Asymmetry in Multi-Modal White Matter Microstructural Indices

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INTRODUCTION: Asymmetry in structure and function has been reported in humans and animals and is believed to be a result of years of evolutionary interhemispheric specialization. Structural connectivity and the microstructural organization of the pathways connecting these hemispheres are important in our understanding of this specialization. Diffusion weighted imaging is often used to study white matter, and measures such as FA and radial diffusivity incorrectly used as an indicator of myelination.. We propose that other quantitative microstructural imaging methods, such as magnetization transfer imaging[1,2] and multicomponent T_2 species from relaxometry[3,4] might be more sensitive indicators of asymmetries in microstructure. Quantitative magnetization transfer (qMT)[1] quantifies the relative density of macromolecules (including myelin) within the brain (f map). Multi-component driven-equilibrium single-pulse observation (mcDESPOT)[3,4] of fast- and slow-T_1 and T_2 provides another putative marker of myelin through myelin water fraction (MWF) maps. This study provides insights into hemispheric asymmetry in whole brain and specific white matter tracts using different metrics - fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), principal eigenvalue (L1), myelin water fraction (MWF), qMT – map f and free water correction (see below) in healthy controls.

Methods: Healthy right-handed volunteers (*N*=28, 31.1±6.7y) were studied using a 3T MRI scanner (HDx system GE Medical Systems, Milwaukee, WI). Cardiac-gated DTI data were acquired with a single-shot spin-echo EPI sequence with the following parameters: b-value = 1200 s/mm^2 along 60 gradient directions; six non-DW images; 60 axial slices, with effective TR = 20 R-R intervals[5]. Sequence specific parameters for mcDESPOT-SPGRs were: TE/TR = 2.1/4.7 ms, flip angle (α) = [3,4,5,6,7,9,13,18]; mcDESPOT-bSSFPs were: TE/TR = 1.6/3.2 ms, α = [10.6,14.1,18.5,23.8,29.1,35.3,45,60][6]. The qMT sequence[1] used a pulsed MT protocol consisted of a 3D MT-weighted spoiled gradient recalled-echo sequence with the following parameters: TR/TE = 26.65/1.86 ms, Gaussian-MT pulses, duration τ = 14.6 ms (duration), with collection of additional B_1 and B_0 mapping. All participants gave written informed consent to participate in this study under a protocol approved by the local Ethics Committee/IRB.

Diffusion images were corrected for CSF-partial volume contamination using the approach detailed in[7], producing free water (FWC) corrected data prior to non-linear registration of non-diffusion metrics to the fractional anisotropy map. Fibre tracking based on fibre orientational density (FOD) peaks from constrained spherical harmonic deconvolution (CSD)[8] was used to reconstruct different fasciculi, in *ExploreDTI*[9]. Whole brain asymmetry measurements for each metric (left greater than right) were performed using tract-based spatial statistics[10] (TBSS). For the uncinate, an asymmetry index along the tract was calculated for each of the 28 participants (Asymmetry Index = 2(L-R)/(L+R)). Using the asymmetry index from all 28 participants a lateralization index was then calculated (Lateralization Index=(# of participants with RS asymmetry -#of participants with LS asymmetry)/(#of participants with RS asymmetry+ #of participants with LS asymmetry)) to assess asymmetry in a control population for specific pathways. (Here we report on the uncinate)

RESULTS: Results from whole brain TBSS asymmetry calculations clearly demonstrate that there is a left lateralization throughout all metrics (Fig 1). Notably, the free water correction (FWC) leftward lateralization is only significant in white matter areas in the frontal cortex, demonstrating that partial volume contamination due to free water is significantly asymmetric in the frontal cortex. The laterality of the uncinate pathway for all metrics is shown in Fig. 2. The metrics that show significant (marked by red star) leftward lateralization are: MD, RD, L1 and FWC, except for MWF that shows a significant rightward lateralization.

DISCUSSION: Whole brain asymmetry measures show a left lateralization in most WM metrics as previously demonstrated in DTI measures[11,12]. FWC is left-lateralised in the frontal cortex – and this has important implications for comparison of metrics in frontal cortex without correcting for partial volume. The spread in asymmetry indices within specific tract measurements (e.g. the uncinate), reflects the fact that the indices are capturing different aspects of microstructure. We are currently investigating the correlation between performance on cognitive tasks and the asymmetry of these different metrics.

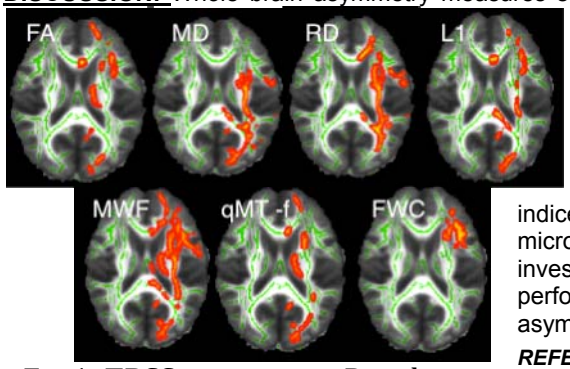
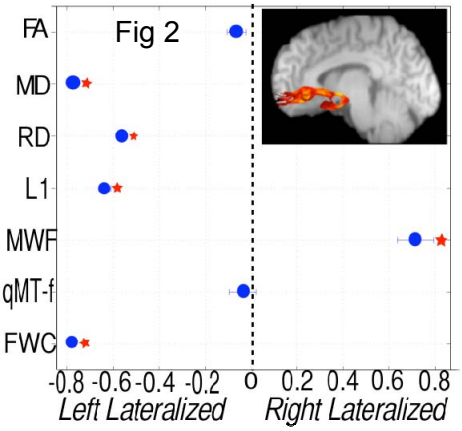


Fig 1: TBSS asymmetry Results



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