A NEW FIBER BUNDLE PATHWAY IDENTIFIED WITH DIFFUSION MRI FIBER TRACTOGRAPHY: FACT OR FANTASY?

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Target audience: Researchers with an interest in diffusion MRI tractography and neuroanatomy.

Introduction: Diffusion-weighted (DW) MRI based fiber tractography (FT) is widely used for investigating microstructural properties of white matter (WM) fiber bundles (e.g., [1]) and for mapping structural connections of the human brain (e.g., [2]). Studying the architectural configuration of the brain's circuitry using this methodology [3-5], however, has sparked a spate of controversy among brain researchers, calling the validity of FT into question [6]. Despite being aware of the well-known pitfalls in analyzing DW MRI data [7] and several other limitations discussed in recent literature [8, 9], we present a description of fiber tract pathways in the orbitofrontal / prefrontal cortex, which – to the best of our knowledge – have not been documented before with DW MRI based tractography with this level of detail. To minimize the possibility that these findings are based on acquisition or processing artifacts, different data sets and processing pipelines have been used to show these fiber trajectories.

Methods: MRI data: Three different type of data sets were used (for detailed acquisition settings and preprocessing, see the corresponding references): *Data A:* A 60 diffusion directions data set with 2.4 mm isotropic voxel size and b = 3000 s/mm^2, which was used in [10] and resampled to 1 mm isotropic voxel size to increase the level of detail [11]; *Data B:* two DW MRI data sets from the Human Connectome Project (HCP), only the b=3000 s/mm^2 shells (90 diffusion directions) were used (isotropic voxel size of 1.25 mm) [12, 13]; and *Data C:* two DW MRI data sets acquired in a sample of the ALSPAC (Avon Longitudinal Study of Parents and Children) participants in the context of a research project entitled "Axon, Testosterone and Mental Health during Adolescence", funded by NIH (5R01MH085772) consisting of 60 diffusion gradients, b = 1200 s/mm^2, and 2.4 mm isotropic voxel size as described in [14]. Fiber tractography: Constrained spherical deconvolution [15] with the recursive calibration method (peak ratio threshold = 0.01) [16] was used to estimate the fiber orientation distribution (FOD) in each voxel (maximum harmonic degree L=8). The deterministic FT framework of [10] was used with parameter settings: FOD threshold = 0.1, angle deviation = 30 deg, step size = 1 mm. Multiple region-of-interest (ROI) "gates" were used for tract selection after performing whole-brain FT with uniform distribution of seed points defined at a 2 mm resolution.

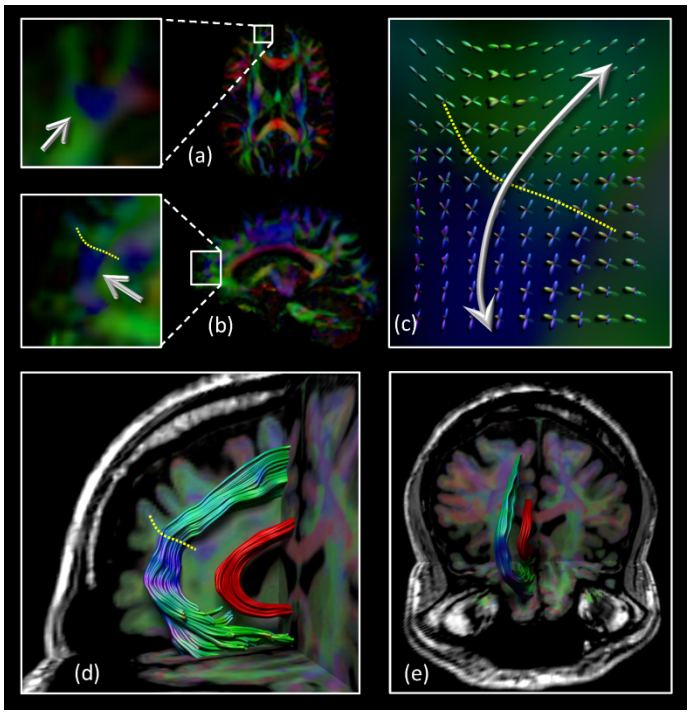

Fig. 1 Overview ROI definition (a-c) and medial (d) / sagittal (e) view of the fiber bundle configuration using "*Data A*" (the cingulum bundle is shown in red to provide anatomical reference).

Results: While the tract pathways were found bilaterally, we focus on only one hemisphere in this work. Fig. 1 shows for *"Data A"* the axial (a) and sagittal (b) view of the ROI (blue region indicated by the arrows) used for tract selection. The complex fiber architecture in this area can be appreciated from the FODs overlaid on the sagittal view in Fig. 1(c) with the dotted yellow line identifying the interface between regions with different dominant fiber populations ("blue" vs. "green" on the DTI based color map). A medial and frontal view of the tract pathway configuration is given in Fig. 1 (d) and (e), respectively (for anatomical reference, the frontal part of the cingulum bundle colored in red is also shown). Fig. 2 shows the fiber bundle trajectory in a sample of subjects from the HCP (*"Data B"*) and ALSPAC (*"Data C"*) cohorts.

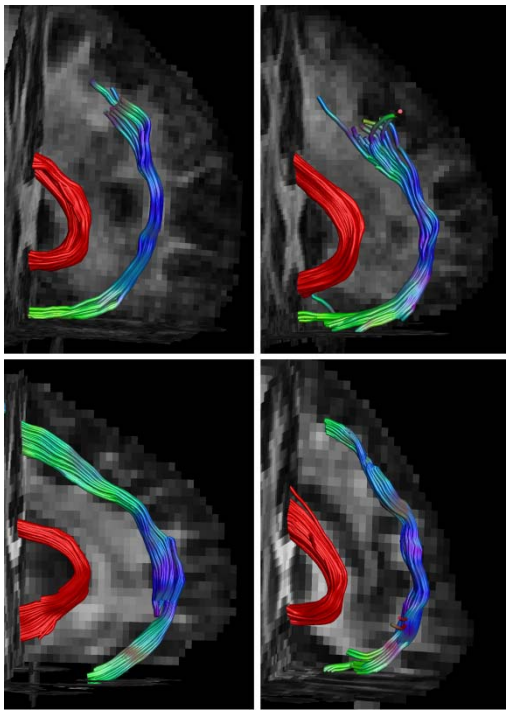

Fig. 2 Fiber tract configurations from the HCP (top) and ALSPAC (bottom) cohorts. Cingulum bundle is shown in red to provide anatomical reference. Left frontal view point.

Discussion and conclusion: Substantial progress in acquisition, processing, and analysis pushes forward the reliability of DW MRI and increases the inherently low accuracy of mapping WM pathways with FT. By taking advantage of state-of-the-art diffusion MRI methodology (e.g., [11, 16]), we have identified a part of an association pathway, most likely an extension of the anterior part of the superior longitudinal fasciculus (part I) given its superior and medial configuration, which has not been described before with DW MRI tractography (e.g., see previous work in [17-19]). Reproducibility across multiple subjects and different data cohorts and acquisition settings boosted our confidence that this finding is not based on artifacts.

References [1] Jones, DK *Diffusion MRI* 2011. [2] Catani, M et al, *Atlas of Human Brain Connections*. 2012. [3] Wedeen, VJ et al. Science, 2012. **335**(6076) [4]Catani, M et al, Science, 2012. **337**(6102) [5] Wedeen VJ et al., Science, 2012. **337**(6102) [6] Thomas, C et al., PNAS, 2014. [7] Jones, DK et al, NMR Biomed, 2010. **23**(7) [8] Jones, DK et al, Neuroimage, 2013. **73** [9] O'Donnell, LJ et al, Schizophr Res, 2014. [10] Jeurissen, B et al., Hum Brain Mapp, 2011. **32**(3) [11] Dyrby, TB et al., Neuroimage, 2014. **103C** [12] Van Essen, DC et al., Neuroimage, 2013. **80** [13] Sotiropoulos, SN et al., Neuroimage, 2013. **80** [14] Vos, SB et al., Neuroimage, 2011. **55**(4) [15] Tournier, JD et al, Neuroimage, 2007. **35**(4) [16] Tax, CM et al., Neuroimage, 2014. **86** [17] Makris, N et al., Cereb Cortex, 2005. **15**(6) [18] Thiebaut de Schotten, M et al., Nat Neurosci, 2011. **14**(10) [19] Catani, M et al., Cortex, 2012. **48**(2).