Microstructural evolution of white matter from macaque to human brain with in vivo DTI

Hao Huang[1,2], Tina Jeon[1], Takashi Yoshioka[3], Virendra Mishra[1], Austin Chen[3], Steven Hsiao[3], Peter C van Zijl[4,5], and Susumu Mori[4,5]

[1]Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States, [2]Department of Radiology, University of Texas Southwestern Medical Center, Dallas, Texas, United States, [3]Mind and Brain Institute, Johns Hopkins University, Baltimore, Maryland, United States, [4]Department of Radiology, Johns Hopkins University, Baltimore, Maryland, United States, [5]F.M.Kirby Research Center, Kennedy Krieger Institute, Baltimore, Maryland, United States

Introduction

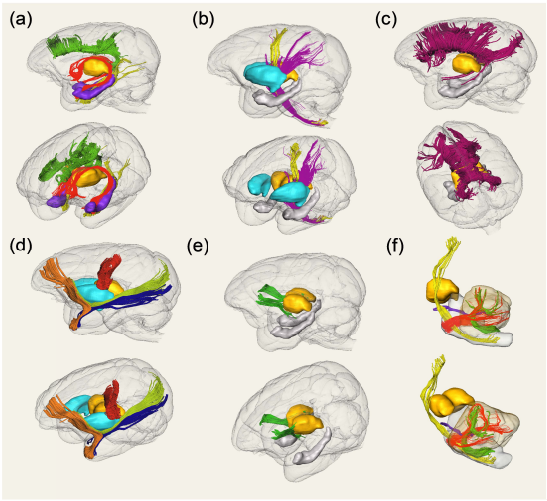
Comparisons of gray matter volumes with MRI have provided us insights on the anatomical evolution from non-human primates (*M. mulatta*) to humans (e.g. 1,2). However, quantified microstructural differences in white matter tracts between these two species have not been reported. Recent improvements in MR technology allow *in vivo* acquisition of high resolution diffusion tensor images (DTI) of macaque brains. High resolution DTI was acquired from 10 *in vivo* macaques and 15 normal young human adults. DTI-tractography was applied to delineate 14 common major tracts which could be consistently traced in both macaque and human brains. These tracts included anterior thalamic radiations (L and R), cingulum bundle in cingulate gyrus (L and R), cingulum to the hippocampus (L and R), cortico-spinal tract (L and R), inferior longitudinal fasciculus (L and R), uncinate fasciculus (L and R), forceps major and forceps minor of corpus callosum. Arcuate fasciculus related to language is unique to human and could not be traced in macaque brains. Fractional anisotropy (FA), mean diffusion (MD), axial (AxD) and radial diffusivity (RD) of these tracts were measured. These metrics characterizing the tract-level microstructures quantitatively were compared between macaque and human brain.

Methods

Macaques and human subjects: Ten young adult macaques (age: 5.3±2.8; body weight=5.7±2.3kg; 6M/4F) were obtained from the rhesus macaque colony. All studies were done with great care to ensure the well being of the monkeys and were approved by Institutional Animal Care and Use Committee. Fifteen healthy young adult (age: 20.5±3.6; 8M/7F) human subjects were also recruited. All subjects were free of current and past medical or neurological disorders. *DTI scanning and measurements of tract-level DTI metrics:* 3T Philips Achieva MR system with 8-channle head coil was used to acquire 1.5x1.5x1.5mm resolution *in vivo* macaque DTI and 2x2x2mm resolution *in vivo* human DTI. Three repetitions for macaque brain DTI and two repetitions for human brain DTI were used to increase SNR. Macaques were scanned under anesthesia. Commonly found white matter tracts including those of limbic, projection, commissural, association, thalamic and cerebellar system were traced with DTI tractography. Same FA and angle thresholds were used for tractography. The DTI metrics FA, MD, AxD and RD were calculated for these tracts with them as binary masks. *Statistical analysis:* Student t-tests were performed to compare the correspondent measurements of macaque and human brains. Bonferroni's correction was used.

Results

Limbic, projection, commissural, association, thalamic and cerebellar tracts of macaque brain: Similar to human white matter tracts (3,4), major white matter tracts of the macaque brain were classified into five functional categories: limbic (Fig. 1a), projection (Fig. 1b), commissural (Fig. 1c), association (Fig. 1d), thalamic (Fig. 1e) and cerebellar (Fig. 1f) tracts, as visualized in 3D in Fig. 1. Topology of corpus callosum of macaque brain (5) (Fig. 1c) is similar to that of human brain (6). Arcuate fasciculus, related to language and other functions unique to humans, could not be reliably traced in macaque brain. Successfully traced other association tracts, including uncinate fasciculus, inferior fronto-occipital fasciculus and inferior longitudinal fasciculus, appeared thinner and narrower in the macaque brain (Fig. 1d) compared to those of human brain (3). The connected cortical regions of these association tracts are also not as widely distributed as those in human brain. *Microstructural evolution of brain white matter from macaque to human brain:* Measurements of microstructural properties of common tracts from all 10 *in vivo* macaque brains and 15 human brains are plotted in Fig 2. Significant differences ($p<0.0036$) of FA and RD are found only with those tracts projecting to prefrontal, limbic and left motor cortical regions, namely left and right cingulum bundle in the cingulate gyrus (cgc-L/R), left and right cingulum projecting to hippocampus (cgh-L/R), left cortico-spinal tract (cst-L) and forcepts minor of corpus callosum (fminor). On the other hand, no statistically significant differences for MD or AxD measurements were found in any tract.



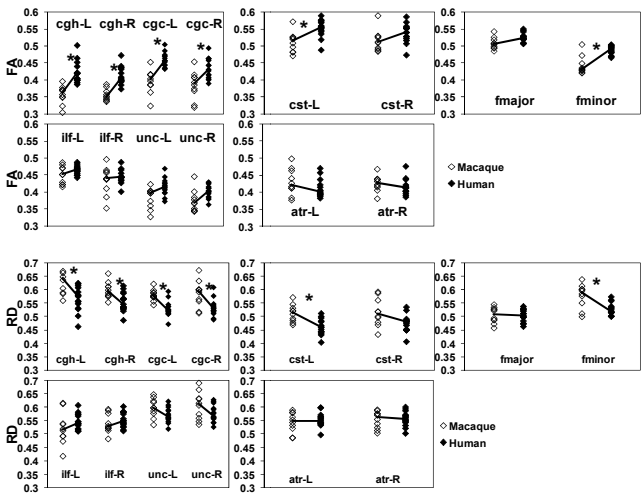


Fig. 1 (left): 3D visualization of limbic (a), projection (b), callosal (c), association (d), thalamic (e) and cerebellar (f) tracts. For anatomical guidance, thalamus (yellow), hippocampus (purple in a and gray in b, c and e) and putamen (cyan in b and d) are also displayed. The color of the tract is as follows. Green: cingulum in a, inferior fronto-occipital fasciculus in d and anterior thalamic tract in e; red: fornix in a, corpus callosum in c, fronto-parietal short tract in d and middle cerebellar peduncle in f; purple: cerebral peduncle; yellow: cortico-spinal tract; blue: inferior longitudinal fasciculus; orange: uncinate fasciculus.

Fig. 2 (right): FA (upper panel) and RD (lower panel) changes from macaque to human brain white matter for all commonly traced white matter tracts. RD is in the unit of $10^{-3}mm^2/s$. Abbreviations: cgh: cingulum projecting to hippocampus; cgc: cingulum bundle in cingulate gyrus; cst:cortico-spinal tract; fmajor/fminor: forceps major/minor; ilf: inferior longitudinal fasciculus; unc: uncinate fasciculus; atr: anterior thalamic radiation.

Conclusion and discussion

In conclusion, the microstructural evolution from macaque to human brain is not homogeneous over the entire brain white matter. Instead, it is characterized with selective enhancement of microstructure of white matter tracts projecting to prefrontal, limbic and left motor cortical areas. In addition, the significant decrease of RD from macaque to human in these white matter tracts and no significant changes of AxD in any tract suggest that one result of evolution from macaque to humans is increased myelination of prefrontal, limbic white matter and left cortico-spinal tract. More analysis is under way to minimize the partial volume effects on these measurements due to brain size difference of the two species.

References: [1] Riling (2006) Evol Anthropol 15: 65-77. [2] Schoenemann et al (2005) Nat Neurosci 8: 242-252. [3] Wakana et al (2004) Radiology 230: 77-87. [4] Mori et al (2005) Elsevier, Amsterdam. [5] Hofer et al (2008) Cereb Cortex 18: 1079-1084. [6] Huang et al (2005) Neuroimage 26: 195-205. Acknowledgements: This study is supported by NIH EB009545.