Gender effect on the asymmetries of brain pathways in the human living brain

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Introduction. Until the advent of diffusion tensor imaging (DTI), our knowledge of white matter anatomy was based on a small number of influential 19th and early 20th century post-mortem dissection atlases. These atlases emphasize the average anatomy of representative subjects and a symmetrical anatomical organization of both brain hemispheres is generally taken for granted (1). Very few post-mortem studies addressed variability of the tracts between the two hemispheres beyond the cortico-spinal tract (CST), which is found larger in the left than the right hemisphere (2). New histological techniques are revealing details about other tracts, like the optic radiations, which are larger in the left hemisphere as compared to the right (3), and the uncinate fasciculus, whose fiber density is on average 30% greater in the right than in the left hemisphere (4). Here, we used diffusion tensor imaging (DTI) tractography to address the question of the white matter interhemispheric differences for the major lateralized tracts.

Material and methods. DTI (2.5*2.5*2.5, bval=1300 s/mm2, 60 directions) datasets from 40 healthy volunteers aged 18-22 (M:F 20:20) were acquired on a 1.5 T GE Signa NV/i LX (General Electric, Milwaukee, WI) (5) and used to perform virtual in vivo dissections. BrainVisa (http://brainvisa.info/) was used to correct for eddy current distortion raw diffusion-weighted data and to calculate the diffusion tensor and the fractional anisotropy for each voxel. A tractography algorithm based on Euler integration (5) was used to propagate streamlines from "seed" regions of interest (ROIs) manually-defined. Following previously described criteria (6) ROIs were delineated around areas of white matter that represent "obligatory passages" along the course of each tract. This allows visualizing all fibres of a single tract without constraining its terminal projections, which may vary from subject to subject. One-ROI approach was used for the anterior commissure, corpus callosum, cortico-spinal tract, internal capsule, fornix. Two-ROI approach was used for the arcuate, cingulum, inferior longitudinal fasciculus, inferior fronto-occipital fasciculus, uncinate, optic radiations, and cerebellar tracts (cortico-ponto-cerebellar, spino-cerebellar tract, and superior-cerebellar tract). Further dissections of the arcuate fasciculus were performed to separate the anterior and posterior indirect segments from the long segment. Tract-specific measurements were extracted (i.e. number of streamlines, volume, and fractional anisotropy) and a lateralization index calculated.
Statistical significance of the degree of the lateralization was determined using one-sample t test for each tract. Only results that survived Bonferroni correction are presented.. Between gender differences have also been assessed using repeated measure ANOVA. The lateralization index of each tract was set as within-subjects factors and the sex as between-subjects factor.

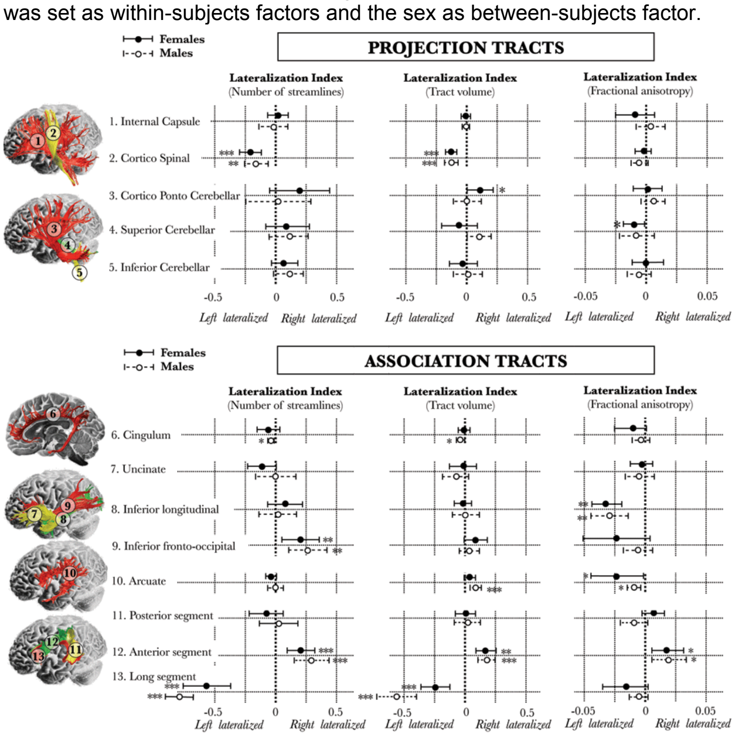

Figure 1. Lateralization index for the number of streamlines, volume and fractional anisotropy (mean±95% confidence interval) of the projection and association pathways.

Results. Males and females differences in the lateralization indexes for the volume, number of streamlines, and FA of the dissected tracts are shown in Figure 1. A statistically significant leftward asymmetry was found for the number of streamlines ($T_{(39)}$= 5.3 p<0.001) and the volume ($T_{(39)}$= 6 p<0.001) of the cortico-spinal tract, and for the volume ($T_{(39)}$= 7.2 p<0.001) and number of streamlines ($T_{(39)}$= 10.9 p<0.001) of the long segment of the arcuate fasciculus. A statistically significant rightward asymmetry was also found for the volume of the arcuate fasciculus ($T_{(39)}$=3.4 p<0.001) and for the number of streamlines ($T_{(39)}$=4.4 p<0.001) of the inferior fronto-occipital fasciculus. Of the three segments of the arcuate fasciculus only the anterior segment showed a rightward asymmetry in volume ($T_{(39)}$=5.6 p<0.001) and number of streamlines ($T_{(39)}$=5.9 p<0.001).
The analysis of the FA measurements revealed a leftward asymmetry for the inferior longitudinal fasciculus ($T_{(39)}$ =6.2 p<0.001). A rightward lateralization was found for the optic radiations ($T_{(39)}$= 5.1 p<0.001) and the anterior segment of the arcuate fasciculus ($T_{(39)}$= 3.7 p<0.001). The ANOVA analysis showed a significant interaction between the lateralization index of the volume and the gender ($F_{(13,494)}$=2.0742 p<0.05) but no interaction for the lateralization index of the number of streamlines and FA.
Post-hoc analysis showed a statistically significant difference between genders for the lateralization index of the volume of the long segment of the arcuate ($T_{(38)}$= 2.57 p<0.05), with males (lateralization index -0.56±0.36) showing a greater left lateralization as compared to females (lateralization index -0.24±0.28).

Discussion and Conclusion. Two important findings emerge from this study. First, tracts like the CST and the long segment of the arcuate fasciculus are left lateralized while the anterior segment of the arcuate fasciculus and the inferior fronto-occipital fasciculus are right lateralized. Secondly, we observed gender differences for the long segment, which is more left lateralized in males than in females. The leftward asymmetries findings from post-mortem dissections, in vivo DTI-tractography, and voxel-based analysis of T1-images (7, 8)
We also report, for the first time, a rightward asymmetry for the volume of the anterior segment and the IFOF. Neglect occurs mostly with lesions to the right hemisphere and the asymmetry of the anterior segment of the arcuate and of the inferior fronto-occipital fasciculus (9) may represent the anatomical substrate of right hemisphere dominance for visuo-spatial processing.

(1) Wakana et al. Radiology (2004). (2) Yakovlev and Rakic (1966). (3) Bürgel et al NeuroImage (2006). (4) Highley et al. Cereb Cortex (2002). (5) Jones et al., Human Brain Mapping (2002). (6) Catani and Thiebaut de Schotten Cortex (2008). (7) Nucifora et al. Neuroreport (2005). (8)Good et al. NeuroImage (2001). (9) Doricchi et al. Cortex (2008).