Supplementary Material: DTT Details and FA Lateralization Results

Diffusion Tensor Tractography

Compact white matter fiber tracking was performed using DTI Studio software (H. Jiang and S. Mori; Johns Hopkins University, Baltimore, MD; **cmrm.med.jhmi.edu**). Three ROI operations namely ***OR, AND, NOT*** operations described in the past were utilized (Mori et al., 1999; 2002; Huang et al., 2004; Wakana et al., 2004; Jiang et al., 2006). In brief, the ***OR*** operation selected all the fibers going through the region-of-interest, ***AND*** operation retained fibers passing through two selected regions of interest and ***NOT*** operation was used to exclude fibers that were either due to contamination from adjacent regions or were artefactual.

Association fibers

Arcuate Fasciculus

We followed the DTT approach described by Catani et al. (2005) to identify and quantify the three distinct white matter segments of the AF namely, the fronto-temporal segment (FT) fronto-parietal segment (FP) and the temporo-parietal segment (TP). Both the FT and FP segments share a common space between the inferior frontal cortex anteriorly to the junction of superior temporal cortex and inferior parietal cortex posteriorly, so they were traced together as follows. First of all, axial slices of the direction encoded color maps were examined to identify the AF with maximum extent in the antero- posterior dimension. The sagittal slice corresponding to this was identified (AF appears green, see Figure 1.A in this Supplement). Coronal slices were located corresponding to the posterior aspect of AF and a region of interest (ROI 1, **OR** operation, Figure 1.A-1, B-1) was drawn manually to include the green fibers. To

increase the specificity, a second ROI (ROI 2, **AND** operation, Figure 1.A-2) was placed on the coronal slice, 2-3 slices from the anterior end of the AF. Resulting fiber tract contained both the FT and FP segments. To isolate the FT segment, a third ROI (ROI 3, AND operation, Figure 1 C-3) was placed on an axial slice where the FT segment curves inferiorly (seen as blue fibers Figure 1.A). The FP segment was isolated by placing a separate ROI (ROI 4, **AND** operation, Figure 1.A-4), on the sagittal slice supero-lateral to the posterior end of AF. The TP segment was isolated by an **OR** operation in the location of ROI 3 and an **AND** operation same as ROI 4.

Inferior Longitudinal Fasciculus and Inferior Fronto-occipital Fasciculus

The inferior longitudinal fasciculus (ILF) and inferior fronto-occipital fasciculus (IFOF) were isolated using three ROIs. The ILF (Figure 1.I-1) was identified on the sagittal slices of the color map. Initial **OR** ROI (ROI 1, Figure 1.J-1) was placed on coronal slices corresponding to the mid portion of ILF/IFOF identified on the sagittal slice and two target **AND** ROIs were placed on coronal slices as follows. The first one (ROI 2, Figure 1.K-2) was placed posterior to ROI 1 (Figure 1.J-1) close to the anterior most part of occipital lobe. This ROI was common for both ILF and IFOF. The second target ROI to separate ILF (ROI 3) and IFOF (ROI 4) were placed anterior to the ROI 1 as shown in Figure 1.K-3, K-4.

Uncinate fasciculus

Tracing the uncinate fasciculus (UF) also requires three ROIs. The first (ROI 1, **OR** operation) was placed on an axial slice (see Figure 1.E-1) and the two **AND** ROIs (ROI 2 & 3, Figure 1.F-2, F-3) were placed on coronal slices corresponding to the locations shown in Figure 1.F.

Projection fibers

Corticospinal Tract

Corticospinal tract (CST) was reconstructed by selecting all the fibers passing through the posterior limb of internal capsule using an **OR** operation. The resulting tract contains the corticospinal tract, corticopontine tract as well as the sensory projections to thalamus. A second ROI was placed over the corticospinal tract in the Pons (seen as blue fibers, Figure1 M, red arrow) at the level of middle cerebellar peduncle (Figure 1.M, yellow arrow). Care must be taken not to include transpontine fibers or pontocerebellar fibers. An axial slice of the B_0 image was identified where the central sulcus can be visualized (inverted omega sign) and a third ROI is placed to enclose the whole precentral region corresponding to the primary motor cortex (Brodmann Area 4; Carpenter, 1983). The final reconstructed fiber tract contained fibers passing through all these three regions.

Somatosensory Tract

The somatosensory pathways (SS) were traced from the level of the medial leminiscus (appear as blue fibers in the Pons; Figure 1.M, white arrow). The first ROI (OR operation) was placed at this level carefully to include only the blue fibers. These fibers were traced upwards and their location in the ventral postero-lateral nucleus of the thalamus (sensory fibers relay in thalamus, Figure 1.N, white arrow) was verified (Carpenter, 1983). Thalamo-cortical projections to the post central cortex (somatosensory cortex, Brodmann Areas 3, 2, 1; Carpenter, 1983) were finally selected and the complete tract was reconstructed from the level of medial leminiscus up to the somatosensory cortex.

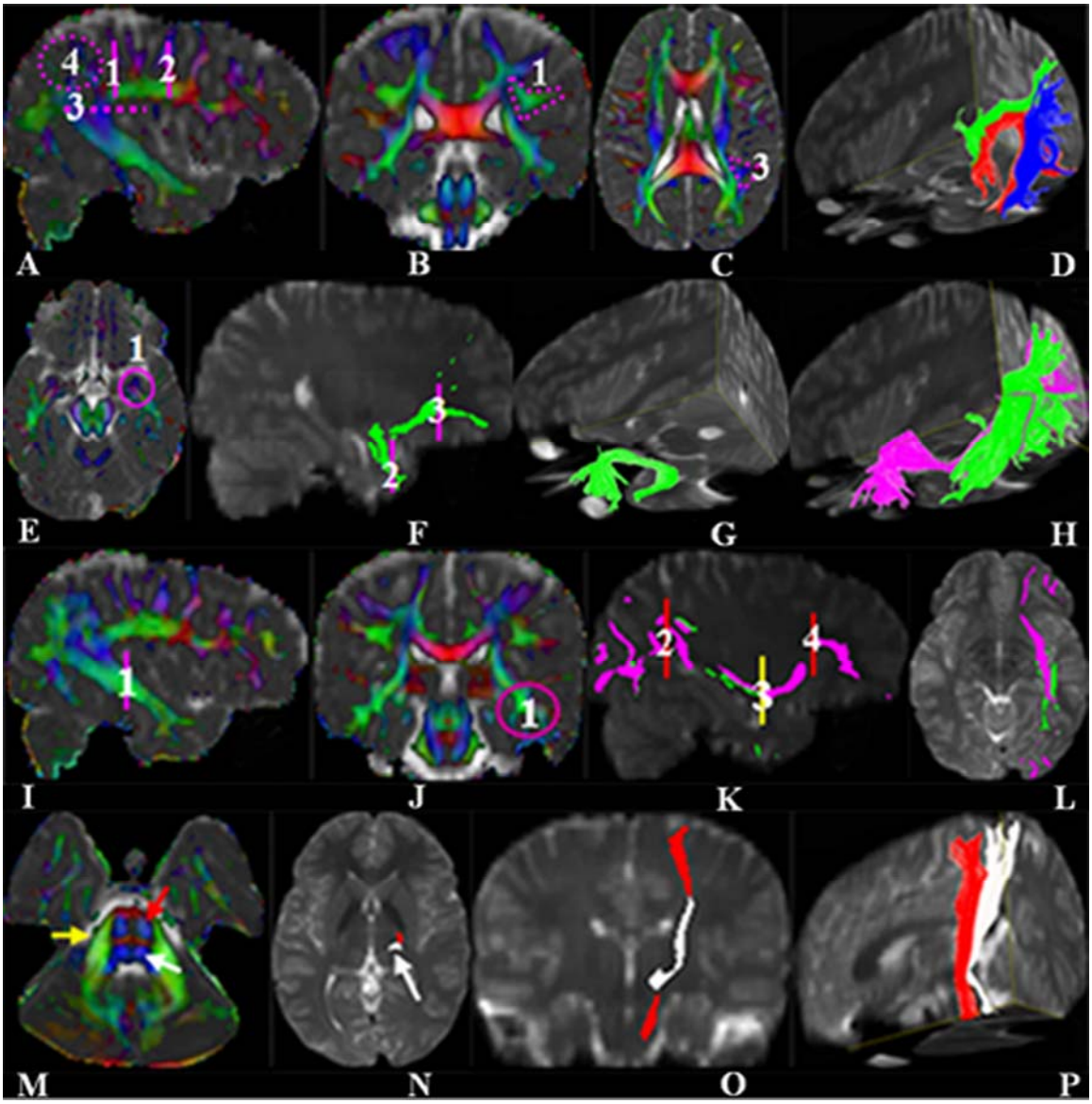

Figure 1. Illustration of the various ROIs used for fiber tracking and the reconstructed fiber tracts (2D and 3D) overlaid on B_0 images. **A, B** and **C** show ROIs for separating the AF. **D** is a 3D view of the reconstructed left AF; red fibers represents FT, green fibers = FP, and blue fibers = TP segments respectively. **E** and **F** show ROIs for isolating UF. **G** is a 3D view of the reconstructed UF; note the shorter inferior and longer superior segment. **I, J** and **K** show ROIs for separating ILF and IFOF. **H, K,** and **L** display reconstructed IFOF (pink) and ILF (green). **M** display the axial 2D view at the level of middle cerebellar peduncle (yellow arrow) showing left CST (red arrow) and medial leminiscus (white arrow). **N**, **O** and **P** display reconstructed CST (red) and SS pathway (white). Note that the SS pathway passes through the thalamus.

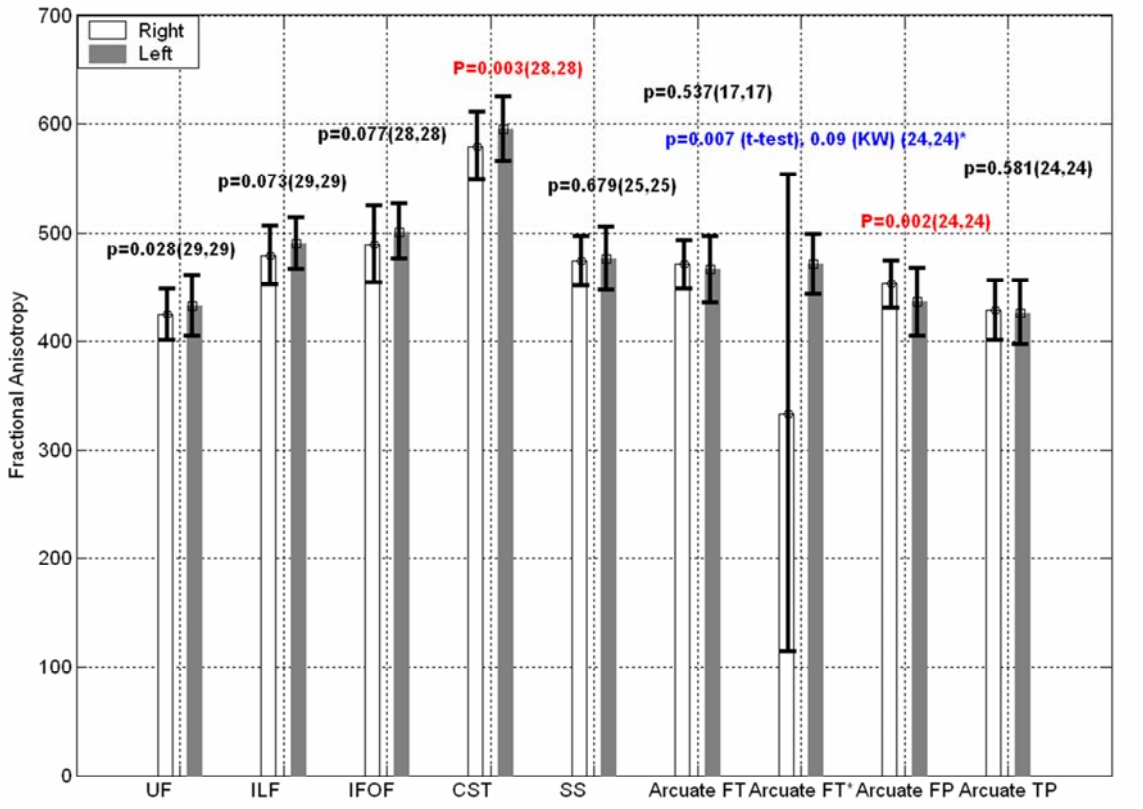

Figure 2. A bar plot of the group mean and standard error to illustrate the lateralization of FA (x 1000) in various white matter pathways studied. Note that the leftward asymmetry of the FT segment of the AF changes with subject inclusion. Seven of twenty-four participants (a total of 31 right-handed) did not have a demonstrable FT segment on the right side (i.e. the maximum asymmetry), excluding these subjects (Arcuate FT) resulted in no asymmetry, whereas including these subjects (Arcuate FT*) in the paired comparison resulted in a significant leftward asymmetry but high observed variability in the FA. A Kruskal-Wallis nonparametric test for paired comparisons performed also showed a trend towards higher FA in the left FT segment. In contrast to the FT segments of AF, the FP segments of AF showed a significant rightward asymmetry in the FA. The leftward asymmetry was also significant for UF and CST while in the ILF and IFOF it was a trend towards significance. The number of participants included in each fiber tract studied is given in brackets. The *p* values given were obtained from the paired t-test, for Arcuate FT*; the p value from the Kruskal-Wallis test (paired nonparametric test) is also reported.