

# Anatomical Cortico-Cortical Networks of the Human Brain Based on Diffusion Probabilistic Tractography

R. Huang<sup>1</sup>, N. J. Shah<sup>1,2</sup>, L. Hoemke<sup>1</sup>, O. Posnansky<sup>1</sup>, K. Zilles<sup>1,3</sup>, and K. Amunts<sup>1,4</sup>

<sup>1</sup>Institute of Neuroscience and Biophysics - Medicine, Research Centre Juelich, Juelich, Germany, <sup>2</sup>Department of Neurology, RWTH Aachen University, Aachen, Germany, <sup>3</sup>C. and O. Vogt Institute for Brain Research, Heinrich-Heine-University of Duesseldorf, Duesseldorf, Germany, <sup>4</sup>Department of Psychiatry and Psychotherapy, RWTH Aachen University, Aachen, Germany

**Introduction:** The cerebral cortex consists of many structurally distinct areas. All cortical areas are interconnected through fibre tracts of the white matters, i.e., each cortical area receives projections from and sends projections to other cortical areas [1] [2] [3]. Such structural organisation can be modelled [4] [5] in a way that BAs are represented by a series of vertices, their connections by lines, and the lines are weighted by the strengths of the interareal connection. Vertices and lines then constitute the human anatomical cortico-cortical connectivity (CCC) network. The cortical network offers a quantitative description of cortical connectivity, which is still largely missing in the human brain [6]. It may also represent a link to studies employing tracers and electrophysiological methods of nonhuman primates as well as mathematical models of primate brain connectivity [1] [2], and, therefore, overcome the often problematic extrapolations from primate to human brain connectivity. The understanding of networks may contribute to our knowledge about how information is processed, disseminated and integrated among multiple specialised cortical areas. Here we attempt to propose a method for building the human anatomical CCC-matrix and investigate the topological properties of the cortical networks using graphical theory [7].

**Methods:** This study was carried out in 14 right-handed healthy males (mean age  $31 \pm 7$  years). Written, informed consent was obtained from all subjects. MR data were acquired using a Siemens Tim-Trio 3T scanner with a 12-channel head coil. DWI data were acquired using a twice-refocused, spin-echo diffusion-weighted EPI sequence (60 volumes with  $b = 800\text{s/mm}^2$  and 7 volumes with  $b = 0$ , voxel-size =  $(1.8\text{mm})^3$ ,  $TE = 88\text{ms}$ , 75 transverse slices). DWI scan was repeated four times. 3D anatomical images were obtained using a T1-weighted MP-RAGE sequence. A brain mask, extracted from the averaged  $b = 0$  volume, was taken as diffusion space and the 3D anatomical images as structural space.

Data analysis was carried out using FSL. Transformation matrices were calculated between diffusion, structural and MNI-152 standard space using FLIRT. BAs were defined using the template of a flattened Brodmann map which contains 41 discrete volume masks (= regions-of-interest, ROI), most of them representing one, but some also representing several BAs. An example of the latter was IPI – the insular and periinsular cortex [8]. Each BA was registered into every individual structural and diffusion space.

Using FDT [9], we performed fibre tracking for all possible pairs of BAs for each subject in diffusion space. Fig. 1 illustrates the steps for constructing the cortical networks: (a) calculating the fibre projection  $d_{\alpha\beta}$ 's from  $\alpha$ -to- $\beta$  BAs, (b) computing the target-based fibre density from  $\alpha$ -to- $\beta$  BA as  $C_{\alpha\beta} = d_{\alpha\beta} / V_{\beta}$ , (c) constructing the atlas-based ICC connectivity matrix,  $C$ , (d) generating the symmetric matrix,  $S$ , and antisymmetric matrix,  $A$ , for each subject and grading matrix elements. Each element of the symmetric matrix was scaled from 5 to 0 indicating the decrease of the strength of ICC connection and each element of the antisymmetric matrix was scaled from 3 to 0 indicating the difference of fibre densities. The group network was constructed by averaging the raw cortical networks from all individuals.

**Results:** (1) *Connectivity-based cortical subdivisions:* We applied an unsupervised learning network approach, a modified  $k$ -nearest neighbour algorithm [10], onto each individual anatomical symmetric CCC-matrix. The re-ordered correlation matrix thus obtained shows clustering structures. After mapping the

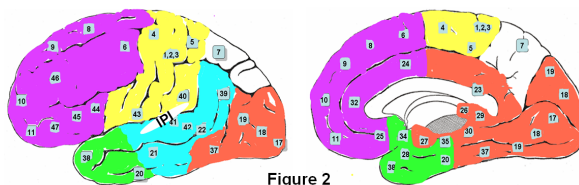
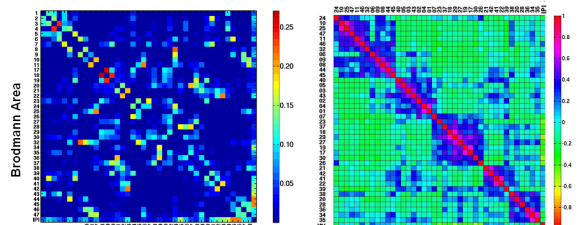
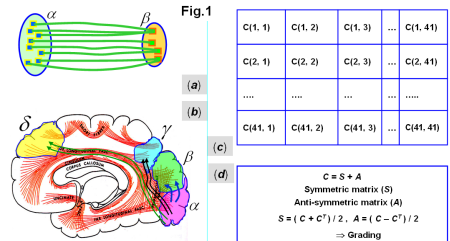


Figure 2

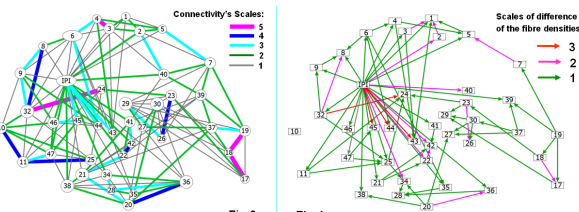


Fig.3

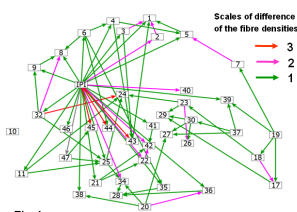


Fig.4

schemes. An alternative strategy is to define the ROIs according to the cytoarchitectonic probabilistic map [13]. A challenge for further research is to explain how the cortical connectivity pattern mediates the behaviour: can the cortical areas be classified as 'relay areas', 'giver areas' or 'taker areas'?

- References:** [1] Felleman DJ, Essen DC, Cereb Cortex 1(1991)1. [2] Young MP, Nature 358 (1992) 152. [3] Zilles K, et al, EU Neuropsychopharmacology 12(2002)587. [4] Hagmann, et al., PLoS Bio 6(2008)e159. [5] He Y et al., J Neurosci 28 (2008) 4756. [6] Pandya DN, Yeterian EH, (1986). [7] Barabasi AL, Oltvai ZN, NRG 5(2004)101. [8] Drury HA, et al., J Cogn Neurosci 8(1996)1. [9] Behrens TE, et al., Nat Neurosci 6(2003)750. [10] Friendly M, The American Statistician 56(2002)316. [11] Essen DCV, Drury HA, Nature 385(1997) 313. [12] Yacoub E, et al., PNAS 105(2008) 10607. [13] Amunts K, Schleicher A, Zilles K, NeuroImage 37 (2007) 1061.