Gender and age dependence of cingulum and corpus callosum in healthy volunteers assessed by diffusion tensor imaging: a virtual dissection study

H. Järnum[1], A-M. Stausholm[1], E. G. Steffensen[1], C. W. Simonsen[1], S. Lundbye-Christensen[2], T. Obel[2], E. T. Fründ[1,3], and E-M. Larsson[1]

[1]Department of Radiology, Aalborg Hospital/Århus University Hospital, Aalborg, Denmark, [2]Center for Cardiovascular Research, Aalborg Hospital/Århus University Hospital, Aalborg, Denmark, [3]GE Healthcare - Applied Science Laboratoy Europe

Introduction: Diffusion Tensor Imaging (DTI) presents an important tool for understanding the complexity of cerebral white matter microstructure. Several studies have demonstrated white matter pathology in schizophrenia, but less is known about white matter abnormalities for the most prevalent psychiatric disease: major depression. The lack of attention, memory and emotions observed in this patient group could possibly be explained by hypothesized changes in fractional anisotropy (FA) and apparent diffusion coefficient (ADC) in the limbic tracts. However, the published results concerning FA and ADC in limbic tracts are divergent, demonstrating a need for a re-evaluation of these findings with a robust DTI postprocessing technique and a comparable healthy control group.

Purpose: To perform virtual dissections of the limbic tract cingulum (left/right) comparing with corpus callosum in healthy volunteers using Catani's tractography approach (1,2), and to study intra-observer repeatability. Meanwhile collecting a reference dataset to utilize in later studies on patients with major depression.

Material & Methods: *Subject group:* Thirty-one healthy volunteers (29 right-handed and 2 left-handed) 16 women, mean age 41 years (age range 23-62 years) and 15 men, mean age 45 years (age range 24-63 years) without history of neurological disease. The cohort group was divided according to sex and age. *MRI protocol:* MRI was performed on a 3T system (Signa HDx, R14M5, GE Healthcare). Axial 2D DTI SE-EPI, 32 directions, b-value 1300, isotropic voxel size of 2.4×2.4×2.4mm^3 40 slices, TR/TE =9000.0/105, FOV 30.7cm, recon. matrix 128x128, scan time 5:42min. *DTI postprocessing:* Eddy current correction was performed with FSL; (http://www.fmrib.ox.ac.uk/fsl. DTI data were reconstructed, displayed and analyzed using Diffusion Toolkit and TrackVis software (3). (www.trackvis.org). The following threshold parameters were used: track turning angle ≤ 60° and FA ≥0.2. *Volumes of interest (VOIs):* "Obligatory passages" VOIs were representing brain regions that all fibers of cingulum (left and right) and corpus callosum had to pass through in order to reach their cortical or subcortical endstations (2) (fig 1). *Reproducibility measurements:* Intra-observer repeatability was assessed on five data sets. *Statistics:* The analyses of differences between gender and trend over age were done by ANCOVA, hereby assuming FA and ADC to be normally distributed. The repeatability is reported by the coefficient of repeatability as described by Bland & Altman (4). The study was approved by the local ethics committee: all participants gave written informed consent.

Results: In contrast to ADC (table 1) FA in both right (fig. 2) and left cingulum (fig. 3) exhibited gender dependency. Neither FA nor ADC in cingulum was age dependent. Corpus callosum (fig.4) showed no gender (table 2) - or age dependence for FA and ADC. Our intra-observer reliability for FA had a repeatability coefficient between $0.3x10^{-3}$ and $1.6x10^{-2}$ in the three tracts. The repeatability coefficient for ADC was less than $1.0x10^{-12}$ m^2/s in all tracts.

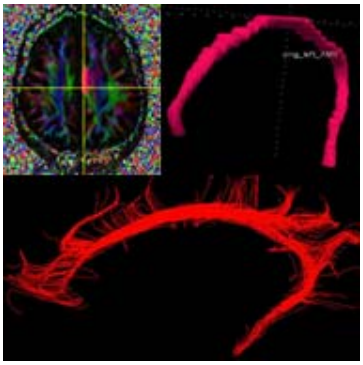

Fig 1. The left cingulum was outlined in TrackVis on axial slices (upper left), resulting in a single volume of interest (upper right). Fibers constituting the tract of interest are visualized (lower image).

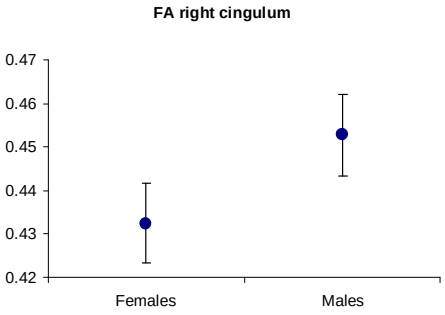

Fig 2. FA for right cingulum.
Females mean FA 0.43 95% CI (0.42;0.44).
Males mean FA 0.45 95%CI (0.44;0.46),
p-value for equal means = 0.003.

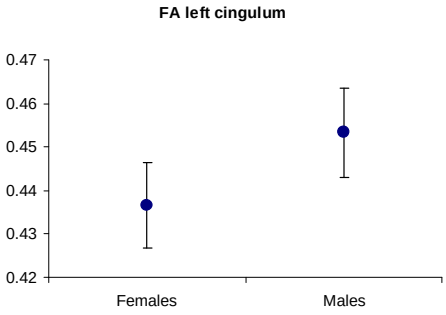

Fig 3. FA for left cingulum.
Females mean FA 0.44 95% CI (0.43;0.45).
Males mean FA 0.45 95% CI (0.44;0.46),
p-value for equal means = 0.02.

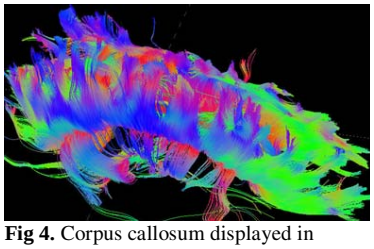

Fig 4. Corpus callosum displayed in TrackVis.

Table 1. ADC (10^{-9}m^2/s) for cingulum

	Females mean & 95% CI	**Males mean & 95% CI**
Cingulum right	0.71 (0.70;0.72)	0.71 (0.70;0.72)
Cingulum left	0.72 (0.71;0.73)	0.71 (0.70;0.73)

Table 2. FA & ADC (10^{-9}m^2/s) for corpus callosum

	Females mean & 95% CI	**Males mean & 95% CI**
FA	0.52 (0.51;0.52)	0.52 (0.51;0.53)
ADC	0.77 (0.76;0.78)	0.77 (0.76;0.78)

Conclusion:
To our knowledge, no previous study has demonstrated a statistically significant different FA for cingulum between healthy females and males. The DTI approach used has been shown to yield reliable descriptions of WM anatomy in post-mortem studies (1). Absence of age dependence concerning FA and ADC in cingulum is in agreement with previous studies. Since no gender differences were found in FA and ADC, corpus callosum may be used as a reference region for our prospective DTI study of major depression. The repeatability coefficient suggests potentials for comparative DTI studies.

References

1. Catani M, Howard RJ, Pajevic S, Jones DK. Virtual in vivo interactive dissection of white matter fasciculi in the human brain. Neuroimage 2002:17:77-94.
2. Catani M, Thiebaut de Schotten M. A diffusion tensor imaging tractography atlas for virtual in vivo dissections Cortex 2008:44:1105-1132.
3. Ruopeng Wang, Thomas Benner, Alma Greg Sorensen, Van Jay Wedeen. Proc. Intl. Soc. Mag. Reson. Med.15(2007)3720.
4. Altman DG, Bland JM. Measurement in Medicine: the Analysis of Method Comparison Studies. The Statistician 1983:32:307-317.