Comparison of probabilistic diffusion tensor tractography with histological tracer studies and RSFC in the rhesus macaque

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Introduction: Diffusion tensor imaging (DTI) may be used to estimate the local orientation of WM fiber bundles in the brain [1]. This directional information allows for noninvasive estimation and reconstruction of axonal pathways using tractography methods [2]. Probabilistic tractography generates a spatial distribution of estimated tract connections and associated confidence. Much of the extant knowledge about the structural connectivity of the primate brain has been revealed by careful examination of injected tracers, designed to travel along the axons of WM, in rhesus macaque monkeys. Because differences between DTI-based tractography measures in humans and injected tracer studies in monkeys can be attributed to both technique and species differences, it is important to study these differences within the same species. Therefore, we performed DTI tractography in a DTI template generated from a large sample of rhesus monkeys and compared the resulting tracts to published results performed using more invasive methods. In this study, we performed probabilistic tractography from regions in the precuneus, an area of the brain that is a major connectivity 'hub', and part of the default-mode network, and which appears to have distinct connections with different functional domains. The precuneus subregions were recently investigated using resting-state functional connectivity (RSFC) [3] and compared to tracer studies. Here we compare the results from probabilistic tractography from the precuneus with tracer and functional connectivity data.

Methods: A rhesus DTI template [4] was created from 271 individual DTI scans and the template was resampled to 0.5x0.5x0.5 resolution and registered with affine transformation to a GM rhesus atlas [5] using DTI-TK, an advanced DTI spatial normalization and atlas construction tool [6]. The atlas-based ROIs were used to identify brain regions for anatomical reference points. We attempted to replicate the injection sites from two tracer studies by cross-referencing anatomical references in the papers' illustrations with the atlas regions and the shapes of major sulci. Seed regions were drawn by hand and and probabilistic tractography was performed using the "PICo" algorithm in Camino [7] with probability density functions (PDF's) from the Bingham distribution, which allows elliptical probability density contours. Streamlines were generated with 2000 iterations at each voxel. A minimum FA value stopping criteria of only 0.05 was used, to allow the tracts to cross into GM if possible, but a curvature threshold was used to terminate streamlines if curvature between current and previous directions is greater than 80°. A visual comparison of these probability maps with both the original tracer study and the published RSFC results.

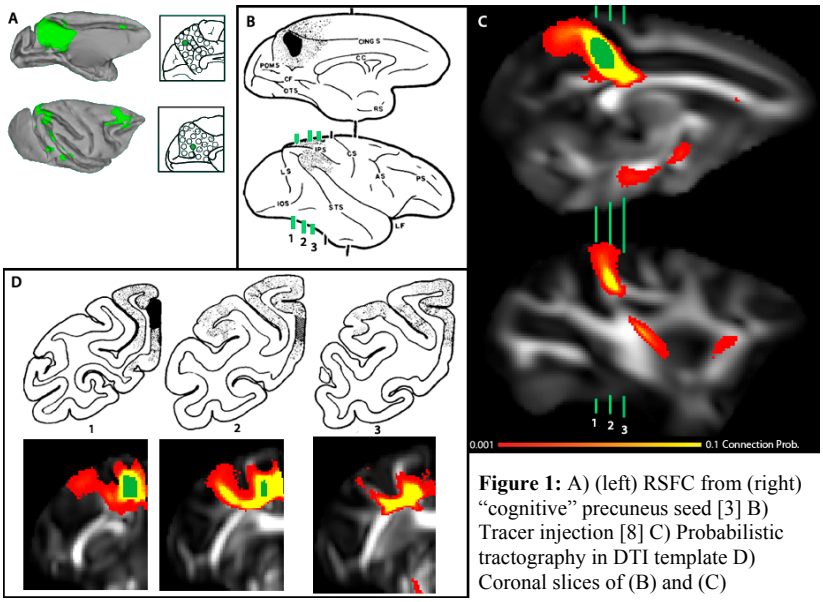

Figure 1: A) (left) RSFC from (right) "cognitive" precuneus seed [3] B) Tracer injection [8] C) Probabilistic tractography in DTI template D) Coronal slices of (B) and (C)

Results: Figure 1 shows connectivity from a precuneus seed region associated with cognitive/associative functions [3]. (A) shows the RSFC results (inset square colored circle shows which seed region these results correspond to), while the rest compare the original tracer paper [8] with our connection probability maps in visually matched sagittal (B,C) and coronal (D) slices. Probability maps show similar patterns to those made by labeled cells in the tracer paper, and additionally replicate parts of paths heading inferior and anterior to the seed region. Figure 2 shows connectivity from a region associated with the limbic system in RSFC (A), another tracer study [9] (B), and probabilistic tractography (C). The connection path running ventrally towards the temporal lobe was identified in all three methods. The lack of connections to the superior parts of the prefrontal cortex could be attributed to a less accurate recreation of the seed region, caused by lack of additional slices or sagittal views in the original tracer study's illustrations.

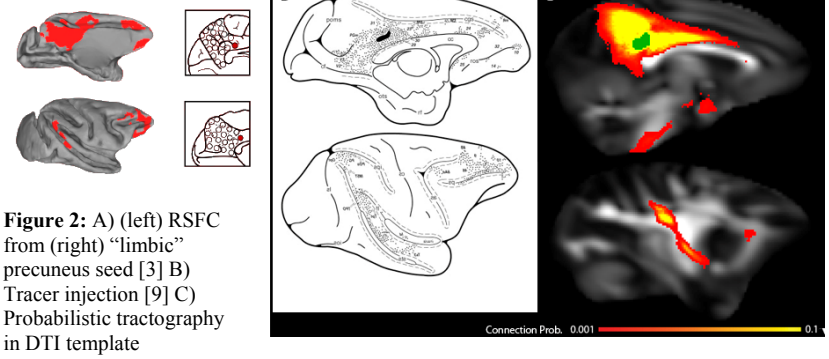

Figure 2: A) (left) RSFC from (right) "limbic" precuneus seed [3] B) Tracer injection [9] C) Probabilistic tractography in DTI template

Discussion: These results provide a qualitative visual comparison between probabilistic tractography on a 271-subject rhesus DTI template and reported tracer studies. While this type of analysis has its limitations, we believe it demonstrates a substantial degree of correspondence between DTI-based tractography and tracer studies. There could be several reasons why probabilistic connectivity cannot fully reconstruct tracer maps. For example, the diffusion tensor model cannot resolve crossing fibers, tractography errors increase with the length of the WM pathway, or the precision of ROI selection may be also limited. Injection sites in tracer studies are identified by reconstructed drawings and relative descriptions, and there is no cytoarchitectonic information available from the animals used in the template. This study is an important first step in evaluating tractography reconstructions and connectivity mapping from specific cortical areas. Despite the limitations of the techniques used, there is good qualitative correspondence between tractography and tracer studies, and future studies with higher-resolution images may provide a more accurate representation of WM connectivity in the primate brain.

References: [1] Basser et al. J Mag Res Ser B. 3;103(3):247-54, 1994. [2] Melhem et al. AJR 178(1):3-16, 2002. [3] Margulies et al. PNAS 106(47):20069-74, 2009. [4] Adluru et al. NeuroImage, 2011. [5] Zakszewski et al. MICCAI CDMRI 2011. [6] Zhang et al. Med Image Comput Comput Assist Interv. 8(Pt 1):172-9, 2005. [7] Cook et al.14th ISMRM 2759, 2006. [8] Pandya et al. J Comp Neurol 204:196–210, 1982. [9] Morecraft et al. 2004 J Comp Neurol 469:37–69 2004.