

Effects of Sleep Deprivation on Brain Functional Network

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Abstract Sleep deprivation adversely affects the brain and cognitive function. Few studies have analyzed effect of the sleep deprivation and partial sleep restriction on rest-state brain functional network. In this study, we investigated the changes of rest-state functional magnetic resonance imaging (fMRI) in topological architectures of brain functional networks in sleep deprivation among 36 samples in sleep deprivation and 40 normal sleep controls. Our analysis revealed that the brain functional network of the clustering coefficient, characteristic path length and local efficiency are significantly increased but the global efficiency decreased significantly in sleep deprivation. Additionally, significant alterations in nodal efficiency were also found in sleep deprivation, involving anterior cingulate, inferior parietal, supramarginal gyrus, caudate nucleus, thalamus are significant decreased, and themiddle temporal gyrus are significant increased. Our results suggested that the groups of sleep deprivation were associated with disruptions in the topological structure of brain functional networks.

Keywords: Sleep deprivation; Global efficiency; nodal Efficiency, Small world properties

1. Introduction

Sleep deprivation can adversely affect the brain and cognitive function. A 2000 study, by the UCSD School of Medicine and the Veterans Affairs Healthcare System in San Diego, used functional magnetic resonance imaging (fMRI) technology to monitor activity in the brains of sleep-deprived subjects performing simple verbal learning tasks[1,2,3]. The study showed that regions of the brain's prefrontal cortex, an area that supports mental faculties such as working memory and logical and practical ("means-ends") reasoning, displayed more activity in sleepier subjects. Researchers interpreted this result as indicating that the brain of the average sleep-deprived subject had to work harder than that of the average non-sleep-deprived subject to accomplish a given task. They therefore concluded that the brains of sleep-deprived subjects were attempting to compensate for adverse effects caused by sleep deprivation. In 1998, Watts and Strogatz found the small worm's neural network shows the feature of small world [4, 5, 6], and concluded that human brain system also has a complex network of small-world properties, then studies confirm the inference [7, 8, 9]. Since then, human brain research became the branch of the complex networks, which widely used to study brain diseases [10, 11, 12], cognitive tasks [13, 14], and the others. Many brain diseases reflects the small world property degenerate, which tend to random networks when compared with the normal control, such as Alzheimer's patients [15,16], and attention-deficit/hyperactivity disorder (ADHD) patients [17, 18].

This study based on a common phenomenon in current society - lack of sleep. Studies have shown that adequate sleep is an important basis of human health. In current social environment, overtime work is widespread. In order to study how the lack of sleep affect our brain, researchers began to use an experiment, sleep deprivation, to study changes in our brain. Sleep deprivation is an experiment that to study the change of cognitive and neural activity via sleep restriction. Nowadays researches mainly through functional magnetic resonance imaging (fMRI), electroencephalography (EEG) and other data analysis to reflect the changes in human cognitive activity. Previous studies have shown that sleep deprivation has effects on human cognitive reaction speed, learning, work memory, attention, vigilance, and Inhibition [19, 20], participates has fatigue, drowsy, unresponsive, action instability and other physiological phenomenon. Individual cognitive impairment will be sustained serious with the time of sleep deprivation increasing. It is a very fatal problem for drivers, pilots, hospital staffs, astronauts, etc.

In the current study, we specifically focused on the brain network of sleep deprivation by the disruption of small-world properties and efficiency based on resting-state fMRI data. First, we construct binary brain networks of each participate with 90 brain regions as nodes extracted by an automated anatomical labeling (AAL) template. Second, calculating the parameters of the brain network (clustering coefficient,

characteristic path length, local efficiency, global efficiency and nodal efficiency) in different connection densities. Third, statistical analysis the differences between the sleep deprivation group and normal sleep group. Finally, to evaluate the effects of sleep deprivation.

2. Materials and methods

2.1 Image Acquisition and Preprocessing

A total of 76 volumes of resting-state functional images were obtained for each subject using an echo planar imaging (EPI) sequence through a 3T Siemens Trio scanner (TR/TE = 2000/30ms, flip angle = 90°, acquisition matrix = 64×64, field of view = 220×220mm², axial slices = 32, and thickness/gap = 3/1mm). Functional data preprocessing was carried out using SPM8. The entire process included removal of the first 10 volumes, slice timing correction, realignment to the first volume for head-motion correction, filtering (0.01~0.08 Hz), normalization to the EPI template with a resampling voxel size of 3×3×3 mm³, smoothing with a 6mm full-width at half-maximum Gaussian kernel. No subjects were excluded because all the head motions were <2 mm or 2°.

2.2 Construction of Functional Brain Network

To construct a functional brain network, we firstly employed the automated anatomical labeling (AAL) template [21] to parcellate the brain into 90 regions of interest (ROIs). Secondly, the time series was acquired on each ROI by averaging the signals of all voxels within that area and then linearly regressing out the influences of head motion and global signal. Thirdly, by calculating the Pearson correlation coefficients in the residual time courses between each pair of ROIs, a correlation matrix was obtained for each subject. To improve the normality, the correlation map was Fisher transformed (r-z) [22]. Finally, the absolute z values were converted into a binary connection matrix to make a graphic model of a brain network. That is, if the absolute z_{ij} (Fisher r-to-z of the Pearson correlation coefficient) of a pair of brain regions, i and j , exceeded a given threshold T (Fisher r-to-z), an edge was said to exist; otherwise it did not exist. The degree of each node, D_{nod} , is the number of connections that link it to the rest of the network. The total number of edges in a network, divided by the maximum possible number of edges $(N^2-N)/2$, is called the connection density or the cost of the network [23]. Given that there was no accurate way to choose a threshold in studies of brain networks, so the functional brain networks were constructed over the whole value of costs (0.03~0.50) at the interval of 0.01 (see Fig 1.). Because a similar trend for between-group differences was observed over the range of 0.03~0.50, and the biggest difference between MDD patients and healthy controls was found when cost is 0.21 for global measures, only results using a cost of 0.21 were reported for regional nodal analyses [24].

Where NG_i is the nodes of the sub-graph G_i , The local efficiency of node is a measure of the fault tolerance of sub-graph, which indicates that higher local efficiency is more stable while the node was eliminated.

The mean local efficiency of network is the average of the local efficiency of nodes.

$$E_{local} = \frac{1}{N} \sum_{i \in G} E_{i-local} \quad (1)$$

The node efficiency is defined as the inverse of the harmonic mean of the minimum length of path between node i and all other nodes in the network.

$$E_{nodal}(G,i) = \frac{1}{N-1} \sum_{j \in G} \frac{1}{L_{i,j}} \quad (2)$$

3. Functional Brain Network Analysis

3.1 Altered network features of brain functional network in sleep deprivation

In term of different threshold T (Fisher's r-to-z) to the partial correlation coefficients, we get network density K_{cost} in range of 0.3-0.5 and calculate the clustering coefficient, characteristic path length, local efficiency, global efficiency (Fig.2 A, B, C, D). Statistical analysis reveal that clustering coefficient and local efficiency are significant differences in K_{cost} (Fig.1A, B), suggesting that local processing efficiency

enhanced; the characteristic path length is significant increased and global efficiency is significant decreased, suggesting that the brain functional network has lower messaging capabilities in sleep deprivation. Despite sleep deprivation is negative impact of our body, the brain improve the local processing capability through self-regulation to resist the impact (Drummond et al. 2004).

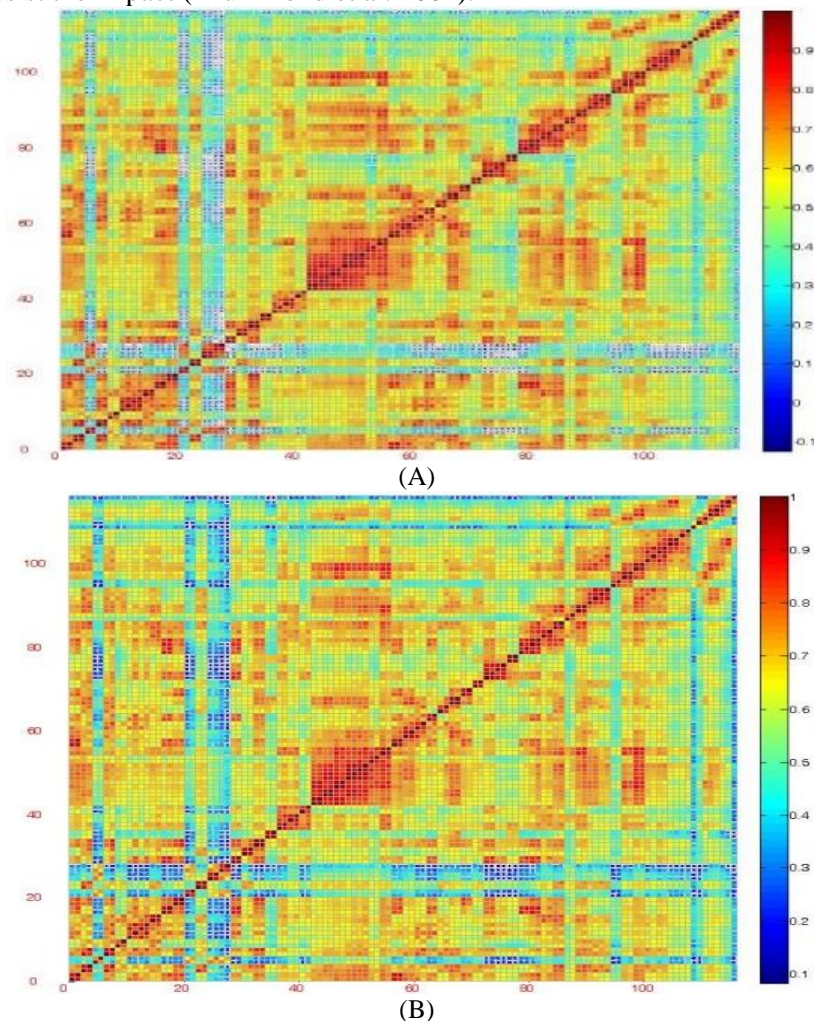


Fig 1 Brain Functional Networks. (A) brain functional networks of sleep deprivation groups (B) brain functional networks of normal sleep controls

3.2 Altered Nodal Efficiency in Sleep Deprivation

To further reveal the influence of the sleep deprivation, the two group difference in nodal efficiency was tested at the connection density of 0.41. We find that the nodal efficiency in anterior cingulate (ACG.R), inferior parietal (IPL.R), supramarginal gyrus (SMG.R), caudate nucleus (CAU.L, CAU.R), thalamus (THA.L) are significant decreased. And the temporal pole: middle temporal gyrus (TPOmid.L, TPOmid.R) are significant increased (see Fig 3. , Fig 4., Table 1). At the same time, we also conclude that the nodal efficiency is affected by sleep deprivation obviously.

The anterior cingulate is effect on inhibitory control, attention and vigilance. Suggesting that human may distracted easily and lapse. The thalamus (THA.L) is also effect on attention. The angular gyri (IPL) and supramarginal gyrus (SMR) is important cause of semantic processing and somatosensory. In contrast, the middle temporal gyrus is increased, which indicate that not all effect of nodal efficiency is decreased in sleep deprivation. It may confirm the compensatory mechanism of the brain to prevent the affection of sleep deprivation.

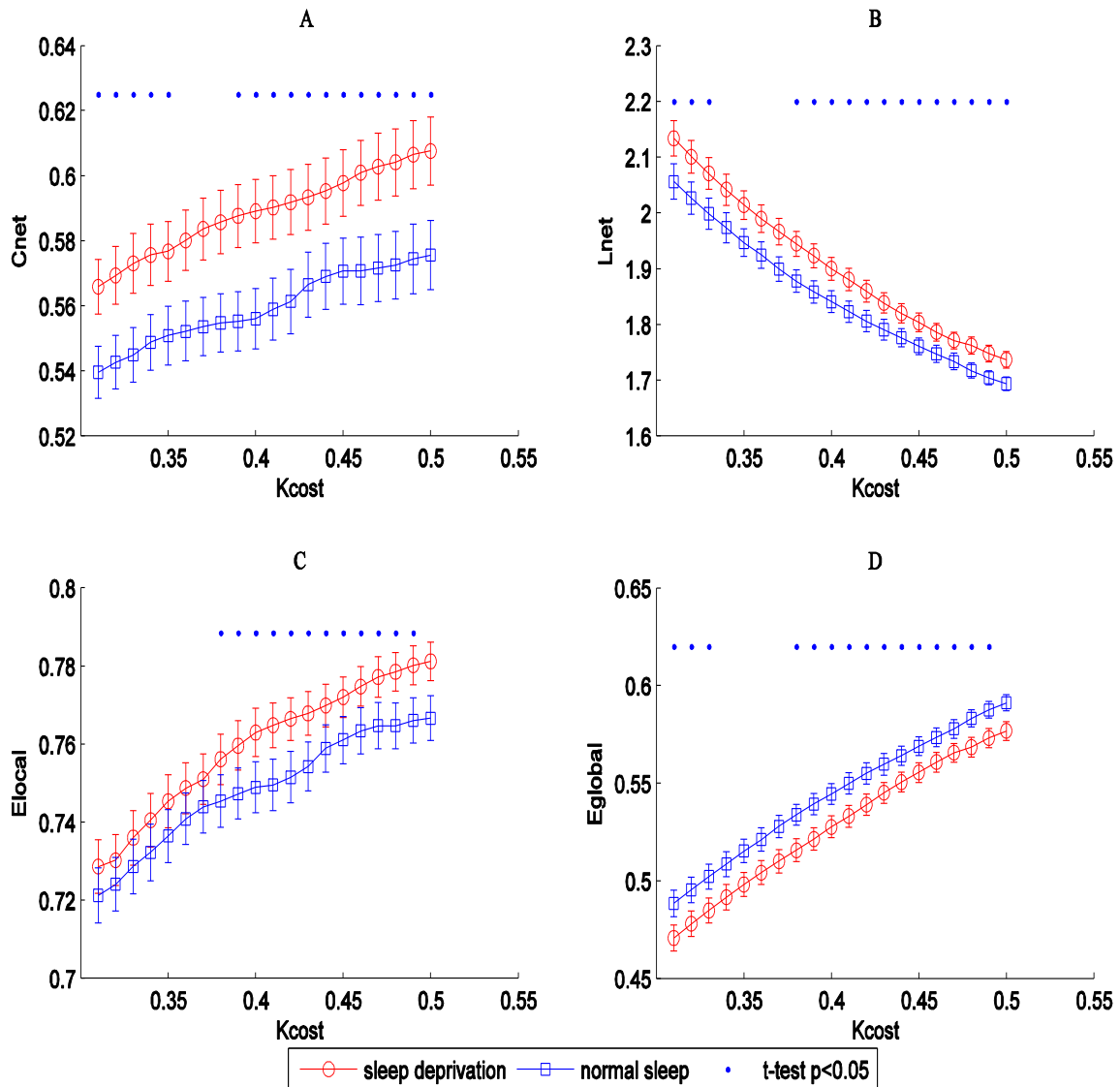


Fig 2 . Network properties of each group. Clustering coefficient (A), characteristic path length (B), local efficiency (C), and global efficiency (D) of sleep deprivation (red circles) and normal sleep (blue squares) as a function of cost K_{cost} . Error bar corresponding to standard error of the mean (21 subjects). Blue dot illustrate significant difference of two group (two sample t -test, $p < 0.05$, uncorrected)

Table 1 Regions showing significant changes in nodal efficiency in sleep deprivation ($K_{cost} = 0.41$)

Abbr.	Brain region	p-value	t-value
ACG.R	Anterior cingulate and paracingulate gyri	0.021	-2.39
IPL.R	Inferior parietall, but supramarginal and an g-ular gyri	0.027	-2.29
SMG.R	Supramarginal gyrus	0.046	-2.05
CAU.L	Caudate nucleus	0.004	-3.00
CAU.R	Caudate nucleus	0.003	-3.08
THA.L	Thalamus	0.030	-2.24
TPOmid.L	Temporal pole: middle temporal gyrus	0.035	2.17
TPOmid.R	Temporal pole: middle temporal gyrus	0.042	2.03

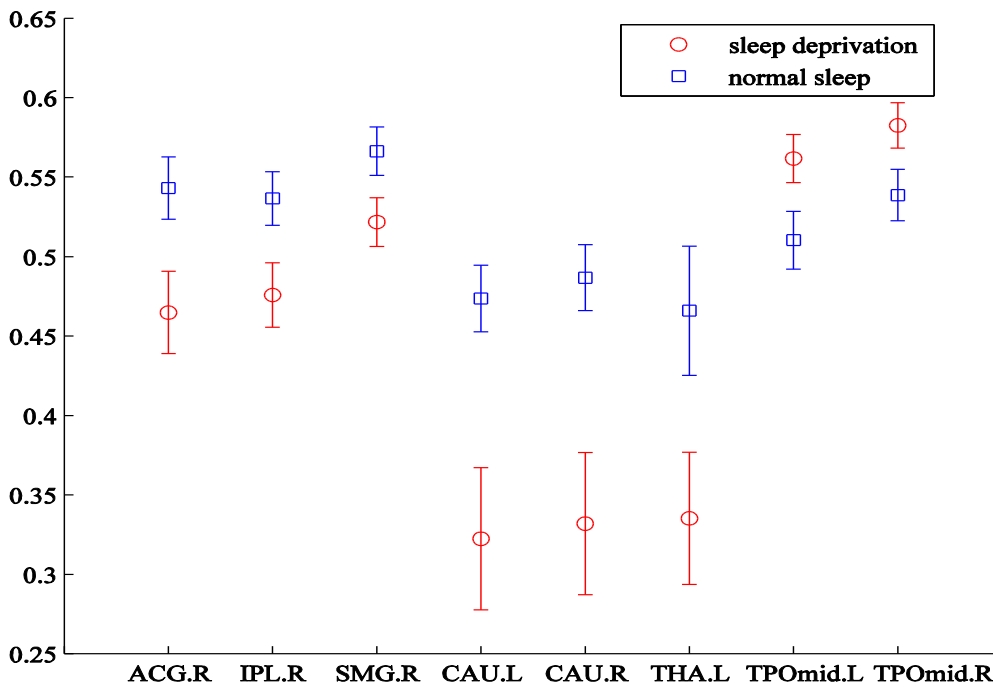


Fig 3. Nodal efficiency significant changes at cost of 0.41, Red and blue error bars correspond to the mean and standard error of the two group. See Table 1 for the detail of the regions.

3.3 Altered Small-World properties in abnormal sleep groups

In this paper, we constructed functional brain networks on the global scale for normal sleep controls and abnormal sleep groups. Graph theory analyses revealed that the global efficiencies of functional brain networks in MDD patients and healthy controls were greater than regular networks but less than random networks, and the local efficiencies were greater than random networks but less than regular networks over the whole range of 0.03~0.50 (Fig 5.). These results were typical features of small-world and were compatible with previous studies of small-world brain network.

Through the clustering coefficient, characteristic path length compare with random network, there are three parameters. The definition as follow:

$$\gamma = C_{real} / C_{random} \tag{3}$$

γ is the ratio of clustering coefficient between real and random network.

$$\lambda = L_{real} / L_{random} \tag{4}$$

λ is the ratio of characteristic path length between real and random network.

$$\sigma = \gamma / \lambda \tag{5}$$

σ is the ratio of γ and λ , which represent the small-worldness of a network.

When $\gamma > 1$, $\lambda \approx 1$, $\sigma > 1$, the network fit the definition of the small-worldness. σ increase significantly in range of connection density (Kcost) in sleep deprivation(see Fig 3C), which indicate that the small-worldness enhanced in sleep deprivation. The γ values is increased in whole range of Kcost (Fig. 5A), the λ and σ is significant in range of 0.38 and 0.5 (Fig. 5B, C).

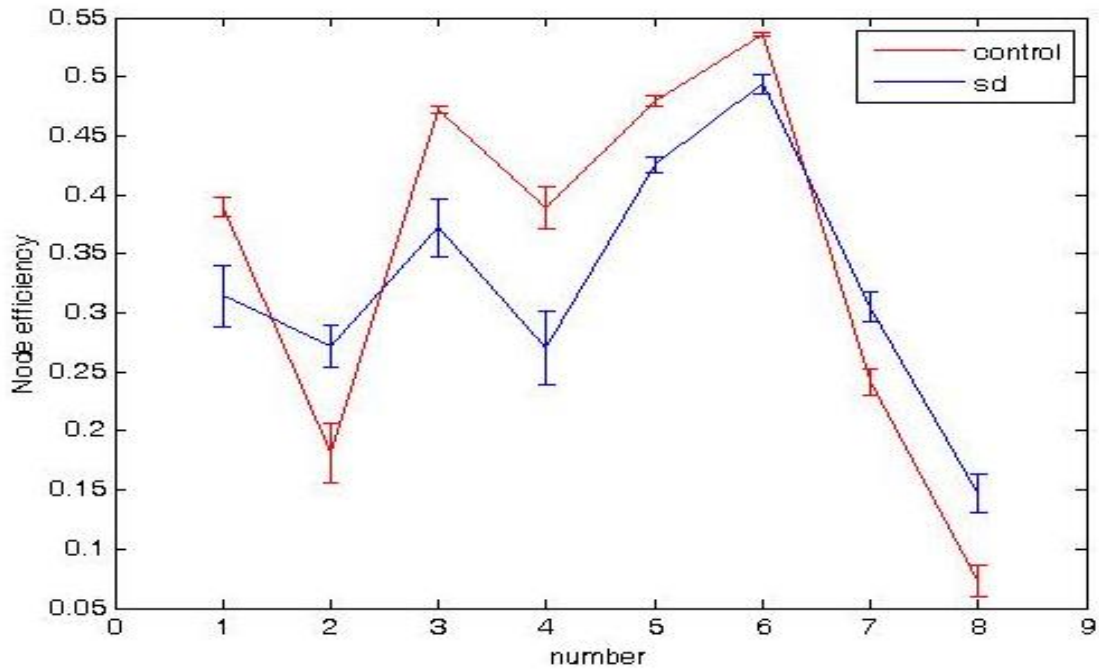


Fig 4. Compared node efficiency between normal sleep controls and groups of sleep deprivation

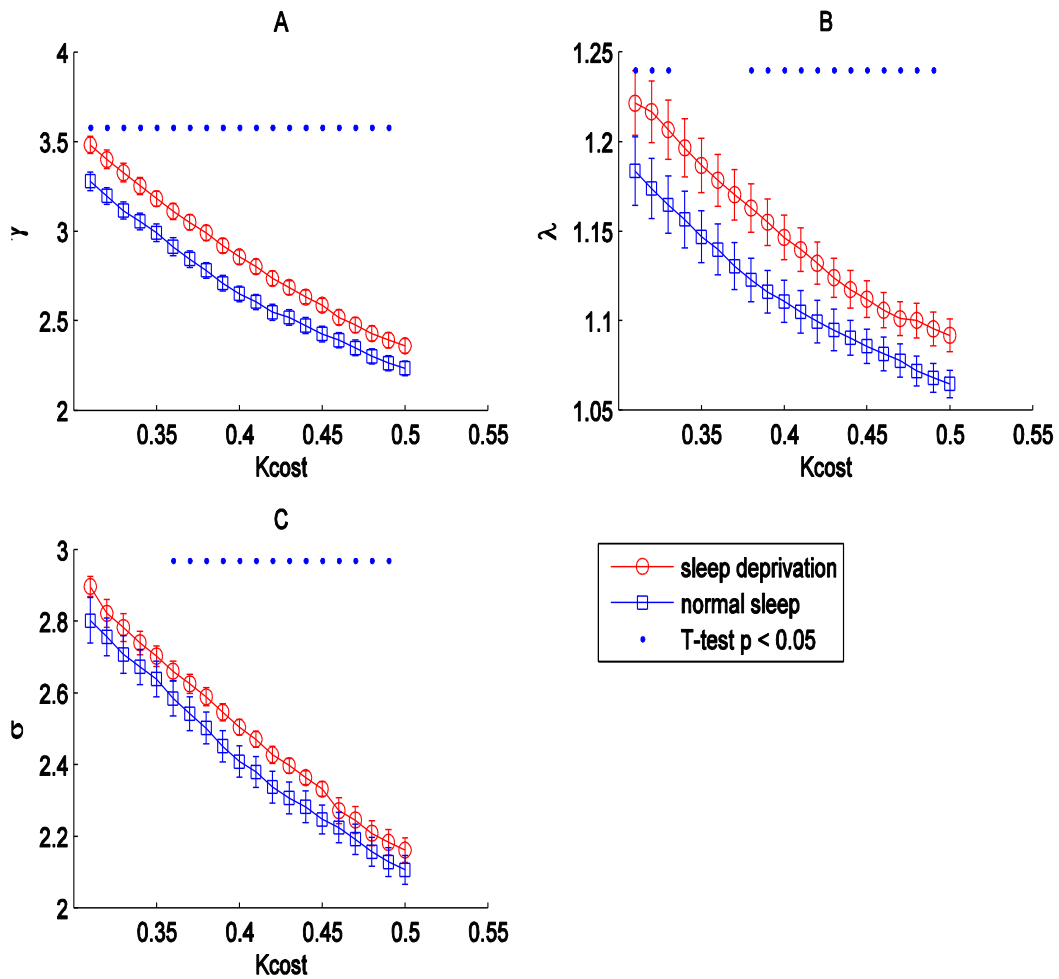


Fig 5. Network properties of each group. Sleep deprivation (red circles) and normal sleep (blue squares) as a function of cost K_{cost} . Error bar corresponding to standard error of the mean (21 subjects). Blue dot illustrate significant difference of two group (two sample t-test, $p < 0.05$, uncorrected)

4. Conclusion

In summary, our study concentrate on small-world properties, which is disrupted in sleep deprivation. Efficiency of parallel information transfer is reduced because of global efficiency significantly increased.

In addition, the nodal efficiency is profoundly affected, our attention may distracted easily and lapse (micro-sleep) duo to the anterior cingulate and thalamus decreased, and the vigilance is also decreased which is important of us to avoiding danger. And the small-worldness is significantly increased in sleep deprivation, suggesting that the processing efficiency is improved in sleep deprivation.

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