA maps of the subject. The ROIs were anatomically defined according to information on WM anatomy in previous neurological and dissection studies [8,11,18–20], and aimed to extract the CB and the IFO. The CB was extracted by the use of four paramedian ROIs; the first one superior to the genu of the corpus callosum, the second one superior to the mid body of the corpus callosum, the third one superior to the splenium, and the fourth posterosuperior to the splenium. The IFO was extracted by the use of three ROI: s; the first one in the frontal deep WM in the lateral part of the frontal lobe, the second one in the occipital deep WM parieto-occipitally and lateral of the lateral ventricle, and the third one in the external capsule, specifically in the deeper subinsular WM. The IFO is divergent in the frontal lobe and in the occipital lobe, but is compressed in the region of the external capsule and the temporal stem.

Segments of each tract were extracted in each hemisphere by drawing new ROIs for use as borders when dividing the tract into segments. These ROIs were also drawn in MNI space and projected back into native space, followed by, if necessary, manual corrections in each individual. In the CB, three segments were extracted: one anterior segment which was defined by the first and the second ROI, one posterior segment which was defined by the second and the third ROI, and one inferior segment that captured the part of the tract that connects to the temporal lobe and was defined by the third and the fourth ROI. In the IFO, three segments of approximately equal lengths were extracted, with the first and the third ROI as outer borders for the IFO, and two ROIs with approximately equal lengths in between. The middle segment captured the part of the tract that is compressed compared to the other parts of the tract. Parts of the tracts extending beyond the segment borders were removed before subsequent analysis. For each subject, four DTI parameters (FA, MD, RD, and AD) were extracted for each segment of the two tracts. In order to not encounter problems with multiple comparisons, corrections to check for stable significant results were performed.

Since no information about handedness, and thereby neither about the dominant hemisphere, was available for any of the subjects, the segment-specific parameter values were averaged across the two hemispheres resulting in one value per subject and segment.

2.4. Correcting for tract size, gender, and site of examination

To correct for covariates that otherwise may confound the results, such as tract size, gender, and the site at which the imaging was performed, the acquired values were adjusted using multiple linear regression. Tract size was calculated for each tract segment by counting the number of voxels containing at least one reconstructed streamline and multiplying by voxel volume. This procedure yielded a value of the tract volume, $V = \sum V_i$, where $V_i$ is the volume of the $i$th streamline. The tract volume, $V$, the gender ($0$: Male, $1$: Female), and the site of examination ($0$: Site 1, $1$: Site 2). The result of the regression was used to correct for the three
covariates (tract size, site and gender) by replacing $y$ with $y'$ in the subsequent analysis, with $y'$ defined according to $y' = y - (\beta_1 m_1 + \beta_2 m_2 + \beta_3 m_3)$, where $m_i$ is the centered equivalent of $x_i$, i.e. $m_i = x_i - \left(\text{mean } x_i\right)$. Centered values were used to ensure that the global means were not affected by the covariate corrections. This step also involved outlier rejection, in which data points with residuals above three standard deviations were excluded.

### 2.5. Statistical analysis

The subjects were grouped into the following five age categories, with the number of included subjects mentioned in the parentheses: 13–18 ($n = 23$), 19–27 ($n = 116$), 28–40 ($n = 37$), 41–60 ($n = 23$), and 61–84 ($n = 36$) years of age. The construction of these ranges was based on the maturation and age peaks of the specific tracts [7]. The effects of age on DTI parameters were tested for by using analysis of variance (ANOVA), i.e. testing the null hypothesis that all age groups had equal means. Binning age as a categorical offered a simple means for the purpose of detecting differences in the patterns between segments, with sufficient power due to the large number of subjects in the present study. To test for spatial heterogeneity within tracts, comparisons of age-related changes were performed between the segments of each tract. This type of analysis was selected because data points from the different tract segments were paired (from the same subject), and hence we performed the analysis on a differential metric defined by $\Delta y = y_1 - y_2$, where $y_1$ and $y_2$ represents the values from the first and the second segment, respectively. Testing for age-group differences in $\Delta y$ using ANOVA yields the probability of whether the difference between the segments is the same in two segments. This analysis yielded three comparisons (segment 1 versus segment 2, segment 1 versus segment 3, and segment 2 versus segment 3). If the result shows present differences between any segments, this would mean that a spatial heterogeneity is present within the tracts.

### 3. Results

In the CB, an age-related pattern of FA change was observed in the anterior and posterior segments, whereas no significant effect of age was found in the inferior segment (Fig. A.1.a–c; Table A.1). The maximum FA was found in the posterior segment in the age interval 19–40 years of age (Fig. A.1.b). In the anterior part of the CB, the RD values increased from the age of 28 years, and reached its maximum value in the oldest age group (Fig. A.2.a). In the posterior segment, the RD values were lowest in the middle-aged group, and increased thereafter with age (Fig. A.2.b). A significant age-related pattern of RD was present in the inferior segment (Fig. A.2.c). The overall pattern of the RD values were reversed compared to the pattern of the FA values. The pattern of the MD values was also reversed compared to the pattern of the FA values, and a significant effect of age was observed for MD values in the inferior segment. Also for the AD values, significant effects of age were observed in the inferior segment.

The IFO showed a similar pattern for FA, as did the CB, with effects of age present in two of three segments (Fig. A.3.a–c; Table A.1). The maximum value for FA was found in the posterior segment in the young adult group; 19–27 years of age, and the strongest effect of age as observed in the anterior segment (Fig. A.3.c). The middle segment showed no significant effects of age (Fig. A.3.b). The pattern of RD was increasing in the anterior and the posterior segments, while in the central segment, the RD was low in the youngest group and quite stable in the other age groups (Fig. A.4.a–c). The RD parameter was stable in its lowest values for all segments and reached its maximum values in the central segment of the young adult group, and the strongest effect of age on RD was observed in the anterior segment (Fig. A.4.a–c). With regard to MD, the largest effects of age were observed in the anterior and central segments, and MD was lowest in the anterior segment in the middle-aged group; 28–40 years of age (Table A.1). The effects of age on AD were similar in all segments (Table A.1). The overall pattern of the RD values was reversed compared to the pattern of the FA values.

The results summarized in Table A.1 show age-related changes in DTI parameters of the analysed WM tracts. The hypothesis that these age-related changes are inhomogeneous within tracts was tested by analysing data obtained by subtracting parameter values between pairs of segments at a subject level, where the subtraction addressed the paired nature of values from different segments in a single subject. If two segments would exhibit identical effects of age, the mean of the resulting difference parameter would be equal across all age groups. This hypothesis was tested using ANOVA, and the results are shown in Table A.2. For the CB, the posterior and anterior segments showed similar patterns of aging in all DTI parameters (i.e. no significant effect of age on the difference between the two segments). Comparisons between the anterior and inferior segments and between the posterior and inferior segments showed differences in the age-effect pattern in all parameters but AD (Table A.2). A similar picture emerged for the IFO, in which the anterior and posterior segments showed similar patterns of age-effects in all parameters except AD. The age-related pattern of change in the middle segment differed compared with that in the posterior and the middle segments (Table A.2). FA and RD captured age differences in the most stable way, since their overall pattern were well consistent in regard to each other. Thereby, FA and RD in combination seems to be a sensitive measure of age-related patterns and differences and provide a good opportunity to perform subtractions between segments.

Results were corrected for tract size, gender, and site of examination. Results from corrected analyses showed some minor differences when compared to results from uncorrected analyses, but the over-all pattern was not affected by the correction. In general, the findings regarding age-related changes in the WM were robust and stable, Table A.1 and A.2 both featured 24 hypothesis tests. A conservative Bonferroni adjustment of the significance threshold, from 0.05 to 0.002, resulted in 13 instead of 18 significant effects for Table A.1 and 12 instead of 15 significant effects for Table A.2.

### 4. Discussion

Diffusion MRI and tractography has emerged as valuable tools for analyses of age-related changes in the tissue microstructure of the brain, and has enhanced our understanding of normal aging and age-related neurodegeneration [4,7,23–25]. However, most tractography-based studies are based on investigations of average effects on whole tracts, which may pass through multiple regions in the brain. From whole-brain analysis using, for example, tract-based spatial statistics (TBSS), we know that effects of aging show a considerable spatial variability [6,23,26]. It is not clear whether the spatial variability arises only from difference between tracts or if there are also differences within tracts. Deterministic tensor-based tractography is capable of capturing the large fiber pathways of the brain with sufficient quality [27]. In this study, we aimed to investigate whether aging affects DTI parameters uniformly along the tract, or whether there is heterogeneity between segments of tracts. Previous results suggest this to be the case, for example, in the corpus callosum (CC) [24,28]. However, different parts of the corpus callosum contain different fibers, and can thus be considered as different tracts. Our results showed that there are differences in the effects of aging on DTI parameters also between segments of individual tracts, such as the CB and the IFO. In one perspective, the CB resembles the corpus callosum, as it contains different types of fibers; both long fibers that potentially connect the frontal and the temporal lobe, as well as short association fibers that run along the CB only for part of its course [15,29]. Due to its composition of multiple fiber components with potentially distinct functional roles, segment-specific responses to aging may thus be expected. The IFO, on the other hand, is composed of longer fibers that connect the frontal, the temporal, and the occipital lobes. Here, global effects may be expected.
to be prevalent, since damage to one part of the tract would be reflected in other parts of the tract, for example, due to Wallerian degeneration [30]. On the contrary, our results show that in addition to the global effects that were in agreement with previous studies [31], there were also local segment-specific effects of aging in the IFO. The middle segment of the IFO showed a different age-related change of both FA and RD compared to the anterior and posterior segments, which were of similar age-related patterns of change. This finding may be related to the fact that the middle segment is more compressed and the fibers are not as dispersed as in the other parts of the IFO as, for example, the posterior segment which has a fan-like shape as it enters the occipital lobe.

There are multiple explanations possible as to why there may be segment-specific effects of aging on DTI parameters. For example, there may be variations in microstructural properties along the course of a tract [32], and thus local sensitivity to aging. The relative importance of confounders for the DTI analysis, such as crossing fibers or partial volume effects may also vary along the tract [8,21–22]. Crossing fibers leads to reduced FA, and selective degeneration of subpopulations of fibers within voxels can counter intuitively result in elevated FA [43]. Partial volume effects driven by tract volume can also confound measurements of FA since thicker tracts will have a lower contribution of partial volume effects to the entire tract than thinner bundles [21–22]. The width of tracts and consequently also the relative contribution of contaminated voxels contaminated by partial volume effects may change with age, and can also differ between tract segments. Although some potential effects may be controlled for in the data analysis, for example, by adjusting for tract size as in the present study, pinpointing whether effects on DTI parameters are driven by changes in myelination, axon density, prevalence of crossing fibers et cetera requires data acquired with imaging protocols more capable than those required for DTI [34–35]. Our main conclusion is thus that segment-specific effects of aging on DTI parameters, but that further studies are required in order to find the reasons for these effects and determine the degree to which they represent localised effects in specific tracts, versus partial volume effects with crossing tracts.

Our results illustrate the advantages of dividing tracts into segments before performing an analysis of DTI parameters. The nice comprehensive analysis of WM tracts done by Lebel et al. demonstrated regionally varying non-linear age-related changes across a wide age range, supporting quadratic age effects on DTI measures [7]. Our work was built upon previous works that support the age-related changes in the degree to which they represent localised effects in specific tracts, and the middle segment is more compressed and the fibers are not as dispersed as in the other parts of the IFO as, for example, the posterior segment which has a fan-like shape as it enters the occipital lobe.

There are multiple explanations possible as to why there may be segment-specific effects of aging on DTI parameters. For example, there may be variations in microstructural properties along the course of a tract [32], and thus local sensitivity to aging. The relative importance of confounders for the DTI analysis, such as crossing fibers or partial volume effects may also vary along the tract [8,21–22]. Crossing fibers leads to reduced FA, and selective degeneration of subpopulations of fibers within voxels can counter intuitively result in elevated FA [33]. Partial volume effects driven by tract volume can also confound measurements of FA since thicker tracts will have a lower contribution of partial volume effects to the entire tract than thinner bundles [21–22]. The width of tracts and consequently also the relative contribution of contaminated voxels contaminated by partial volume effects may change with age, and can also differ between tract segments. Although some potential effects may be controlled for in the data analysis, for example, by adjusting for tract size as in the present study, pinpointing whether effects on DTI parameters are driven by changes in myelination, axon density, prevalence of crossing fibers et cetera requires data acquired with imaging protocols more capable than those required for DTI [34–35]. Our main conclusion is thus that segment-specific effects of aging on DTI parameters, but that further studies are required in order to find the reasons for these effects and determine the degree to which they represent localised effects in specific tracts, versus partial volume effects with crossing tracts.

Our results illustrate the advantages of dividing tracts into segments before performing an analysis of DTI parameters. The nice comprehensive analysis of WM tracts done by Lebel et al. demonstrated regionally varying non-linear age-related changes across a wide age range, supporting quadratic age effects on DTI measures [7]. Our work was built upon previous works that support the age-related changes in the degree to which they represent localised effects in specific tracts, and the middle segment is more compressed and the fibers are not as dispersed as in the other parts of the IFO as, for example, the posterior segment which has a fan-like shape as it enters the occipital lobe.

<table>
<thead>
<tr>
<th>Parameter Segment</th>
<th>13–19 (n = 26)</th>
<th>20–27 (n = 122)</th>
<th>28–40 (n = 40)</th>
<th>41–60 (n = 24)</th>
<th>61–84 (n = 45)</th>
<th>p (ANOVA)</th>
<th>F value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cingulate bundle (CB)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior FA</td>
<td>0.50 (0.03)</td>
<td>0.50 (0.03)</td>
<td>0.50 (0.03)</td>
<td>0.48 (0.03)</td>
<td>0.47 (0.04)</td>
<td>p &lt; 10^(-4)</td>
<td>7.45</td>
</tr>
<tr>
<td>Posterior FA</td>
<td>0.55 (0.03)</td>
<td>0.56 (0.03)</td>
<td>0.56 (0.03)</td>
<td>0.54 (0.03)</td>
<td>0.53 (0.03)</td>
<td>p &lt; 10^(-3)</td>
<td>5.27</td>
</tr>
<tr>
<td>Inferior FA</td>
<td>0.42 (0.02)</td>
<td>0.41 (0.03)</td>
<td>0.41 (0.03)</td>
<td>0.42 (0.02)</td>
<td>0.42 (0.02)</td>
<td>n.s.</td>
<td>0.67</td>
</tr>
<tr>
<td>Anterior MD</td>
<td>0.79 (0.03)</td>
<td>0.79 (0.03)</td>
<td>0.78 (0.02)</td>
<td>0.79 (0.03)</td>
<td>0.79 (0.03)</td>
<td>n.s.</td>
<td>1.36</td>
</tr>
<tr>
<td>Posterior MD</td>
<td>0.74 (0.02)</td>
<td>0.74 (0.02)</td>
<td>0.74 (0.03)</td>
<td>0.74 (0.03)</td>
<td>0.73 (0.02)</td>
<td>n.s.</td>
<td>0.86</td>
</tr>
<tr>
<td>Inferior MD</td>
<td>0.83 (0.02)</td>
<td>0.85 (0.03)</td>
<td>0.84 (0.02)</td>
<td>0.83 (0.03)</td>
<td>0.82 (0.03)</td>
<td>p &lt; 10^(-8)</td>
<td>11.84</td>
</tr>
<tr>
<td>Anterior AD</td>
<td>1.27 (0.05)</td>
<td>1.28 (0.05)</td>
<td>1.28 (0.03)</td>
<td>1.27 (0.04)</td>
<td>1.25 (0.05)</td>
<td>p = 0.015</td>
<td>3.14</td>
</tr>
<tr>
<td>Posterior AD</td>
<td>1.25 (0.05)</td>
<td>1.27 (0.04)</td>
<td>1.26 (0.04)</td>
<td>1.26 (0.04)</td>
<td>1.24 (0.05)</td>
<td>p = 0.035</td>
<td>2.63</td>
</tr>
</tbody>
</table>

5. Conclusion

We show that differences in age-related changes exist not only between regions and between different tracts of the brain, but also between segments within white matter tracts. We found a regionally varying pattern of the aging process within the CB and the IFO, which suggests that tractography studies could benefit by applying the analysis to segments of tracts instead of whole tracts. The reason for segment-specific effects of age on DTI parameters is yet unknown.
Table A.1 (continued)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Segment</th>
<th>13–19 (n = 26)</th>
<th>20–27 (n = 122)</th>
<th>28–40 (n = 40)</th>
<th>41–60 (n = 24)</th>
<th>61–84 (n = 45)</th>
<th>p (ANOVA)</th>
<th>F value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FA</td>
<td>Center</td>
<td>0.44 (0.02)</td>
<td>0.44 (0.02)</td>
<td>0.44 (0.02)</td>
<td>0.43 (0.03)</td>
<td>0.41 (0.02)</td>
<td>p &lt; 10&lt;sup&gt;−9&lt;/sup&gt;</td>
<td>13.44</td>
</tr>
<tr>
<td>D</td>
<td>Posterior</td>
<td>0.50 (0.03)</td>
<td>0.50 (0.03)</td>
<td>0.50 (0.03)</td>
<td>0.50 (0.03)</td>
<td>0.50 (0.03)</td>
<td>p &lt; 10&lt;sup&gt;−9&lt;/sup&gt;</td>
<td>10.73</td>
</tr>
<tr>
<td>RM</td>
<td>Center</td>
<td>0.40 (0.02)</td>
<td>0.40 (0.02)</td>
<td>0.40 (0.02)</td>
<td>0.39 (0.03)</td>
<td>0.37 (0.02)</td>
<td>p &lt; 10&lt;sup&gt;−6&lt;/sup&gt;</td>
<td>6.38</td>
</tr>
<tr>
<td>RM</td>
<td>Posterior</td>
<td>0.56 (0.03)</td>
<td>0.56 (0.03)</td>
<td>0.56 (0.03)</td>
<td>0.56 (0.03)</td>
<td>0.56 (0.03)</td>
<td>p &lt; 10&lt;sup&gt;−6&lt;/sup&gt;</td>
<td>6.38</td>
</tr>
<tr>
<td>RM</td>
<td>Center</td>
<td>0.50 (0.03)</td>
<td>0.50 (0.03)</td>
<td>0.50 (0.03)</td>
<td>0.50 (0.03)</td>
<td>0.50 (0.03)</td>
<td>p &lt; 10&lt;sup&gt;−6&lt;/sup&gt;</td>
<td>6.38</td>
</tr>
<tr>
<td>RM</td>
<td>Posterior</td>
<td>0.66 (0.04)</td>
<td>0.66 (0.04)</td>
<td>0.66 (0.04)</td>
<td>0.66 (0.04)</td>
<td>0.66 (0.04)</td>
<td>p &lt; 10&lt;sup&gt;−6&lt;/sup&gt;</td>
<td>6.38</td>
</tr>
<tr>
<td>Inferior</td>
<td>Posterior</td>
<td>0.57 (0.02)</td>
<td>0.57 (0.02)</td>
<td>0.57 (0.02)</td>
<td>0.58 (0.03)</td>
<td>0.60 (0.02)</td>
<td>p &lt; 10&lt;sup&gt;−6&lt;/sup&gt;</td>
<td>6.38</td>
</tr>
</tbody>
</table>

Table A.2

Differences in DTI parameters between segments. Differences between segments of the tracts in the fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD), significance-tested using ANOVA with p and F values reported. The parameter values represent the mean difference between each pair of segments, in the same tract, and the standard deviation is given in the parentheses.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Segments compared</th>
<th>13–19 (n = 26)</th>
<th>20–27 (n = 122)</th>
<th>28–40 (n = 40)</th>
<th>41–60 (n = 24)</th>
<th>61–84 (n = 45)</th>
<th>p (ANOVA)</th>
<th>F value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cingulate bundle (CB)</td>
<td>Posterior-Anterior</td>
<td>0.05 (0.04)</td>
<td>0.06 (0.03)</td>
<td>0.05 (0.03)</td>
<td>0.06 (0.03)</td>
<td>0.07 (0.03)</td>
<td>n.s.</td>
<td>0.78</td>
</tr>
<tr>
<td>FA</td>
<td>Anterior-Inferior</td>
<td>0.08 (0.04)</td>
<td>0.08 (0.04)</td>
<td>0.09 (0.04)</td>
<td>0.07 (0.03)</td>
<td>0.05 (0.04)</td>
<td>p &lt; 10&lt;sup&gt;−4&lt;/sup&gt;</td>
<td>7.05</td>
</tr>
<tr>
<td>MD</td>
<td>Anterior-Inferior</td>
<td>0.03 (0.03)</td>
<td>0.04 (0.03)</td>
<td>0.05 (0.03)</td>
<td>0.06 (0.03)</td>
<td>0.07 (0.03)</td>
<td>n.s.</td>
<td>0.18</td>
</tr>
<tr>
<td>RD</td>
<td>Anterior-Inferior</td>
<td>0.03 (0.05)</td>
<td>0.03 (0.05)</td>
<td>0.03 (0.05)</td>
<td>0.04 (0.04)</td>
<td>0.04 (0.04)</td>
<td>n.s.</td>
<td>0.85</td>
</tr>
<tr>
<td>Inferior fronto occipital fasciculus (IFO)</td>
<td>Anterior-Center</td>
<td>0.01 (0.03)</td>
<td>0.01 (0.02)</td>
<td>0.01 (0.02)</td>
<td>−0.00 (0.02)</td>
<td>−0.02 (0.03)</td>
<td>p &lt; 10&lt;sup&gt;−7&lt;/sup&gt;</td>
<td>10.93</td>
</tr>
<tr>
<td>FA</td>
<td>Anterior-Inferior</td>
<td>0.08 (0.02)</td>
<td>0.09 (0.02)</td>
<td>0.08 (0.02)</td>
<td>0.08 (0.02)</td>
<td>0.09 (0.02)</td>
<td>n.s.</td>
<td>1.46</td>
</tr>
<tr>
<td>MD</td>
<td>Anterior-Inferior</td>
<td>−0.01 (0.02)</td>
<td>−0.02 (0.02)</td>
<td>−0.02 (0.02)</td>
<td>−0.02 (0.02)</td>
<td>−0.03 (0.03)</td>
<td>n.s.</td>
<td>1.53</td>
</tr>
<tr>
<td>RD</td>
<td>Anterior-Inferior</td>
<td>−0.01 (0.02)</td>
<td>−0.01 (0.02)</td>
<td>−0.01 (0.02)</td>
<td>−0.01 (0.02)</td>
<td>−0.01 (0.02)</td>
<td>n.s.</td>
<td>1.53</td>
</tr>
</tbody>
</table>

Fig. A.1 a–c. Age-related effects on fractional anisotropy in the cingulate bundle. The cingulate bundle was divided into three segments: the anterior (red), the posterior (green), and the inferior (purple) segment. Columns show the average fractional anisotropy value in each age category, with error bars showing the standard error of the mean in each age category.
Fig. A.2. a–c. Age-related effects on radial diffusivity in the cingulate bundle. The cingulate bundle was divided into three segments: the anterior (red), the posterior (green), and the inferior (purple) segment. Columns show the average radial diffusivity value in each age category, with error bars showing the standard error of the mean in each age category.

Fig. A.3. a–c. Age-related effects on fractional anisotropy in the inferior fronto-occipital fasciculus. The inferior fronto-occipital fasciculus was divided into three segments: the anterior (red), the middle (green), and the posterior (purple) segment. Columns show the average fractional anisotropy value in each age category, with error bars showing the standard error of the mean in each age category.

Fig. A.4. a–c. Age-related effects on radial diffusivity in the inferior fronto-occipital fasciculus. The inferior fronto-occipital fasciculus was divided into three segments: the anterior (red), the middle (green), and the posterior (purple) segment. Columns show the average radial diffusivity value in each age category, with error bars showing the standard error of the mean in each age category.
References


