Characterization of white matter asymmetries in the healthy human brain using diffusion MRI fixel-based analysis

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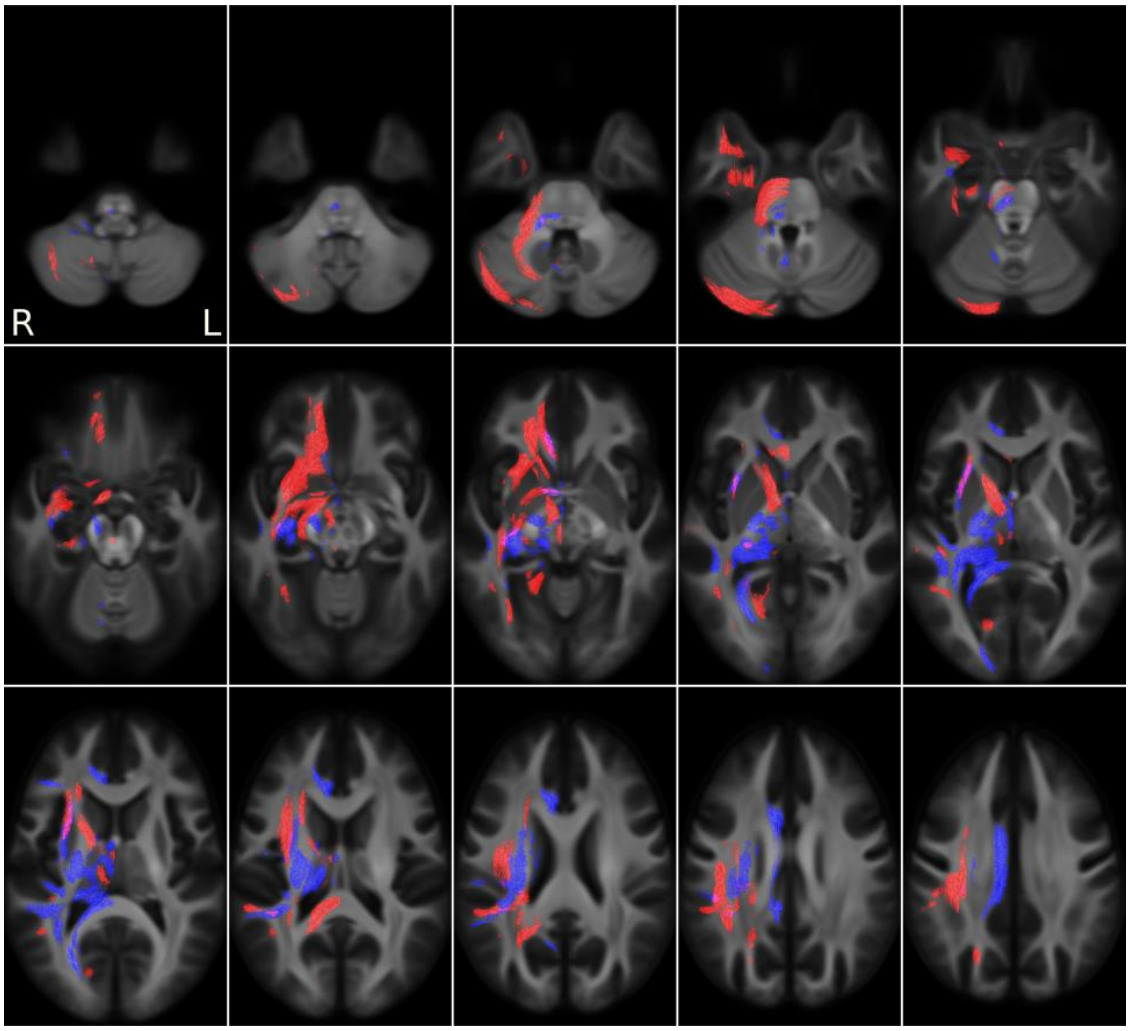
Supplementary Material



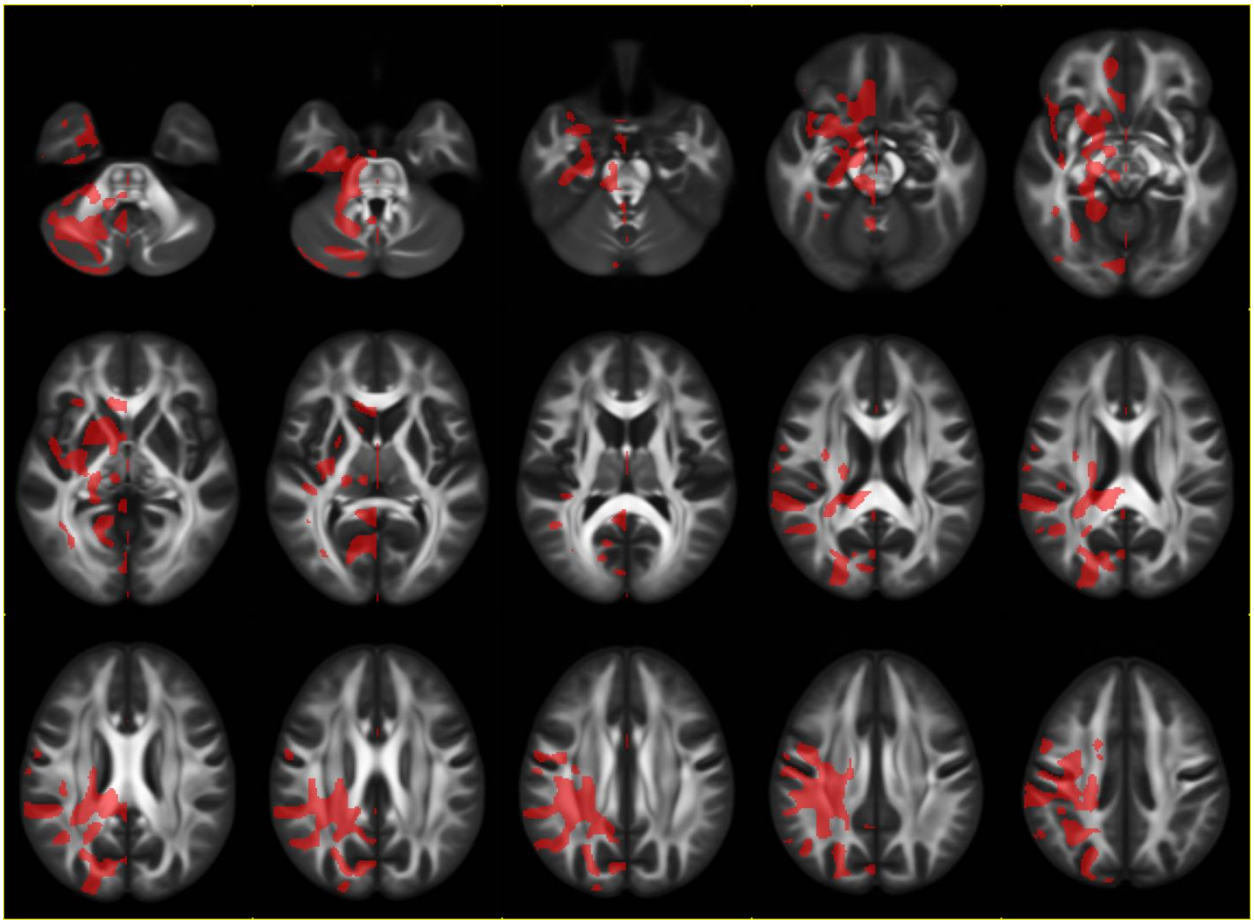
Supplementary Figure S1- ***Significant fixels displayed red in color for Right>Left and blue in color for Left >Right asymmetry (FWE corrected, p<0.05) in Fibre Density and Cross-section (FDC).*** *Fixels are displayed in the right hemisphere of the brain as seen on axial slices, to help visualise the relative spatial locations.*

Voxel-based FA analysis

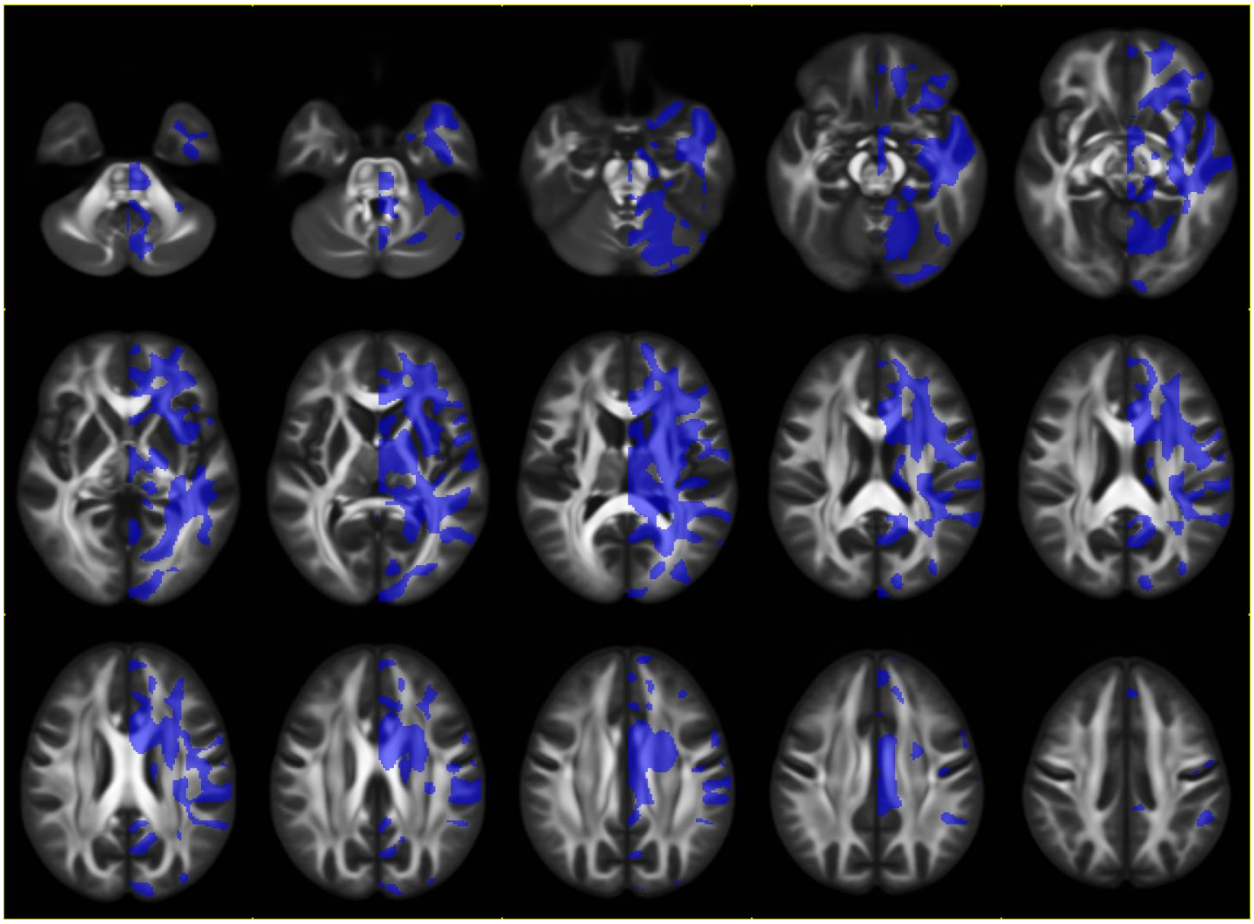
To facilitate a direct comparison of some of the prior DTI-based voxel-based results cited in Table 1 to the related results but computed based on the same HCP data used in our study, we include in this section the results of performing a more traditional voxel-based analysis of the tensor-based fractional anisotropy (FA). To this end, the same HCP MRI dataset (n=100) as that used for FBA analysis was used to perform voxel-based FA analysis.

An FA map was computed for each subject from the pre-processed data using an iteratively re-weighted, linear least square estimator (Veraart et al., 2013). All 100 subjects were used to create a symmetric template, through iterative registration of original and left-right flipped FA maps of each subject. Each transformed FA map in template space was smoothed using a 6 mm full width at half-maximum Gaussian kernel. The difference between the left and right hemispheres for the FA metric was computed for each subject (FA_R - FA_L). Two independent one sample t-tests were performed (i.e., $H_{R>L}$: $FA_R - FA_L > 0$; $H_{L>R}$: $FA_L - FA_R > 0$), with age, sex, and handedness included as covariates. Threshold-free cluster enhancement was performed with default parameters (dh=0.1, E=0.5, H=2).

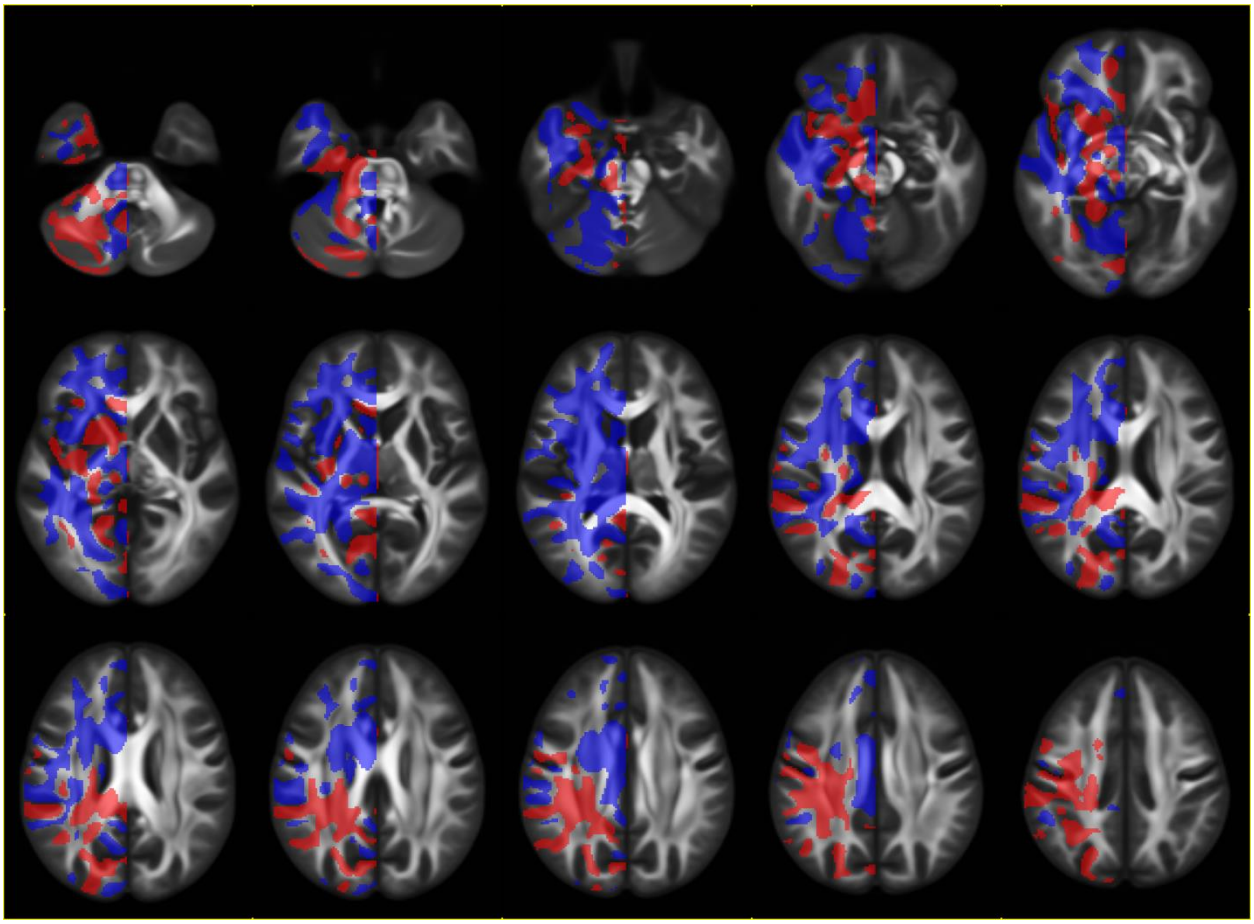
Supplementary Fig. S2 and Fig. S3 show example axial slices of the VBA template image, overlaid with significant voxel-based asymmetry results (FWE-corrected *p*-value < 0.05) demonstrating rightward dominance (i.e., FA_R>FA_L) and leftward dominance (i.e., FA_L>FA_R) respectively. For their relative spatial distributions, Supplementary Fig. S4 shows the significant voxel asymmetry results for both FA_R>FA_L (red) and FA_L>FA_R (blue) results overlaid on the same hemisphere of the template.



Supplementary Figure S2: ***Voxel-wise significant Right > Left asymmetry (FWE corrected, p<0.05) for Fractional Anisotropy (FA) metric overlaid on a voxel-based template.***



Supplementary Figure S3: ***Voxel-wise significant Left > Right asymmetry (FWE corrected, p<0.05) for Fractional Anisotropy (FA) metric overlaid on a voxel-based template.***

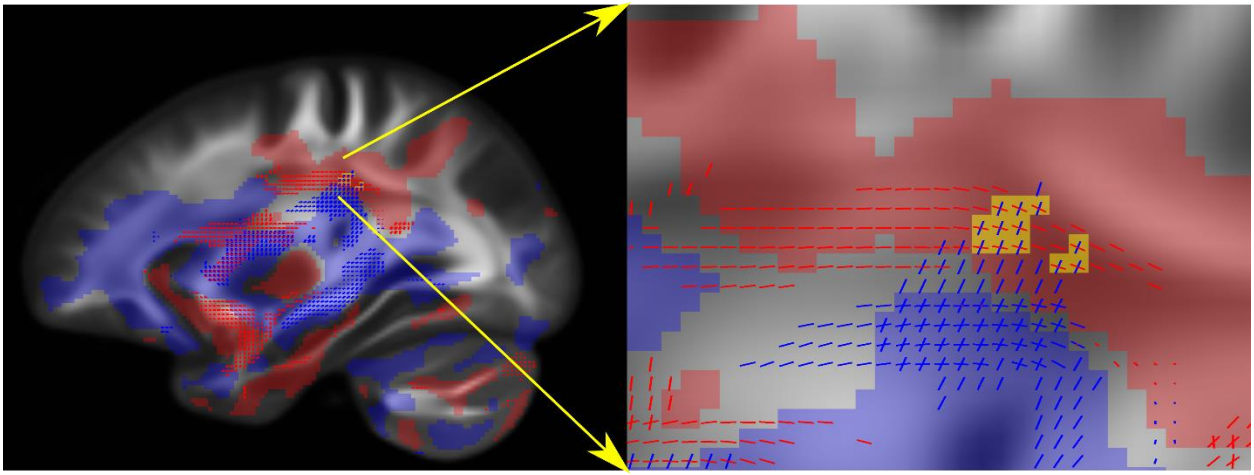


Supplementary Figure S4: - ***Significant voxel-based asymmetry results displayed in red for Right>Left and in blue for Left >Right asymmetry (FWE corrected, p<0.05) in Fractional Anisotropy (FA).*** *Significant results are displayed in the right hemisphere of the brain as seen on axial slices, to help visualise the relative spatial locations.*

Similar to FBA experiment, areas with asymmetry were labelled based on the white matter atlas (Cho et al., 2015). Labelled significant results are listed in the last column of Table 1.

VBA identified extensive areas with significant hemispheric asymmetry of FA. Interpretation of these results and their relation to the FBA requires some caution, as a number of factors are different between the two analysis pipelines. FA can be influenced also by the relative proportion of fibres in areas with multiple fibre populations, such as in areas where two or more major bundles cross. One such region is shown in Supplementary Fig. S5: FDC is capable of detecting

asymmetries (even with R>L and L>R in the same voxel); however, FA is interpreted as representing only R>L asymmetry (voxels in red) in some of these voxels. Please refer to Discussion section for more details about tensor-related limitations and the benefits of our FBA approach.



Supplementary Figure S5: Example of detected asymmetries in fixel and voxel-based asymmetry analysis. Red fixels/voxels denote R>L asymmetry; blue fixels/voxels denote L>R asymmetry. Yellow voxels indicate overlapping fixels of right/left asymmetry.

References

Cho, Z.-H., Chi, J.-G., Calamante, F. (Eds.), 2015. 7.0 Tesla MRI Brain White Matter Atlas, 2nd ed. Springer-Verlag, Berlin Heidelberg.

Veraart, J., Sijbers, J., Sunaert, S., Leemans, A., Jeurissen, B., 2013. Weighted linear least squares estimation of diffusion MRI parameters: strengths, limitations, and pitfalls. NeuroImage 81, 335–346. https://doi.org/10.1016/j.neuroimage.2013.05.028