Different topological organization of human brain functional networks with eyes open versus eyes closed

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ABSTRACT

Opening and closing the eyes are fundamental behaviors for directing attention to the external versus internal world. However, it remains unclear whether the states of eyes-open (EO) relative to eyes-closed (EC) are associated with different topological organizations of functional neural networks for exteroceptive and interoceptive processing (processing the external world and internal state, respectively). Here, we used resting-state functional magnetic resonance imaging and neural network analysis to investigate the topological properties of functional networks of the human brain when the eyes were open versus closed. The brain networks exhibited higher cliquishness and local efficiency, but lower global efficiency during the EO state compared to the EC state. These properties suggest an increase in specialized information processing along with a decrease in integrated information processing in EO (vs. EC). More importantly, the "exteroceptive" network, including the attentional system (e.g., superior parietal gyrus and inferior parietal lobule), ocular motor system (e.g., precentral gyrus and superior frontal gyrus), and arousal system (e.g., insula and thalamus), showed higher regional nodal properties (nodal degree, efficiency and betweenness centrality) in EO relative to EC. In contrast, the "interoceptive" network, composed of visual system (e.g., lingual gyrus, fusiform gyrus and cuneus), auditory system (e.g., Heschl's gyurs), somatosensory system (e.g., postcentral gyrus), and part of the default mode network (e.g., angular gyrus and anterior cingulate gyrus), showed significantly higher regional properties in EC vs. EO. In addition, the connections across sensory modalities were altered by volitional eye opening. The synchronicity between the visual system and the motor, somatosensory and auditory systems, characteristic of EC, was attenuated in EO. Further, the connections between the visual system and the attention, arousal and subcortical systems were increased in EO. These results may indicate that EO leads to a suppression of sensory modalities (other than visual) to allocate resources to exteroceptive processing. Our findings suggest that the topological organization of human brain networks dynamically switches corresponding to the information processing modes as we open or close our eyes.

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Introduction

While vision has featured centrally in prominent scientific theories of consciousness (Crick and Koch, 2003), we spend a considerable portion of our lives with our eyes closed, thereby attenuating the potential contributions of vision. Interestingly, a recent study suggested that momentary closing of the eyes (blinking) not only occurs more often than would be necessary for ocular lubrication, but that these blinks are

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associated with subtle shifts in neural activity (Nakano et al., 2013). While awake, awareness shifts based on whether our eyes are open or closed; awareness has been described as "exteroceptive" when the eyes are open (EO) and "interoceptive" when the eyes are closed (EC). These states correspond to focus on the "outside" versus the "inside", respectively, and each has different psychophysiological characteristics and underlying brain mechanisms (Marx et al., 2003).

Compared to EC, an increased attentional load and raised level of arousal is present in EO (Hufner et al., 2009). The differences attributable to these states may have more to do with the simple processing of visual information; even in the darkness, where little to no visual input is present, these two states reveal distinct neural activation patterns (Hufner et al., 2009). Attentional and oculomotor systems (e.g., superior parietal gyrus and frontal eye fields) show activation in EO, while sensory systems (e.g., visual, auditory, and somatosensory) show activation in EC (Bianciardi et al., 2009; Hufner et al., 2008, 2009; Marx et al., 2003, 2004; McAvoy et al., 2008; Niven and Laughlin, 2008). These findings suggest two different states of mental activity: an "exteroceptive" state characterized by overt attention and ocular motor activity (during EO) and an "interoceptive" state characterized by imagination and multisensory activity (during EC) (Hufner et al., 2009; Marx et al., 2004). The corresponding differences of spontaneous neural activity between these two states have been characterized in previous resting-state functional magnetic resonance imaging (R-fMRI) studies (Bianciardi et al., 2009; McAvoy et al., 2008; Yan et al., 2009; Yang et al., 2007; Zou et al., 2009).

More recently, an R-fMRI study, by manipulating both eyes open/closed and lights on/off, found that there were significant differences between EO and EC in both spontaneous brain activity and functional connectivity but no differences in whole brain topological organization other than connection distance (i.e., the Euclidean distance between each pair of regional nodes) (Jao et al., 2013). Given that the topological properties of human brain networks have shown correlations with various cognitive functions and pathologies (Bullmore and Sporns, 2009; He and Evans, 2010), it is curious that there were widespread influences of EO and EC on the spontaneous activity and connectivity but not on the topological organization of the networks (Jao et al., 2013).

Given that there are critical influence of different acquisition parameters and analytic strategies in R-fMRI data but lacking consensus about the best way to deal with it (Murphy et al., 2009; Wang et al., 2009; Wig et al., 2011; Zuo et al., 2013), we acquired human R-fMRI data and constructed whole brain functional networks with different brain parcellation templates and presence/absence of global signal regression (GSR) to compare topological parameters (e.g., small-world, network efficiency and nodal efficiency) of brain networks between the EO and EC states. We hypothesized that the "exteroceptive" state and the "interoceptive" state were associated with different topological organizations of brain networks corresponding to different information processing modes. Specifically, we predicted that there would be an "exteroceptive" network, characterized by attention and ocular motor system during EO, and an "interoceptive" network characterized by imagination and multisensory system during EC.

Materials and methods

Subjects

Twenty-three right-handed healthy volunteers (11 females; mean age $\pm$ SD, 20.17 $\pm$ 2.74 years) participated in this study. All participants were undergraduate/graduate students and had no history of neurological and psychiatric disorders or head injury. Written informed consent was obtained from each participant prior to the MRI acquisition. The study was approved by the Institutional Review Board of Beijing Normal University.

Data acquisition

MRI data were acquired on a Siemens Trio 3 T MRI scanner powered with a total imaging matrix technique at the Imaging Center for Brain Research, at Beijing Normal University. Both the R-fMRI and high resolution 3D structural brain data were obtained using a 12-channel phased-array receiver-only head coil with the implementation of parallel imaging scheme GRAPPA (GeneRalized Autocalibrating Partially Parallel Acquisitions) (Griswold et al., 2002). For scanning, we selected the acceleration factor 2. The R-fMRI data were acquired using gradient-echo echo-planar imaging (EPI). The sequence parameters were as follows: TR = 3000 ms, TE = 30 ms, slice thickness = 3.5 mm with no gap, flip angle = 90°, FOV = 224 mm $\times$ 224 mm, data matrix = 64 $\times$ 64, interleaved 40 transversal slices giving spatial coverage 140 mm and 160 volumes. Each subject underwent the R-fMRI scans in two runs, EC state and EO state, each lasting 8 min. The order of the R-fMRI data acquisitions (corresponding to the two states) was counterbalanced across all subjects. In addition, we also acquired the 3D high-resolution brain structural images (1 mm³ isotropic) for each subject using a T1-weighted MP-RAGE sequence. The sequence parameters were TR/TE = 1900 ms/3.44 ms, flip angle = 9°, data matrix = 256 $\times$ 256, FOV = 256 mm $\times$ 256 mm, BW = 190 Hz/pixel, and 176 images along sagittal orientation, obtained in about 6 min.

Data preprocessing

The data preprocessing was conducted using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/) and DPARSF (Yan and Zang, 2010). For each subject, the two R-fMRI runs (EO and EC) were processed separately. For each run, the first 10 volumes were discarded to account for the MR signal equilibrium. The remaining functional images were first corrected for timing, and then realigned to the first volume to correct for head motion, which did not exceed 2.0 mm of displacement or 2.0° of rotation in any direction, in any subject. To account for the influence of head motion on R-fMRI (Mowinckel et al., 2012; Power et al., 2012; Satterthwaite et al., 2012; Van Dijk et al., 2012), the root mean squares of both overall head displacement and head rotation were calculated under EO and EC, and no significant differences were found between EO and EC (ps > 0.2). Subsequently, the functional images were spatially normalized to the standard MNI-152 template and re-sampled to a voxel size of 3 $\times$ 3 $\times$ 3 mm³. The waveform of each voxel was finally passed through a band-pass filter (0.01–0.08 Hz) to reduce the effects of low-frequency drift and high-frequency physiological noise.

Construction of brain functional networks

The functional connectivity matrix of each subject was constructed based on the automated anatomical labeling (AAL) (Tzourio-Mazoyer et al., 2002), which parcellated the brain into 90 regions of interest (ROIs; Table S1). The mean time series of each ROI was calculated by averaging the time series of all voxels within that ROI. The effects of head-motion profiles and global signal were regressed out with multiple linear regression analyses as described in previous studies (Fox et al., 2005; Van Dijk et al., 2012; Wang et al., 2009). Given that the impact of global signal regression (GSR) is important and its contributions, intensely debated (Chai et al., 2012b; Fox et al., 2009; Murphy et al., 2009; Van Dijk et al., 2010; Weissenbacher et al., 2009), we repeated the data analysis without GSR to check the reliability of the results (Supplementary materials). Regression residuals were then substituted for the raw mean time series of the corresponding ROIs. Pearson's correlation between the residual time series of each pair of the 90 ROIs was calculated to obtain a symmetric correlation matrix, the functional connectivity matrix for each subject. Finally, all elements of the correlation matrix were truncated and binarized by using a pre-selected value of sparsity (the ratio between total number of edges and the maximum possible number of edges in a network). To ensure that the brain