A Framework to Derive and Analyze Anatomical Brain Networks in Chimpanzees using Diffusion Tractography

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Introduction: Recently, mapping anatomical brain circuitry in humans via diffusion tractography and analyzing resultant brain networks using graph theory have gained significant attention, as such studies can reveal crucial information on brain functions (*1*). However, same effort has not been reported in chimpanzees. Chimpanzees are our closest living relatives, and mapping their brain connectivity may provide insight into the unique evolutionary changes of human brains. To map brain networks of chimpanzees and compare them with those of human beings, several key technical challenges must be overcome. In contrast to humans and macaques, studies of chimpanzees' brain are scarce and no digitally available parcellation scheme currently exists. Moreover, their brain size is only the third of that of humans. As a result, an unbiased parcellation of chimpanzee and human brains for an objective comparison is a challenge that must be solved. Here we tested multiple relatively high-resolution parcellation schemes (>500 cortical regions) on chimpanzees and studied the effect of nodal number on the cross-subject nodal correspondence and on the graph theoretic measures. This is the first step toward establishing a robust framework for deriving and comparing anatomical brain networks across three species (humans, chimpanzees and macaques) to try to understand the evolution of the human brain.

Methods: ***Subjects:*** Three chimpanzee subjects (Wenka, Cheeta, and Lulu: all females, age: 54, 54, 56 yrs) were used in this study. ***MRI acquisition:*** MRI was performed on a Siemens 3T Trio scanner (Siemens Medical System, Malvern, PA). High-resolution MPRAGE T1 scan protocol, optimized at 3T, used a repetition time/inversion time/echo time of 2600/900/3.06 msec, a flip angle of 8°, a volume of view of 205×205×154 mm, a matrix of 256×256×192, and a resolution of 0.8×0.8×0.8 mm, NEX=2. Diffusion MRI data were collected with following parameters: voxel resolution of 1.8×1.8×1.8 mm^3, 41 slices covering the whole brain, 60 diffusion weighted directions and a b value of 0, 1000 sec/mm^2, repetition time/echo time of 5900/86 msec, field of view of 130×230 mm^2, matrix size of 72×128, partial fourier option of 6/8, NEX=8, with phase reversal method to correct for susceptibility distortion (*2*). ***Parcellation Method:*** First, gray-matter/white-matter (GMWM) interface masks were generated based on partial volume images generated by the FAST function (www.fmrib.ox.ac.uk/fsl/). Initial seed points were then iteratively added to the interface mask such that the distance to the nearest node remained a static value, and the nodes were simultaneously grown taking into account the relative position and current size of all of their neighboring nodes. The generated parcellation mask was then dilated to aid in the mask transformation to each subject's diffusion space. Using FNIRT registration tools in FSL (fmrib.ox.ac.uk/fsl/) and empirically optimized parameters, the parcellation scheme was projected from the template space into the diffusion space of each subject. For quantitative evaluation of the nodal overlapping, the parcellation schemes with 500, 1000, and 2000 nodes from each subject's diffusion space were non-linearly registered onto one subject (Wenka), and then the distance between the centers of the gravity (cog) locations for each node across subjects were calculated. ***Diffusion Tractography and Graph Theory Measures:*** The high angular resolution diffusion imaging datasets were processed through a global tractography algorithm (*3*) to reconstruct the connections between each nodal pairs. The number of tracts were added and compiled into a 1000×1000 adjacency connectivity matrix using each projected parcellation scheme, and then analyzed using the Brain Connectivity Toolbox (*4*). Measures of nodal degree were computed and then mapped back to their corresponding nodes for visualization purpose.

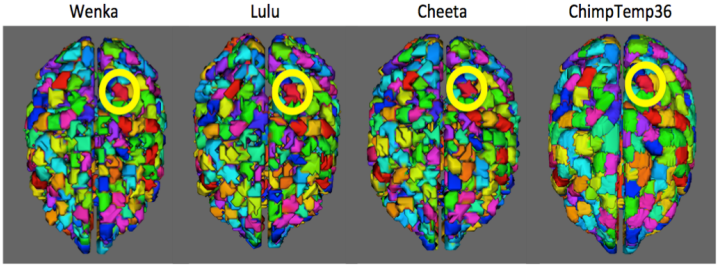

Figure 1. Parcellation schemes in the diffusion space of each chimpanzee subject and the original one derived on the chimpanzee T1-weighted template.

Results: The parcellation schemes with 1000 nodes number in each individual's diffusion space as well as in the template space are shown in Fig.1. It can be seen that with 1000 nodes, there is a good correspondence in terms of nodal location across subjects (yellow circle). The quantitative measure of the distances of the nodal cog between Lulu and Cheeta after registering to Wenka shows mean differences of 0.79, 0.83, and 0.94 voxels for parcellation schemes of 500, 1000, and 2000 nodes, respectively. If a spherical nodal shape is assumed, these values correspond to 19.8%, 26.3%, and 37.4% of the average nodal radii in each scheme. With regards to the degree maps for each subject, although there are observed differences in the location of high degree nodes, the pivotal nodes remain consistent across all subjects (Fig.2). It is also noteworthy that the topology of the degree map derived in our study resembles that derived in humans using the same nodal number (*5*), inferring a possibly conserved architecture of the brain networks between human and chimpanzee.

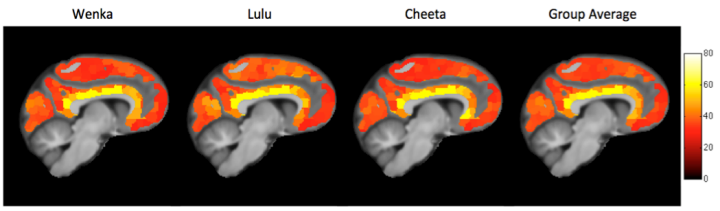

Figure 2. Comparison of nodal degree maps using 1000 nodes parcellation method for three subjects and the group mean.

Conclusions: We demonstrated an approach for generating a relatively high-resolution parcellation of the cerebral cortex that is independent of existing parcellation scheme for cross-species comparisons. Our results indicate that with nodal number up to 1000, there is still a good correspondence of node locations across subjects. This effort on carefully examining the effects of nodal and edge selections on the characteristics of brain networks is a prerequisite of a robust mapping of brain connectivity for cross-species comparisons.

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References: 1**.** P. Hagmann *et al.*, *PLoS Biol* **6**, e159 (Jul 1, 2008), 2. J. L. Andersson, S. Skare, J. Ashburner, *Neuroimage* **20**, 870 (Oct, 2003), 3. M. Reisert *et al.*, *Neuroimage* **54**, 955 (Jan 15, 2011), 4. O. Sporns, G. Tononi, R. Kotter, *PLoS Comput Biol* **1**, e42 (Sep, 2005), A. Zalesky *et al.*, *Neuroimage* **50**, 970 (Apr 15, 2010).