Constructing structural connectivity in rat brain based on inter-regional gray matter volume covariations

Ziyu Cao[1], Liqin Yang[1], Xuxia Wang[1], Fuchun Lin[1], and Hao Lei[1]

[1]*State Key Laboratory of Magnetic Resonance and Atomic and Molecular Physics, Wuhan Institute of Physics and Mathematics, Chinese Academy of Sciences, Wuhan, Hubei, China*

Introduction Network analysis has been used to understand structural/functional connectivity of human brain [1] and functional connectivity of rodent brain [2,3]. Structural connectivity for rodent brain has not been reported. It has been demonstrated in human studies that cross-subject variability of brain morphometric features, such as gray matter (GM) density and cortical thickness, can potentially be utilized to construct structural connectivity of the brain [4,5]. In this study, we acquired high resolution anatomical images from 152 adult Sprague-Dawley rats, and used cross-subject inter-regional covariation in GM volume to construct structural connectivity in rat brain. The network properties, such as small-worldness and community structures, were analyzed.

Materials and methods One hundred and fifty two male Sprague-Dawley rats, weighing 200-300 g, were imaged on a Bruker Biospec 7.0 T/20 cm scanner under 1.5-2.0% isoflurane anesthesia using a volume coil as transmitter, and a 4-channel phase-array surface coil for reception. For each rat, 52 contiguous coronal T_2-weighted images were acquired by a RARE pulse sequence, with RARE factor 4, TR 5800 ms, TE_{eff} 40 ms, FOV 35 mm×35 mm, matrix size 512×384, slice thickness 0.58 mm and 8 averages. SPM8 was used for image segmentation and co-registration. The image data from each animal were first segmented into GM, white matter (WM) and cerebrospinal fluid matter (CSF) probability maps, using a set of 68 μm×68 μm×68 μm GM/WM/CSF templates built in-house. The GM and WM probability maps of all animals were then entered into the DARTEL algorithm to obtain co-registered unmodulated/modulated GM/WM maps, followed by smoothing with a 0.2-mm FWHM Gaussian kernel and dimension reduction in the slice direction to a slice thickness of 340 μm. Group-average unmodulated GM and WM maps were calculated, from which binary masks of GM and WM were generated using a threshold of GM/WM probability>0.4. The masks were then applied to the individual modulated data to produce a GM+WM volume map for each rat. The GM+WM volume maps from all animals were then entered into group ICA, which was carried out using the Infomax algorithm within the GIFT software (http://icatb.sourceforge.net/). The number of independent components was estimated automatically to be 29. By inspection, 9 components were considered artifacts and discarded. The remaining 20 components were z-thresholded. The partial correlation coefficient between each pair of the 20 components was calculated, yielding a 20×20 partial correlation matrix, which was binarized with a threshold of $p<0.01$. The small-worldness properties and modularity were calculated.

Results The binarized partial correlation matrix is shown in Fig. 1. The small-worldness coefficient (σ) for this network was found to be 1.42, with global clustering coefficient γ=1.42, mean shortest path length λ=0.99. Modularity analysis yielded 6 communities, among which 5 are shown in Fig. 2a-e, respectively. The combination of the 5 communities is shown in Fig. 1f. Community (a) included mainly the basal ganglia; community (b) included mainly white matter and hippocampus; community (c) included mainly visual, motor and somatosensory cortex; community (d) included mainly temporal association cortex and ectorhinal cortex; community (e) included mainly amygdala. The combination of the five communities is shown in Fig. 2f.

Discussion We used cross-subject inter-regional covariation in GM volume to construct structural connectivity in rat brain. It was shown that the structural connectivity constructed using the anatomical measures exhibits certain degree of small-worldness and community structures that are comparable to that have been reported for functional connectivity in rat brain [2].

Acknowledgements Supported by grants from Natural Science Foundation of China (30870674 and 20921004) and Chinese Ministry of Science and Technology (2011CB707800).

References [1] Bullmore et al, Nat Rev Neurosci, 10:186-198, 2009. [2] Liang et al, J Neurosci, 31:3776-3783, 2011. [3] Lu et al., Proc Natl Acad Sci USA, 109:3979-3984, 2012. [4] Bassett et al., J Neurosci, 28: 9239-9248, 2008. [5] He et al., Cereb Cortex, 17:2407-2419, 2007.

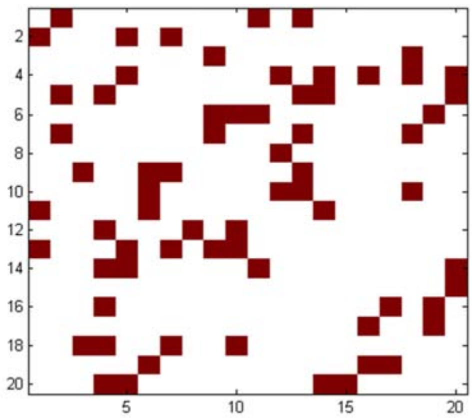

Figure 1. The binarized partial correlation matrix. Red squares indicate significantly correlated component pairs.

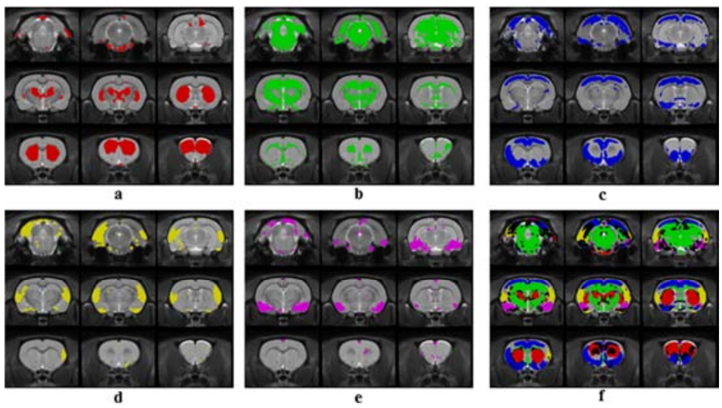

Figure 2. Community structure of the structural network of rat brain. Five out of the six communities derived from modularity analysis are shown in a-e. The combination of the 5 communities is shown in f. The black color indicate overlap among different communities.