

A Diffusion Tensor Imaging based semi-automated segmentation and subdivision of the human corpus callosum: correlation of anisotropy and callosal area and application to gender based differences

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Introduction: Corpus callosum (CC) is the largest commissural fiber network in the brain and plays an important role in inter-hemispheric communication and is implicated in various neurological and neuropsychological disorders. The CC is a heterogeneous structure with fibers connecting specific cortical areas traveling through distinct callosal regions. The human CC fibers are functionally specialized and have different axonal packing and varied degrees of myelination [1]. Both Fractional anisotropy (FA) and cross sectional areas of CC are affected in a number of neurological, neuropsychological, and neuropsychiatric disorders. However, the relationship between the regional cross sectional areas and the corresponding FA values and how this might be affected by gender are not known. Since the regional areas of CC depend on the axonal morphology, such a relationship could provide a rational basis for interpreting FA changes as a result of pathology. In addition, most of the published FA values on the CC have been based on manually driven ROI analysis that could introduce significant operator bias. In this work, we present DTI based semi automated subdivision of the CC into seven segments based on Witelson's scheme [2] to compute both FA and the corresponding CC callosal sub regional areas on age matched males and females.

Subjects and Methods: Whole brain DTI data were acquired from thirty two healthy adults (age-matched 16 females, 16 males; age = 38.1±12.1 years) on a GE 1.5 T scanner as described elsewhere [3]. Diffusion-weighted image distortion correction, tensor decoding, interpolation and analysis were performed using an in house developed multidimensional DTI toolbox. The mid-sagittal section was identified based on the interpolated and FA modulated principal eigenvector (P_{vec}) overlaid on the mean diffusivity (D_{av}) maps (Figure 1.a). The identification was assisted by an experienced neurosurgeon based on the appearance of the interthalamic mass and the fornix. The CC was then segmented on the mid-sagittal slice based on FA, D_{av} and P_{vec} fiber orientation, and coherence. To isolate the CC from the other segmented tissues we adopted the blob coloring procedure. The reliability of the present segmentation procedure was verified on 10 control subjects by comparing the segmented CC areas with the corresponding manually outlined CC areas on T_1 weighted images acquired in the same scan session. The procedure outlined provides the seven segments of CC (Figure 1b): CC1-rostrum, CC2-genu, CC3-rostral midbody, CC4-anterior midbody, CC5-posterior midbody, CC6-isthmus and CC7-splenium along with the mean, SD of the $b=0$, and DTI metrics (FA, eigenvalues, coherence etc.)

Results: FA regional values and cross sectional areas (Figure 2) for each segmented CC subdivision were compared for their gender dependence using the unpaired two-tailed Student t-test. No significant differences between gender and FA or gender and cross sectional area were found for any of the subdivisions of the CC ($p>0.2$). Figure 3 shows the plot of regional FA values and the corresponding cross sectional areas along with linear regressions. Table 1 summarizes the Spearman's rank correlation coefficient between the 7 cross sectional areas of the CC and their corresponding regional FA values for males and females. The FA values of CC1 and CC2 show significant positive correlation with the cross sectional area for both males and females. Such a gender independent correlation was not observed for other regions.

Discussion and Conclusions: These are the first studies that examined the relationship between the seven regional FA values and the corresponding cross sectional areas in CC. The variation in the cross sectional areas across the seven segments in CC is consistent with histology [5]. The use of semiautomatic technique for segmenting and subdividing CC should minimize operator bias in the estimation of both FA and cross sectional areas. Such a method should be particularly useful in handling large amount of data that is typically acquired in multi-center clinical trials. Our observation that the regional cross sectional areas in CC are gender independent is also consistent with histological results [2, 4]. These studies also show that the FA values in CC6 and CC7 exhibit significant correlation only in females and not in males. On the other hand, a significant positive correlation was observed for CC4 only in males, but not in females. The reasons for the selective gender dependence on the observed correlations are unclear. These preliminary results need to be confirmed using larger cohorts.

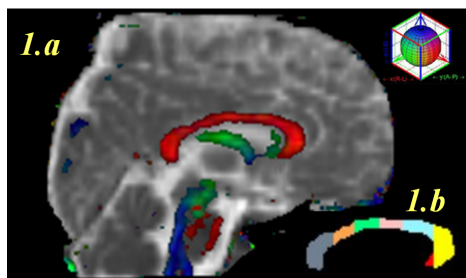


Figure 1.a: Illustration of overlay of the FA modulated by P_{vec} on the D_{av} map. The directional DTI color map is shown for clarity.

Figure 1.b: Witelson's seven subdivisions of the segmented CC: CC1 (red), CC2 (yellow), CC3 (blue), CC4 (pink), CC5 (green), CC6 (brown), CC7 (gray).

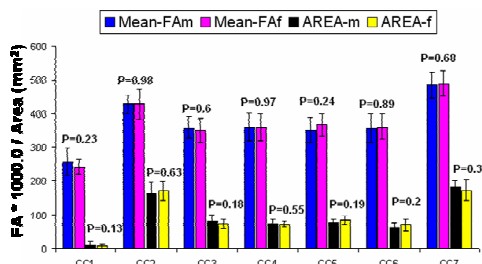


Figure 2: Bar plots of mean FA (males:blue, females:magenta) and mean cross sectional areas (males:black, females:yellow) for seven subdivisions of CC.

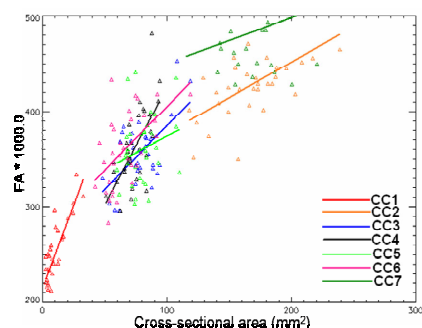


Figure 3: Scatter plot of FA vs Cross-sectional area in seven segments of all 32 subjects (16 males + 16 females). Plotted linear regression fit for each subdivision demonstrates the trend.

	Area - Males r (P)	Area - Females r (P)
FA(CC1)	0.7938 (0.0002)	0.5817 (0.0180)
FA(CC2)	0.5861 (0.0170)	0.5707 (0.0209)
FA(CC3)	0.3254 (0.2186)	0.3269 (0.2164)
FA(CC4)	0.7402 (0.0010)	0.4660 (0.0688)
FA(CC5)	0.2369 (0.3769)	0.1766 (0.5129)
FA(CC6)	0.3475 (0.1871)	0.7564 (0.0006)
FA(CC7)	0.1533 (0.5705)	0.7902 (0.0002)

Table 1: Spearman's correlation coefficient between regional FA and the corresponding cross sectional area for each segment of CC in males and females. P values are shown in parentheses.

References

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