Comprehensive high-resolution macaque DTI atlas in in-vivo space

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Introduction

The neuroanatomical atlases play an essential role for brain-related research in multiple aspects, finding and identifying the unknown structures based on known ones, guiding the invasive operations, carrying the knowledge of brain structures for education and serving as registration references for mapping the functional information. Currently available macaque atlases based on histology, conventional T1 weighted MRI (e.g. 1,2) or chemical tracing (3) have played important roles as anatomical references. However, few of them are digital, comprehensive including anatomical information of cortical gyri, subcortical nuclei and white matter tracts, established in *in-vivo* space or have 3D presentations. An unsolved challenge of invasive neuroscientific experiment is to link the peripheral head landmarks to the targeted brain locations. In this study, we established a comprehensive high-resolution macaque DTI atlas in *in-vivo* space by integrating high resolution *ex-vivo* DTI data into *in-vivo* space. This high resolution DTI atlas provides rich anatomical information with comprehensive labeling. To better serve as anatomical guidance for the invasive operations, this atlas is uniquely characterized with both *ex-vivo* resolution and *in-vivo* space so that both anatomical details of brain and head landmarks are included. In addition, the digital labeling can be conveniently loaded by the users to interpret functional results.

Methods

Macaques: Ten young adult macaques (age: 5.3±2.8; body weight=5.7±2.3kg; 6 Male and 4 Female) were obtained from the macaque colony. All studies were done with great care to ensure the well-being of the monkeys. After *in-vivo* MRI/DTI, 4 macaque brains were fixed by perfusion fixation with 4% paraformaldehyde. *In-vivo acquisition of DTI and T1 weighted image:* A Philips 3T Achieva MR system was used. Anesthesia was maintained by either sodium pentobarbital (25mg/kg IV) or a mixture of ketamine (7mg/kg) and xylazine (0.5-2mg/kg). EPI SENSE was used for DTI with isotropic 1.5x1.5x1.5mm resolution and b value 1000s/mm^2. T1 weighted (MPRAGE) images at resolution of 0.75x0.75x0.75mm were also acquired. *Ex-vivo high resolution DTI acquisition:* 3D multiple spin echo diffusion tensor imaging was performed in 4.7T Bruker scanner. Multiple echo (number of echoes = 8) DTI sequence will be adopted to improve the SNR. The nominal resolution was 0.3x0.43x0.45 mm. *Establish high resolution DTI atlas in in-vivo space:* A median-sized macaque brain with both *in-vivo* and *ex-vivo* scanning was chosen for making the atlas. Shrinkage or distortion of the brain tissue caused by the fixation and confinement of the container during lengthy *ex-vivo* scanning was minimized by LDDMM elastic warping (4), as shown in Fig. 1. In this way, high resolution DTI data was transformed into *in-vivo* space. *Comprehensive gray and white matter labeling:* Cortical gyral parcellation was performed by painting 3D surface first and then transferring the surface labeling into volume labeling to label 2D cross-sectional slices. White matter was labeled with cross-section of fibers traced from DTI tractography in 2D plane.

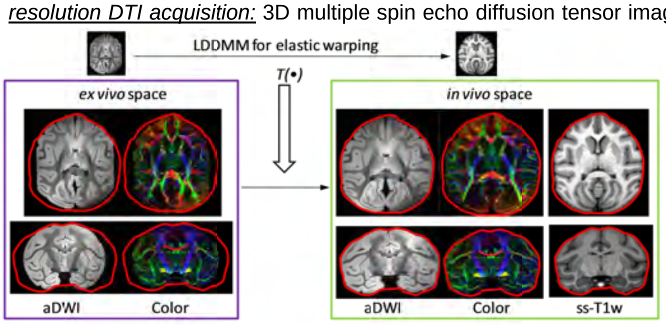
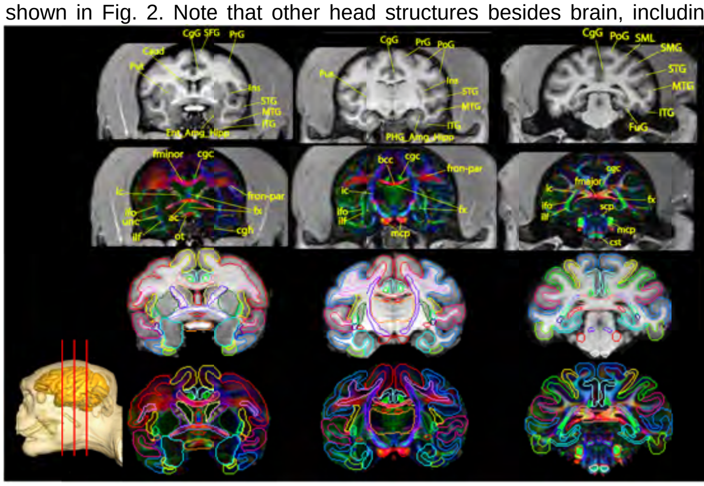


Fig. 1: Illustration of integrating the ultra high resolution *ex-vivo* macaque brain DTI data into the *in-vivo* space. The ultra high resolution DTI data in *ex-vivo* space (left) was elastically warped into *in-vivo* space (right) with LDDMM transformation T(•). The identical red contour, characterizing the brain tissue boundary of *in-vivo* space, was delineated from *in-vivo* T1 weighted images and overlaid on each image to demonstrate the warping effects. aDWI: averaged diffusion weighted image; ss-T1w: skull-stripped T1 weighted image.

Results

Digital macaque atlas in in-vivo space with comprehensive gray and white matter labeling: The comprehensive labeling of all major gray and white matter structures in axial, coronal and sagittal view was obtained. Due to limited space, only several snapshots of the labeling in coronal slices are shown in Fig. 2. Note that other head structures besides brain, including bony, facial and sinus structures, are included for anatomical guidance of invasive experiment. *Parcellation of cortical gyri:* Fig. 3 shows 3D views of parcellated cortical gyri represented by different colors.



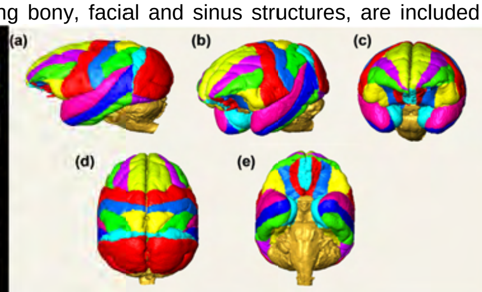


Fig. 2 (left): The comprehensive annotation and labeling of all cortical gyri, subcortical nuclei and white matter tracts on coronal T1 weighted images (first and third row) and orientation-encoded DTI colormaps (second and fourth row). All images are presented in *in-vivo* space after integration of *ex-vivo* DTI colormaps into the *in-vivo* space. The annotation of cortical gyri and subcortical nuclei are displayed on top of the T1 weighted images of the whole head (first row), while annotation of the white matter tracts are displayed on top of the DTI colormaps transferred into the *in-vivo* intracranial space (second row). Comprehensive labels of all structures are displayed on top of the skull-stripped T1 weighted images (third row) and orientation-encoded DTI colormaps (fourth row). The geometric locations of these coronal images are indicated by the red lines on top of a 3D reconstructed whole head with brain highlighted with solid yellow color. Labeling colors are consistent to the 3D reconstructions in Fig. 3.

Fig. 3 (right): The lateral (a), oblique (b), anterior (c), superior (d) and inferior (e) view of the parcellated cortical gyri of a macaque brain. Same colors were used for the identical gyrus in both left and right hemisphere.

Conclusion and discussion

By integrating the ultra high resolution *ex-vivo* DTI data and *in-vivo* T1 weighted images, we have constructed a comprehensive digital atlas in *in-vivo* space. For anatomical guidance of the invasive experiments, the facial and bony landmarks from the head were also included. This digital atlas is easy to be downloaded and can be readily applied to the design and data analysis for the neuroscientific experiments with macaque brains. It will be a complementary resource of the histology-based atlas. With inter-subject registration, we will establish probabilistic atlas with these data sets.

References: [1] Martin R and Bowden DM (1996) Neuroimage 4:119. [2] Saleem KS and Logothetis NK (2007) Elsevier. [3] Schmahmann JD and Pandya DN (2006) Oxford Univ. Press. [4] Miller, MI et al (2002) Annu Rev Biomed Eng 4: 375. **Acknowledgement:** This study is sponsored by NIH MH092535 and NIH EB009545.