Lateralisation of connective pathways between language centres demonstrated using group analysis of fibre tracking incorporating crossing fibre information

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Introduction It has recently been demonstrated that voxels containing crossing fibres may be identified using spherical harmonic fits to diffusion orientation profiles derived from HARDI[1] data acquisitions[2,3], and that the orientations of the underlying fibre populations may be estimated[4-6]. This is of particular importance in certain areas of the brain where major fibre bundles cross. For the purpose of this work we are interested in the region where the superior longitudinal fasciculus (SLF) crosses the corona radiata. The SLF is thought to link two grey matter regions involved in language understanding and production: Broca's area (BA) and Wernicke's area (WA). BA is the main centre for word generation, whilst WA is likely to play a crucial role in word comprehension. We set out to see whether connectivity between these regions is indeed via the SLF, and whether it is stronger on in the left hemisphere (containing the language centres).

Methods HARDI brain data were acquired using a GE Signa 1.5 T scanner with a standard quadrature head coil. 11 right-handed normal volunteers were studied (6 male, 5 female). Sequence parameters: cardiac gating (TR = 20 RR ~ 20 s); 60 axial slices; TE = 95 ms; 54 weighting directions at b = 1156 smm^{-2}; 6 acquisitions at b ~ 0 smm^{-2}; δ = 34 ms; Δ = 40 ms; gradient strength G = 22 mTm^{-1}; 96 × 96 acquisition matrix, interpolated to 128 × 128; 220 mm field of view, generating 2.3 × 2.3 × 2.3 mm^3 voxels as acquired, reconstructed to 1.72 × 1.72 × 2.30 mm^3 [1,7].

We used spherical harmonic voxel classification[3] to identify voxels in which the single tensor model is poor and in these cases fit a mixture of two Gaussian densities; otherwise we use the single tensor model. The principal diffusion directions of the tensors in the mixture model provide estimates of the crossing fibre orientations[4-6].

BA, WA, and homologous regions in the right hemisphere were identified in standard space and volumes of interest (VOIs) defined to encompass neighbouring white matter to allow fibre tracking. VOIs were transformed back to native space for streamline tracking modified to trace through the multi-tensor field. Paths were terminated if they extended into grey matter. No penalty was imposed on curvature. Step size was set to 0.23 mm. Propagation was constrained using the pairs of VOIs and was started from the centre of every voxel in the white matter[8]. A path was accepted if it intersected BA and WA or the homologous areas in the right hemisphere. Voxels that were encountered by an accepted pathway were recorded to generate maps of voxels that were connected to the two areas of interest.

Variability group maps were constructed using spatially normalised connected volumes from each individual. Volumes were averaged at each point in standard space, thus indicating the degree of spatial variability and overlap of the identified connections between subjects[9]. A voxel *commonality value C* of 1.0 indicates that each individual had a connection identified in this voxel; C = 0.0 indicates that none of them did. We calculated the lateralisation index (*LI*) of the connected volumes between hemispheres at a range of C thresholds to determine whether lataeralisation was caused by more or less variable connected volume within the group.

Results The group variability maps for the volume of connection in the left and right hemispheres can be seen in Fig. 1. Consistent connection is observed between BA and WA via the SLF (left hemisphere). Connection is also apparent between BA and WA via the external capsule (EC), although this is not apparent in all subjects. Consistent connection is observed to area 40, implying a pathway connecting this region to BA and WA. Connection to the superior temporal gyrus (STG) and the middle temporal gyrus (MTG) is apparent, again implying connection to both BA and WA. Two subjects showed no connections between BA and WA, likely due to a failure in the voxel classification stage of the data processing, apparently due to poor signal to noise ratio.

A smaller volume of connection is observed overall in the right hemisphere (Fig. 2), although the consistent connections between BA and WA via the SLF and to area 40 are comparable to that seen in the left hemisphere (Fig. 1). Evidence for connections to the STG, MTG, and via the EC is lacking.

The lateralisation index *LI* is shown as a function of commonality value C in Fig. 2. The left hemisphere is shown to have a larger connected volume at all values of C; *LI* is positive for all values of C.

Conclusion Our results provide a quantification of the volume of white matter involved in linking Broca's area and Wernicke's area. We also demonstrate the differences and similarities in the roles played by the white matter, in particular the SLF, in the two hemispheres and show that these findings are largely consistent across a group of normal individuals. The differences between left and right hemispheres reflect the well-known lateralisation of language processing in the brain; however, this is to the best of our knowledge the first time this has been demonstrated in white matter pathways connecting important processing centres. Although the connection between BA and WA via the SLF is expected, the evidence for a possible connection via the external capsule is less so, and the possibility of erroneous connection due to partial volume effects cannot be dismissed. However, if this connection is confirmed in future studies this may add to our knowledge of cerebral interconnections involved in the processing of speech and language. This is one of the first examples of the use of crossing fibre orientation information, and the first that we know of to demonstrate quantifiable observations over a group of individuals. The ability to extract complex crossing fibre information is vital for accurate fibre tracing in regions such as the SLF that demonstrate significant partial volume effects with other fibre tracts.

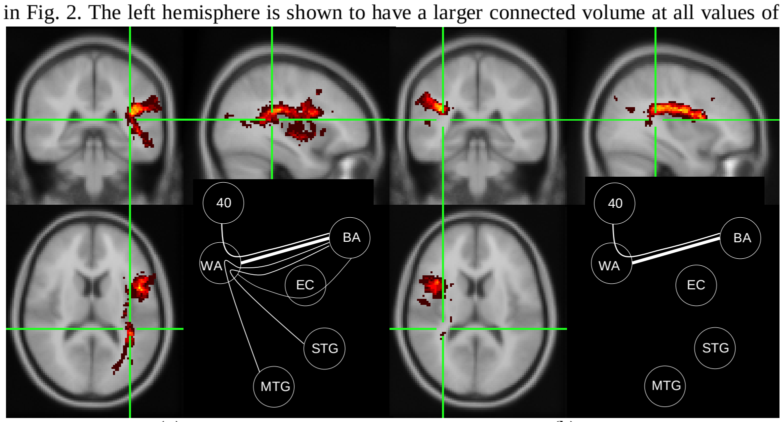

Figure 1. Commonality maps. Hotwire scale indicates 0 < C ≤ 1. Schematics indicate routes of connections and weight of line indicates commonality of connection. (a) Left hemisphere. (b) Right hemisphere (radiological convention).

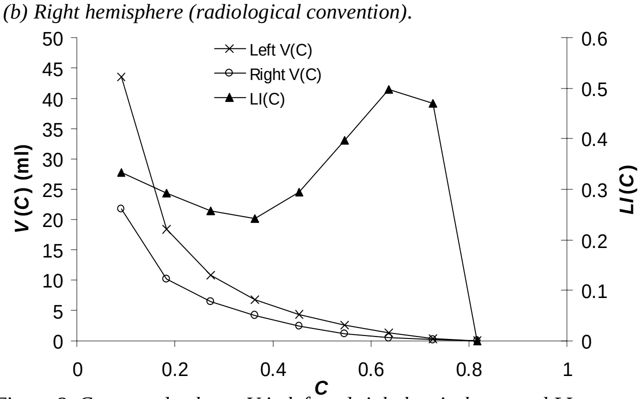

Figure 2. Connected volume, V in left and right hemispheres and LI as a function of commonality, C.

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