Computational White Matter Atlas for Young Rhesus Macaques

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Introduction: Diffusion Tensor Imaging (DTI) studies of non-human primates (NHP) are becoming increasingly common. Recently, many DTI analysis methodologies have been developed for human brain studies; however, few are directly applicable to NHP. The Rhesus Macaque (*Macaca mulatta*) is a commonly studied NHP species for which anatomical atlases exist, although they are based on post-mortem slices [1,2,3]. A T1-weighted atlas using 112 aging Rhesus was recently developed [4]. To the best of our knowledge, there are no DTI templates publicly available for young Rhesus Macaques. A prerequisite for most statistical analyses using DTI for localizing white matter (WM) differences across populations is to spatially normalize the individual scans to a representative template. In human studies, the accuracy of spatial normalization of white matter has been shown to improve with tensor-based image registration [8,13] and by using a population-specific DTI template that is, morphologically, most similar to the subjects in the population of interest. Here, we report the development of a population-specific DTI template for young adolescent Rhesus Macaque monkeys using 271 high-quality scans. NHP atlases that are based on a large number of animals capture more of the variability in the species from which they were drawn, and for this reason may be preferable to single-subject atlases. This DTI template will be made publicly available along with six major WM fiber bundles obtained using tractography. It is anticipated that these tools will help facilitate both voxel-based and tract specific WM analyses ([17,18]) in non-human primate species, which in turn may increase our understanding of brain function, development, and evolution.

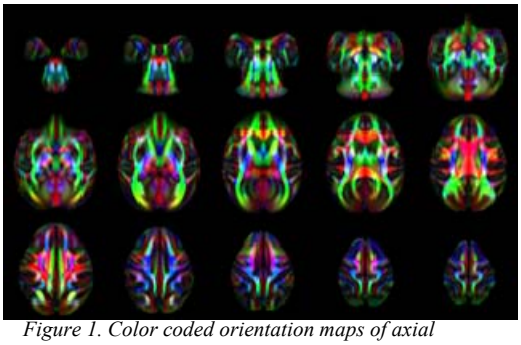

Figure 1. Color coded orientation maps of axial slices of the DTI template.

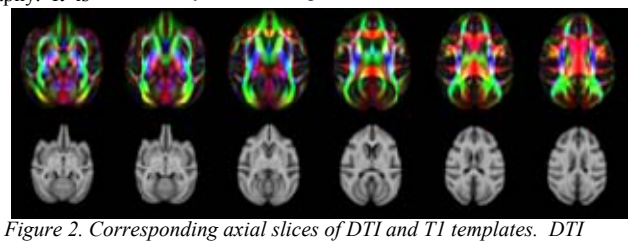

Figure 2. Corresponding axial slices of DTI and T1 templates. DTI shows more anatomical information about WM organization than T1.

Methods: 271 young rhesus macaques in the age-range of 1-3.5 years were scanned. Before undergoing MRI acquisition, the monkeys were anesthetized with an intramuscular injection of ketamine (15mg/kg). DT-MRI data were collected using a GE SIGNA 3T scanner with a 16cm diameter quadrature birdcage coil using an axial three-dimensional scan with the following parameters: repetition time: 10s; echo time: 77.2ms; field of view: 14cm; matrix: 128x128 (interpolated to 256x256 on the scanner); 2.5 mm thick slices; echo spacing: 800μs. Diffusion-weighted imaging (b=1000s/mm^2) was performed in 12 non-colinear directions with 1 non-diffusion weighted image and the acquisition was repeated 12 times and averaged. The DWI volumes were eddy-current corrected using the implementation in FSL [5]. Field inhomogeneity correction was performed using the method described in [6]. The brain tissue was carefully extracted for each subject using a rigorous semi-automatic setup described in [7]. The population-averaged DTI template was constructed from the DT-MRI images of all the 271 animals using DTI-TK (http://www.nitrc.org/projects/dtitk). "DTI-TK" is a non-parametric, diffeomorphic deformable image registration [8] that incrementally estimates its displacement field using a tensor-based registration formulation [9]. It is designed to take advantage of similarity measures comparing tensors as a whole via explicit optimization of tensor reorientation [9]. By computing image similarity on the basis of full tensor images, rather than scalar features, the algorithm incorporates local fiber orientations as features to drive the alignment of individual WM tracts. The initial average image is computed as a log-Euclidean mean [10] of the input DT images. The average is then iteratively refined by repeating the following procedure: (1) register the subject images to the current average, (2) compute a refined average for the next iteration as the mean of the normalized images. This procedure is repeated until the average image converges. The resulting template is unbiased towards any single subject and captures the average diffusion properties of the population at each voxel with a diffusion tensor. Subsequently, the template is "shape-corrected" to ensure that it also represents the average shape of the population, using the strategy proposed by [11]. This is achieved by first computing an average of the deformation fields that warp each subject into alignment with the template, then warping the template with the inverse of the average deformation field.

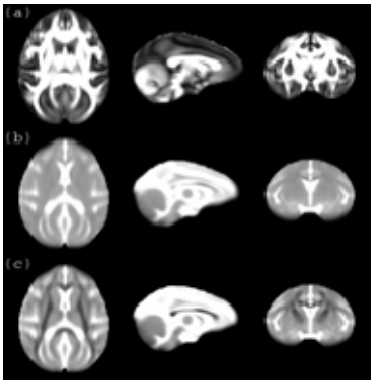

Figure 3. (a) FA, (b) MD, (c) RD of the template.

Results: Axial slices of the population-averaged DTI template using 271 subjects are shown in Fig. 1 as a RGB-encoded fiber orientation map. Fig. 2 shows slices of the T1 template ([4]) corresponding to the DTI template. One can see that DTI provides more anatomical information about the white matter than T1. Further, DTI allows computing various rotationally invariant measures such as fractional anisotropy (FA), mean diffusivity (MD), and radial diffusivity (RD) for population-based studies. Sample FA, MD, and RD slices from the average template are shown in Fig. 3. Fig. 4. shows six WM pathways identified using techniques described in [12].

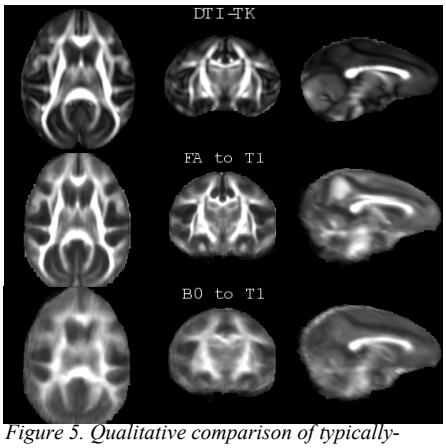

Figure 5. Qualitative comparison of typically-used T1-based methods to DTI-TK

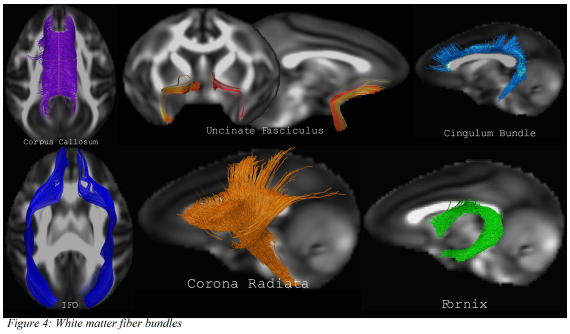

Figure 4: White matter fiber bundles

Discussion: The factors that contributed to the quality of our template are: (a) The large DTI sample from 271 monkeys, (b) High-dimensional spatial normalization using full-tensor information. As shown in studies on human and infantile data, using tensor-based registration can improve detection of WM differences [8,13]. Hence, DTI templates for human studies are becoming increasingly common [14,15,16]. This DTI template will significantly facilitate future DTI analyses with robust voxel-based and tract-specific analyses [17,18] in NHP. The current DTI template is in Paxinos [3] resolution i.e. 256x256x240,0.5mm^3. Fig. 5. shows our preliminary qualitative comparisons to the T1-based registration via mapping the diffusion data onto T1 space using two different intra-subject registration (FA-T1, B0-T1) methods. Visually it's evident that B0-T1 strategy is poor while FA-T1 gives reasonably sharp atlas but WM areas exhibit spurious high curvatures. More rigorous comparison to T1-based registration and establishing stereotaxic correspondence is part of our on-going work.

References: [1] Martin et al. NIMG 4:119-50,96 [2] Mikula et al. NIMG 35:9-15,07 [3] Paxinos et al. Acad Press,09 [4] McLaren et al, NIMG 45:52-9,09 [5] Smith et al. NIMG 23:208--19,00 [6] Jezzard et al. HBM 8:80-85,95 [7] Bartosic et al. HBM, 10 [8] Zhang et al. TMI 26: 1585–1597,07 [9] Zhang et al. MIA 10: 764-785,06 [10] Arsigny et al. MRM 56:411-21, 06 [11] Guimond et al. CVIU 77:192-210,00 [12] Catani et al. Cortex 44:1105-32,08 [13] Wang et al. CDMRI, 10 S et al. NIMG, 10 [17] Smith et al, NIMG 31:1487-1505,06 [18] Yushkevich et al, NIMG 41:448-61,08.