Altered Small-World Topological Properties of Functional Brain Network in Patients with OSA

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Abstract: Obstructive sleep apnea (OSA) is a common disorder of sleep disorders in which patients often suffer from cognitive impairment. Recent neurological imaging studies have shown that cognitive impairment in OSA patients is closely related to the extensive brain regions with abnormal neural activity. However, it remains unclear whether the topological properties of function networks in OSA patients have changed. Based on resting-states functional magenetic resonance imaging (rs-fMRI) and graph-analysis methods, this study explores the different orgnization in functional brain network between OSA patients and healthy volunteers. The brain connectome of patients with OSA exhibited small-worldness, but existed significant statistical difference compared with health controls. Besides, the betweenness centrality and degree centrality of right dorsolateral superior frontal gyrus and right hippocampal gyrus were significantly different in OSA patient group. The aberrant topological properties illustrated that the functional integration and segregation of brain networks in patients with OSA were disrupted.

1 INTRODUCTION

Obstructive sleep apnea (OSA) is the most common adult respiratory disease in which patients suffer from frequent apnea or hypoventilation due to recurrent complete or incomplete upper airway obstruction during sleep (Zhang, 2012). The main manifestations of OSA patients are snoring during sleep with apnea and superficial breathing, recurrent hypoxemia, hypercarbia and sleep architecture disorders at night. This leads to daytime sleepiness, cardio-pulmonary vascular complications and even multi-organ damage, which seriously affects the quality of life and life expectancy of patients (He, 2009). OSA is an independent risk factor for a variety of systemic diseases and may significantly affect cognitive function in addition to increasing the incidence of hypertension, diabetes, respiratory failure and cardiovascular disease (He, 2009). Current studies have shown that OSA can extensively impair cognitive function, including attentional alertness, executive ability, memory and motor coordination, and severely affect patient outcomes and prognosis (Verstraeten, 2007; Aloia, 2004; Decary, 2000).

Resting-state functional magnetic resonance imaging (MRI) provides a non-invasive and effective technique for studying brain function. Previous studies based on fMRI data have found that some functional measures of regions exhibited functional abnormalities in patients of OSA, such as the regional homogeneity (ReHo) in the right temporal, parietal and frontal regions (Santarnecchi, 2013), the decreased ALFF of regions in default mode network (DMN) (Li, Ma, 2016; Li, Nie, 2016). And researchers have found that all these abnormal regional alterations may be correlated to cognitive dysfunction.

However, brain is a complex information processing system (Khazaie, 2017). Any neurological activity can't occur as a result of a single neuron or brain region working alone, but rather a collection of neurons or several brain regions acting in concert with each other to transmit and integrate information. The complex network-based graph theory analysis has been widely applied to characterize such complex systems. The so-called network is a mathematical representation of a real complex system, defined as a collection of nodes and edges. For a brain network,

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the nodes can be brain regions or voxels, or even neurons, while edges can be identified by anatomical connectivity, functional connectivity depending on the characteristics of the data set. Functional connectivity indicates a correlation in time between the neurophysiological activity of two points. Based on graph theory, Chen found that the whole brain network of OSA patients exhibited decreased smallworld topological property (Chen, 2018). However, Huang found that the smallworld property of the OSA brain network was not significantly different to HC's, but OSA performed significantly lower in Cp and higher in Lp (Huang, 2019). Hence, it follows that the functional network organization of OSA patients are not clear yet.

In this paper, we intend to explore the impact of OSA disease on patients' functional brain networks from a complex network perspective.

2 MATERIAL METHOD

2.1 Data Acquisition

The data of this experiment were divided into two groups, the OSA patient group and the healthy controls group (HC), which included 24 OSA patients with typical indications of OSA disease and met the diagnostic criteria for the disease in the relevant draft; 21 healthy volunteers were also recruited as the control group.

In this study, MRI data were acquired using a GE Signa HDx magnetic resonance scanner with a field strength of 3.0 T. Scans and resting-state fMRI data were acquired using Gradient Recalled Echo (GRE) single excitation planar echo imaging (EPI) sequence with the following parameters: TR=2000ms, TE=30ms, FA=90°, FOV was 240*240mm², a 64*64 matrix was used, thickness =3mm, the layer spacing (gap) was 1mm, a total of 38 layers were divided, and 180 time points were acquired in each volume.

2.2 Data Pre-Processing

The DPARSF (Data Processing Assistant for Resting-State fMRI) software based on MATLAB was used to preprocess the functional MRI data of both OSA and HC related to the following steps.

The images of the first 10 time points were excluded to avoid the potential noise and instability. Slice timing was applied to correct this time difference. Head movement correction was used to avoid a slight head movement. The unified standard spatial EPI template with a voxel size of 3×3×3mm3 was used for transformation in order to facilitate the later study. The whole brain average signal, cerebrospinal fluid and white matter signal and motion signal were regressed out. The linear drift was removed. Then a band-pass filtering (0.01-0.08Hz) was used to remove the interference of low frequency and high frequency signals.

2.3 Construction of Brain Networks and Calculation of Topological Properties

Brain networks were constructed and topological properties were calculated. Based on the human Brainnetome Atlas template (Fan, 2016), the cerebrum of each subject was divided into 246 brain regions (nodes). The Pearson correlation coefficient of the average time series of each two brain regions was calculated as the functional connectivity (edges), then followed by the Fisher r-to-z transformation to normalize it. The z-scored 246×246 correlation coefficient matrix was obtained.

The correlation matrices were binarized by a pre-selected value of sparsity K ($0.05 \leq K \leq 0.5$). For a specific K, we got an undirected binarized network for each subject, then we applied graph theory to calculate the topological properties of each brain network. The global network properties contain clustering coefficient (C_p), characteristic path length (L_p), normalized clustering coefficient (γ), normalized characteristic path length (λ), and small-world property (σ). The nodal properties contain the betweenness centrality (BC) and degree centrality (DC) of each brain regions.

2.4 Statistical Analysis

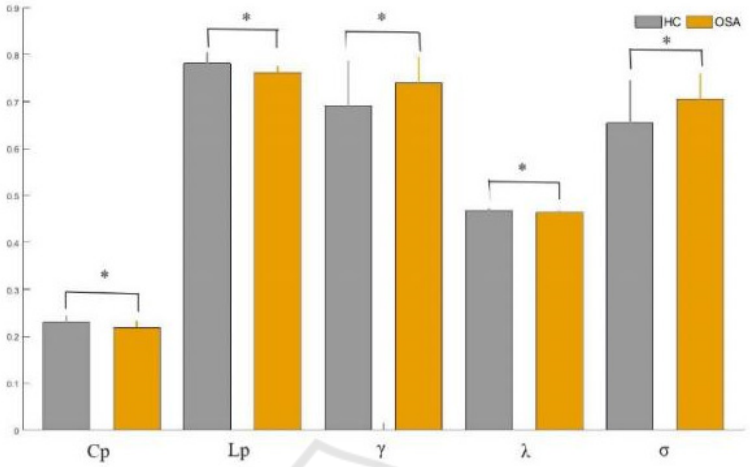
Two-samples t-test was performed for each parameter corresponding to the two groups of subjects. $p<0.05$ is considered to be statistically different.

3 RESULTS AND DISCUSSIONS

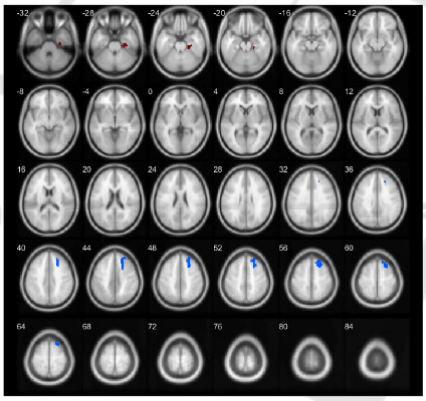
3.1 Global Properties

The area under curve (AUC) of each global parameter (C_p, L_p, γ,λ, and σ) in OSA group and HC group is shown in Figure 1(a). The Cp, Lp,λ of OSA patients were significantly lower than healthy controls ($p < 0.05$), while the$\gamma$and σ of OSA patients were significantly higher than healthy control ($p < 0.05$).

In each sparsity, the small-world property σ was greater than 1, which indicated that the brain functional network in both the HC and OSA groups had the small-world property. But the small worldness of OSA patients was significantly increased compared with healthy controls. These results suggest that the small-world properties of the functional brain network of OSA patients are significantly altered.



(a) The difference of global topological properties



(b) Regions whose DC and BC showed between OSA and HC significantly different

Note: * $p<0.05$, which was considered significantly difference.

Figure 1: The AUC of global properties and local properties comparisons with OSA and HC.

3.2 Local Properties

In this paper, we mainly analyzed the local properties: BC and DC of every brain region, and the regions significantly different between OSA patients and healthy controls are shown in Fig. 1(b) and Table 1. The BC and DC of right dorsolateral superior frontal gyrus (Frontal_Sup_R) was significantly lower in the OSA patient group. The BC and DC of right hippocampal gyrus (ParaHippocampal_R) was significantly increased in OSA group.

Table 1: The P-value of brain regions whose BC and DC were significantly different between OSA and HC..

Brain Regions	BC	DC
Frontal_Sup_R	0.0074	0.0048
ParaHippocampal_R	0.0010	0.0015

4 CONCLUSION

Based on the results and discussions presented above, the conclusions are obtained as below:

(1) The resting-state brain functional networks of both OSA patients and normal controls exhibit small-world property. But the small-world property of OSA patients are significantly altered, which suggest that the functional network organization of OSA patients is altered.

(2) The local property of OSA patients was significantly decreased in superior frontal gyrus, which indicated that the impairment of the superior frontal gyrus is associated with behavioral cognitive dysfunction in OSA patients.

(3) The local property of OSA patients was significantly increased in parahippocampal gyrus, which indicated that the significantly higher value of BC and DC may be related to compensatory mechanisms of memory function impairment.

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