Graph Analyses of the Network Connectivity Changes during Propofol-Induced Sedation and Unconsciousness

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Introduction: Understanding how brain function is affected by anesthetics will help both anesthesiologists and neuroscientists reveal the underlying cognitive processes for consciousness and sleep. Anesthetic effects on the resting-state brain connectivity between regions of interest (ROIs) could be evaluated using graph theory[1], but parcellation of ROIs might be among the critical factors that account for the diversity in the previously observed results[2]. Functional MR image voxels can be grouped into brain ROIs based on the resting-state connectivity coherence[3, 4]. In this study we evaluated the anesthetic effects of propofol on the connectivity between ROIs parcellated based on the similarity of resting-state time courses[4].

Methods: Resting-state fMRI data were acquired on a Siemens 3T whole-body scanner TIM Trio (Siemens Medical Systems, Erlangen, Germany) with a 12-channel phased-array head coil. 33 healthy (19-35 yrs, ASA I) subjects were recruited. During the conditions without and with 0.02μm/ml plasma-level propofol-infusion, two functional BOLD runs of 210 volumes each were acquired with TR = 2 s, TE = 30 ms, FOV = 256×256mm^2, flip angle = 90°, matrix size 64×64, each volume 33 AC-PC aligned slices, 4mm thick with no gap. The first 10 volumes were discarded from each of the BOLD runs, which were then slice-time and motion corrected using SPM5. The BOLD time courses were low-pass filtered with a 4th degree elliptical filter (cut-off frequency: 0.08 Hz) and the 6 motion parameters, the mean signals of white matter and CSF, and linear and quadratic drifts were regressed out from the data[5]. For each subject, two BOLD runs were then concatenated for the anesthesia-free or propofol-infusion condition; the mean time course of all voxels within each of the 278 ROIs was used in cross correlation between ROIs[4]. The resulting 278×278 coefficient maps were used in the group analyses to test the changes in connectivity between ROIs induced by propofol.

Results and Discussion: A 3-view graph showing significant network connectivity changes ($p<0.01$) by propofol is plotted against the 3-view MNI brain template in Figure 1. Nodes (mass centers of ROIs) with degrees (# of connections) ≥ 3 are listed in Tables 1 & 2. Our results: 1) increases were primarily found in the parietal lobe, with the posterior cingulate (R.BA23) serving as a hub center, while decreases occurred largely in the frontal lobe, most associating with the middle pre-frontal gyrus (R.BA 10); 2) no node with both positive and negative changes in connectivity with other nodes was found; 3) overall increases induced by propofol are greater in magnitude than decreases; 4) propofol appeared to have preferential effects on the right side of the brain. Our network analyses show the most affected areas include those overlapping with the DMN[6], e.g., the PCC for increases, and medial PFC for decreases. Neuronal activity increases in the PCC have been found to be closely related to sleeping and unconscious states[7,8]. Our result reveals that, in addition to local increases, e.g., CBF in the PCC[9], the connectivity between the PCC and multiple parietal areas was enhanced during propofol anesthesia. Increases in the DMN activity have also been found as a strong indicator of brain's integrity[10], so the increase within the DMN observed in this study might indicate the brain's integrity is not compromised during propofol anesthesia. The frontal lobe has been long thought to be associated with high order cognitive functions of the brain, such as reward, attention, working memory, planning and motivation, thus the diminishing of these high-order cognitive functions might be accounted for by the reduced connectivity between the frontal lobe and other brain areas.

Table 1 Regions with increased connectivity during propofol anesthesia (#degrees>=3):

ROI[4]	Deg.	Tal-x	Tal-y	Tal-z	ROI_Descriptions		Talairach-Daemon[11]	Parcellation[4]
48	11	13	-54	15	*R CBR*	*Limbic*	*Posterior Cing*	*R.BA23.4*
11	4	6	-12	6	*R CBR*	*Sub-lobar*	*Thal.MedialDorsalNuc*	*R.BA50.1*
29	4	25	-45	60	*R CBR*	*Parietal*	*Sup Parietal L BA 7*	*R.BA7.6*
135	3	7	-38	36	*R CBR*	*Limbic*	*Cing G*	*R.BA23.2*

Table 2 Regions with decreased connectivity during propofol anesthesia: (#degrees>=3):

ROI[4]	Deg.	Tal-x	Tal-y	Tal-z	ROI_Descriptions		Talairach-Daemon[11]	Parcellation[4]
129	8	44	44	-3	*R CBR*	*Frontal*	*Mid Frontal G*	*R.BA10.6*
78	4	44	25	-12	*R CBR*	*Frontal*	*Inf Frontal G*	*R.BA47.3*
179	4	-43	41	-6	*L CBR*	*Frontal*	*Mid Frontal G*	*L.BA47.1*
37	3	14	61	0	*R CBR*	*Frontal*	*Medial Frontal G BA10*	*R.BA10.2*
64	3	18	10	59	*R CBR*	*Frontal*	*Mid Frontal G*	*R.BA6.3*
274	3	-11	56	-14	*L CBR*	*Frontal*	*Sup Frontal G*	*L.BA10.5*

Conclusion: Network analyses based on graph theory have been performed to evaluate the effects of propofol anesthesia in the normal human brain on the parcellation based on the resting-state connectivity consistency. We found that one network with increases in connectivity is located in the parietal lobe and the other with decreases primarily located in the frontal, indicatating the differential network effects of propofol on the brain.

References: 1 Guldenmund et al. Brain Conn 2013; 3(3):273. 2 Nallasamy et al. The Neuroscientists 2011; 17(1):94. 3 Nelson et al. Neuron 2010; 67(1):156. 4 Shen et al. Neuroimage 2013; 82:403. 5 Martuzzi et al. Neuroimage 2011; 58(4):1044. 6 Raichle et al. Neuroimage 2007;37(4):1083. 7 Blumenfeld. Progress in brain research 2005;150:271-286. 8 Laureys et al. Current opinion in neurology 2005;18(6):726-733. 9 Qiu et al. ISMRM 2012; Abs#2152. 10 Grecius et al. PNAS 2004; 101(13):4637. 11 http://www.talairach.org/daemon.html

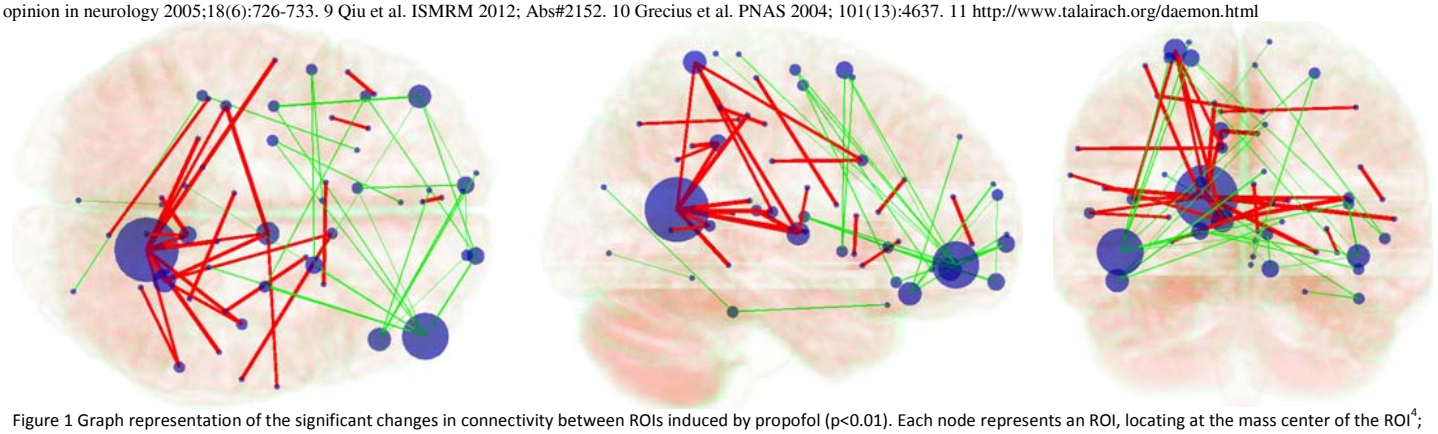

Figure 1 Graph representation of the significant changes in connectivity between ROIs induced by propofol ($p<0.01$). Each node represents an ROI, locating at the mass center of the ROI[4]; the size of the sphere is proportional to the degree, or the number of connections; the thickness of a line connecting 2 nodes represents the magnitude of the increase (red), or decrease (green). Scale: node degree 1- 11; magnitude of connection 0.1-0.25.