Constant and variable features of white matter anatomy in the human brain: an in vivo diffusion tractography study

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Introduction. Increasing knowledge of white matter organization has recently been derived from diffusion tensor tractography *(1, 2, 3)* but access to this knowledge has often been limited to Diffusion Tensor Imaging (DTI) experts. Therefore a tractography atlas of the human brain pathways is timely for a better comprehension of brain function. However, this endeavour may be compromised by methodological limitations of the DTI technique and the high degree of inter-individual anatomical variability *(4, 5)*. Here we combine group effect maps with a spatial overlap approach to develop a 3D probabilistic atlas that provides comprehensive information about inter-subject variability and general morphology of the tract.

Material and methods. DTI 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) *(6)* and used to perform virtual in vivo dissections of 33 major pathways. For each tract, a binary map was computed by assigning each pixel a value of 1 or 0 depending on whether the pixel was visited by the tract streamlines. All binary maps were spatially normalized to the Montreal Neurological Institute (MNI) space and summed to produce tract overlap maps on axial, sagittal, and coronal slices. Statistical parametric mapping analysis of the smoothed (smoothed with an isotropic kernel of 4 mm) visitation maps was applied to create statistically significant maps. We then combined both results to create composite maps (see figure 1).

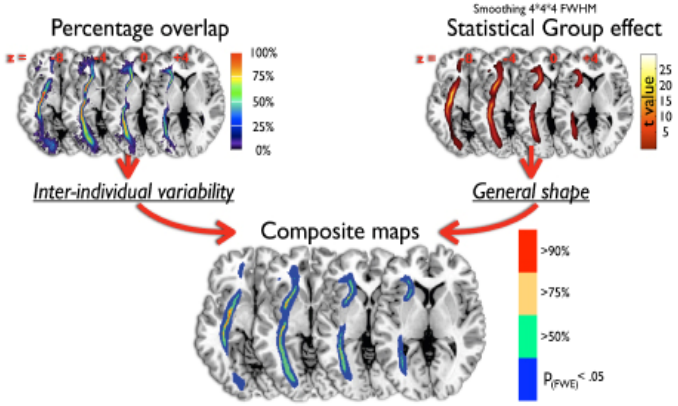

Figure 1. Normalized group atlas of the right inferior occipito-frontal fasciculus. Left, percentage overlap maps show the inter-individual variability along the tract. Right, the statistical group effect maps ($P_{(FWE)}$: probability corrected for multiple comparisons) provide complementary information on the general shape of the tracts, which is representative of the anatomy of the general population. Bottom, the two maps are combined into composite maps that provide comprehensive information about inter-individual variability of the tract and the general shape.

Results. All probability maps had a general correspondence to the already known anatomy of the tracts as derived from a post-mortem white matter atlas *(7)*. However the anatomy of some tracts was incompletely represented. An asymmetrical distribution of the percentage maps was evident for the arcuate fasciculus (AF), with greater percentage of overlap in the left temporal region compared to the right, and the uncinate fasciculus with greater percentage of overlap in the right temporal region compared to the left. The other tracts had minor degrees of asymmetry or no asymmetry. In general the percentage of overlap was higher for the central regions of the tracts than for the peripheral terminations, with very few tracts approaching voxels in the vicinity of the cortex.

Discussion and Conclusion. The percentage of overlap maps varied along the tracts. This is probably due to a combined effect of the true anatomical variability and the presence of false positive and false negative reconstructions of the tracts. By decreasing the percentage of overlap the representativeness of the maps to individual subject data increases however the possibility of generalizing to the general population also decreases. The statistical maps based on a group effect analysis partially overcome this problem by giving results for which there is a statistical confidence, but they lack in any information on inter-individual variability. The composite maps combine percentage overlap with statistical group effect maps to provide precise stereotaxic information about the anatomy and the variability of the tracts. Future studies will be needed to implement this approach with methods aimed at solving multiple-fibre crossing to reduce artefactual representations and false negatives on the maps.

(1) Wakana et al. Radiology (2004) *(2)* Catani et al. Neuroimage (2002) *(3)* Lawes et al. NeuroImage (2008) *(4)* Ciccarelli et al. NeuroImage (2003) *(5)* Catani et al. PNAS (2007) *(6)* Jones et al.. Hum. Brain Mapp. (2002) *(7)* Bürgel et al. NeuroImage (2006)