Derivation of Unbiased Anatomical and Diffusion MRI Templates of Primate Brains for Cross-Species Analysis

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Introduction: The reconstruction and analysis of the anatomical circuitry in the human brain via diffusion tractography has gained significant attention over the last few years [1]. As an extension to these studies, mapping the anatomical circuitry of our closest living relatives, the chimpanzee, as well as that of an extensively studied primate species, the rhesus macaque, has shown potential to provide insight into the unique evolutionary changes in the architecture of the human brain [2,3]. Such studies would greatly benefit from an unbiased and robust method for generating anatomical and diffusion templates across the three species. However, major obstacles exist in 1) defining a template space for a population of subjects to be spatially normalized that is not biased towards any single subject, 2) effectively aligning the low resolution diffusion data with the high resolution T1-weighted (T1w) anatomical data, and 3) appropriately compiling the aligned diffusion data of the primate population analyzed. In this work, we have developed methods that address each of these major obstacles, allowing for the reconstruction of the anatomical circuitry to be applied directly in the template space of all three species. Developed templates for each species are compared in structural morphology, major white matter tract reconstruction, and identified anatomical circuitry hubs.

Materials and Methods: In order to address the first obstacle, subject T1w images were nonlinearly co-registered to an intermediate template brain using four iterations at five decreasing levels of subsampling and blurring kernels. Affine and nonlinear registration was performed using the FLIRT and FNIRT tools in FSL, respectively. Average deformation warps were applied every iteration to reduce bias towards any single subject [4]. In regards to the second obstacle, a recently developed method for creating a psuedo-T1w image from diffusion measures, namely mCHARM, was applied with nonlinear registration to appropriately align the diffusion MRI data to the T1w anatomical images [5]. To address the third obstacle, all of the raw data now projected appropriately into the anatomical template space was concatenated into one large dataset and was directly used for generating diffusion tensor-derived measures and tractography. Diffusion b-vectors necessary for tensor derivation were rotated for each subject by appropriate affine transformation components of the nonlinear registration process. The b-vectors and b-values across all subjects were concatenated alongside the projected diffusion images. Tensor reconstruction and probabilistic tractography was run using the FDT toolbox in FSL, and deterministic tractography based on q-ball reconstruction for dODFs was performed using the TrackVis toolbox.

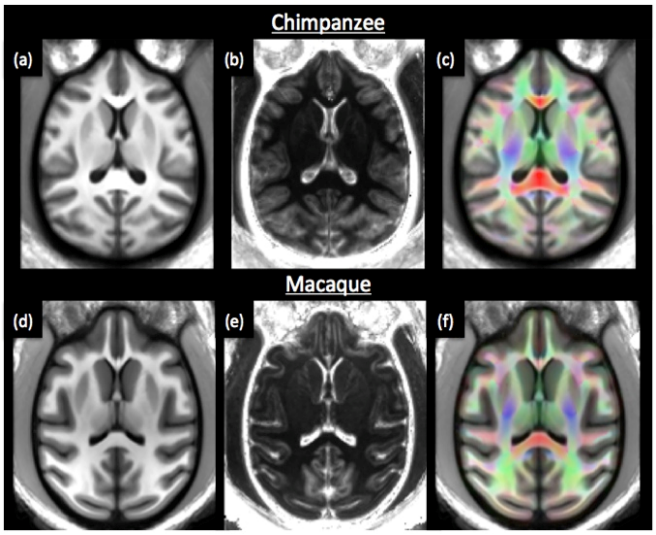

Figure 1. Axial slice of the final chimpanzee (top) and macaque (bottom) anatomical and diffusion templates. The T1w anatomical templates (a,d), coefficient of variance maps (b,e), and DTI templates (c,f) are shown. The DTI color-map indicating the primary orientation of the fibers in each voxel is shown overlaid onto the anatomical template (c,f). Red, blue, and green indicate right-left, superior-inferior, and anterior-posterior orientations, respectively.

Results and Discussion: Visual inspection indicates that the estimations of fractional anisotropy (FA), mean diffusivity (MD), as well as the primary diffusion direction (V1) of the diffusion tensors in the template space resemble those of the major white matter tracts in individual chimpanzee and macaque subjects. Furthermore, as shown in Figure 1, the FA as well as V1 color-maps overlaid onto the anatomical templates demonstrate that the subjects' diffusion data has spatially correct projections onto template space over the whole population. Recent tests have also demonstrated that most major white-matter tracts can be derived based on this population-compiled diffusion MR data, as shown in Figure 2. We also expect the partial volume effects alleviated when the up-sampled population-based diffusion MR data are used for deriving anatomical networks of the chimpanzee brain.

Conclusions: In this study, we present a method to generate unbiased population-based T1w anatomical and diffusion templates for the purpose of reconstructing chimpanzee and macaque anatomical brain networks. We expect such templates to have faithful anatomical correspondence with each other, as well as superior SNR for accurately estimating diffusion measures that are representative of the species, as compared to individual diffusion MR data. The availability of such templates will greatly facilitate our understanding of the similarities and differences between the chimpanzee, macaque, and human brain.

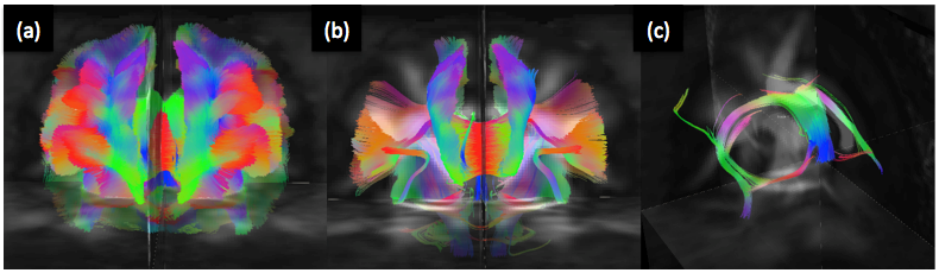

Figure 2. Deterministic tractography of the chimpanzee diffusion template, derived from concatenated population diffusion data, reconstructed using HARDI dODFs. Tracts from the whole brain (a), corpus callosum (b), and fornix (c) are shown, with coloring at each point along the fibers representing the relative orientation of the fiber at that point in space.

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