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Age-related Network Topological Difference based on the sleep ECG Signal

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Abstract

Age has been shown to be a crucial factor for the EEG and fMRI small-world networks during sleep. However, the characteristics of the age-related network based on sleep ECG signal and how the network changes during different sleep stages are poorly understood. This study focuses on to explore the age-related scale-free and small-world network properties of the ECG signal from male subjects during distinct sleep stages, including the wakeful(W), light sleep (LS), deep sleep (DS) and rapid eye movement (REM) stages. The subjects are divided into two age groups: younger (age<=40, n=11) group and older group (age>40, n=25). For the scale-free network analysis, our results reveal a distinctive pattern of the scale free network topologies between two age groups, including the mean degree ($\bar{d}$), the clustering coefficient ($\bar{c}$), and the path length ($\bar{l}$)features, such as the slope distribution of $\bar{c}$ in younger group increased from *1.99* during W to above *2.05* during DS. In addition, the results indicate that the small-world properties can be found across all sleep stages in both age groups. But the small-world index in the LS and REM stages significantly decreased with age (*p=0.0006 and p=0.05 respectively*). The comparison analysis result indicates that the network topology variations of the sleep ECG signals prone to show age-relevant differences which could be used for sleep stage classification and sleep disorder diagnosis.

Keywords: Complex networks; Sleep; Electrocardiography; clustering coefficient; Scale-free and small-world networks

1. Introduction

Sleep is an important biological process which is essential for an individual's performance, learning ability and physical movement. Spatial Complex network (SCN) has been shown to be a powerful approach for quantifying sleep patterns of brain functions. A node of the SCN could be a brain region, a voxel [1] or an EEG channel [2, 3]. An edge of the SCN is presented when there is an anatomical connection or functional correlation between two nodes.

Researchers have highlighted that sleep functions could be measured by network topology indicators of multichannel EEG signals or fMRI signals. Bassett et.al [4] showed that the functions of human brain systems have a small world network property (SWN) which has a high clustering coefficient ($\bar{c}$) and a short path length ($\bar{l}$). The SWN has been shown to steadily increase from the light sleep stage to the deep sleep stage with a higher $\bar{c}$ and lower $\bar{l}$ based on EEGs [2]. Also, study has shown that a brain network of the fMRI data has a higher SWN in the deep sleep stage than those in wakefulness [5]. However, another study of Uehara et al. [6] claimed that $\bar{l}$ actually the SWN showed an increase from the light sleep

stage to the wakeful stage. The exact network properties changes of different sleep stages are still under debate. In addition, the network topology differences between the REM and the light sleep are still unclear. Most existed literature only discussed the wakefulness and the NREM sleep stages without considering the REM stage [5-8]. One of the key reasons is that it is difficult to differentiante the REM sleep stage and deep sleep under a noisy fMRI scanner [6-8]. The general EEG headset has no more than 64 electrodes which results in that the nodes of the corresponding SCNs are less than 64. The limited number of the SCN degree makes the distribution results a weak persuasion. It is rare to see the reports of the clustering distributions from different sleep stages, especially the network models based on ECG signals.

In regard to the age factor, most SCN-based research reveals that there is a decayed SWN in the older adults based on EEG signals. Both clustering and path were found lower in older people group than those in the younger group [10]. Decreased and increased connection in beta and gamma band were found in older adults in the eye opening status [11]. A shorter path length was found in alpha bands in older group compared with the younger group [12]. However, it is difficult to construct the SCNs only from a single biomedical signal channel, such as those from Polysomnography (PSG) which is a routine measurement for sleep quality and usually contains two EEG signals, one ECG and/or one EMG. The typical duration of sleep EEG segments captured using a PSG device in hospital is 30 secs which (assuming the sampling rate is 1000 Hz) only produce a SCN with one node (i.e., one channel used). Thus, the node number of a SCN model with signal from PSG is small and it would also be difficult for the model to process long-term records. In addition, SCNs with different size of nodes have different network properties which cause matter in the consistency of the brain function analysis[1]. Recently, there is a study using complex networks method to study the cardiorespiratory interaction during sleeping, which provides evidence that cardiorespiratory activity contains different characteristics across sleep stages due to the manifestation of autonomic (sympathetic and vagal) nervous activity [28]. However, as far as we know, no research has been done about the age-relevant complex networks properties based on the ECG signals. Also whether there is SWN properties of the sleeping ECG signal in relating to brain function is still unknown.

To fill these gaps, this paper leverages the difference visibility graphs (DVGs) to evaluate sleep patterns difference in four sleep stages based on ECG signals. The aim is to investigate relationships between aging and sleep functions. The SWN is applied to measure the network changes of the younger group compared to the older group during four sleep stages: wakefulness, light sleep (LS), deep sleep (DS) and REM. By probing the local network topologies (such as mean degree $\bar{d}$ and $\bar{c}$), a global network measurement ($\bar{l}$) may provide new sights on brain function across four sleep stages and different ages. The DVGs of the ECGs associated with sleep functions are necessary to understand the critical differences from the wakeful stage to the deep sleep stage during the whole night. In our analysis, the ECG signals of two database from 35 subjects are used to extract the network topologies. Statistical results examine the changes of graph topologies: $\bar{d}$, $\bar{c}$ and $\bar{l}$ of the deep sleep or rapid eye movement (REM) stage of the ECG signals. Then the SWN is evaluated among four sleep stages and the topologies are compared between two age groups.

2. Method

The experimental data is obtained from two public Sleep databases [14, 15]. The data from these two databases were both acquired from PSG devices. In this study, the algorithm for extracting graph topologies is implemented using C++ programming language. The statistical analysis is conducted with R scripts.

2.1 Data sets1- UCDDB Database

UCDDB sleep database [14] contains 25 full overnight PSG from adult subjects (21 male, 4 female) with suspected sleep-disordered breathing. The data was recorded from St. Vincent's University Hospital/ University College Dublin. All subjects were selected randomly over six months period from those patients with suspected sleep-disordered breathing. The ECG sampling rate is 128 Hz and with a resolution of 11-bit. The apnea annotations were scored offline by experienced sleep physicians. In this study, 21 male subjects were selected for analysis.

The original sleep stages in this database were labeled with one of these classes: 0(wakefulness), 1 (REM), 2 (sleep stage 1), 3 (sleep stage 2), 4 (sleep stage 3), 5 (sleep stage 4) etc..

2.2 Data sets2- Slpdb Database

The second EEG database is a collection of recordings for chronic obstructive sleep apnea syndrome in Boston's Beth Israel Hospital Sleep Laboratory [15]. It was denoted as Slpdb in this paper. It contains 16 male subjects and encoded as slp01 to slp67x (the data has 18 recordings in total because two subjects have recorded twice). The sampling frequency is 250 Hz. These recordings always contain two EEG channels, one ECG signals annotated beat-by-beat, and a respiration signals. Similar to UCDDB, the sleep stage was coded as one of six classes: W(wake), 1-4, (sleep stages 1 to 4), and R(REM). In this study, 15 recordings were selected from 15 male subjects (the slp67x was excluded because there is no age information for that subject).

2.3 Difference Visibility Graph

An difference visibility graph (DVG) is a network in which a node is directly mapped from a point of a time series. It is proposed by Zhu et al. [16]. The edges between two points can obliquely see each but cannot see each in a horizontal angle, which can be named as oblique visiblity graph (OVG) as well. Mathematically, given a ECG time series $x_{t=1,\ldots,n}$, it is mapped to a graph G (V, E) by following steps, a data point x_i is mapped into a node v_i in G. An edge between v_i and v_j (i<j) from two points x_i and x_j extists if and only if:

$$\forall k \in (i,j); \frac{(x_j - x_k)}{j-k} > \frac{(x_j - x_i)}{j-i} \wedge (x_k \geq x_i \vee x_k \geq x_j) \wedge (j - i \neq 1) \quad (1)$$

Fig. 1 shows how a time series X is transferred into an DVG, the X comes from 1312th epoch of the ECG signals in a subject slp03 from the slpdb database. For example, in Fig 2, the 1st point can obliquely see the 4th point but cannot obliquly see the 45th point.

It is noted that the graph in Fig. 1 is a spare graph, such as the nodes 2, 3, 5 etc . are isolated nodes, which implies that those isolated nodes could be ignored later when graph features are processed. Thus, the DVG can be efficient to process the long-term time series.

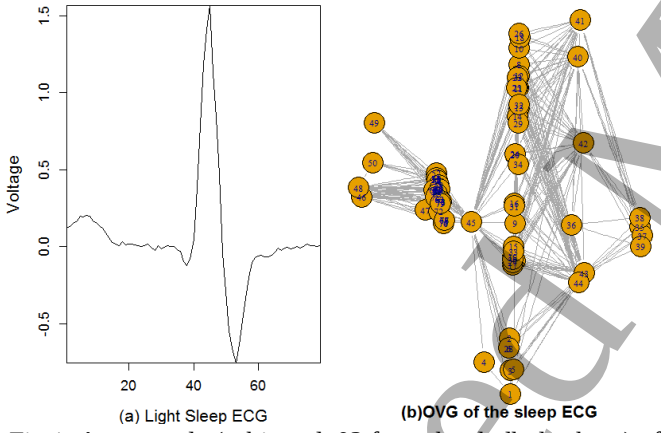

Fig 1. An example (subject slp03 from the slpdb database) of the ECG signal transferring into the DVG

A time series can be characterized with the network topology, such as mean degree, clustering coefficient, average path etc. [17]. A node degree is one of the basic characteristics of a graph. The degree d_i of node v_i is the number of edges from v_i. For example, in Fig. 1 (b), d_1=1 and d_{30}=3 . The average degree $\bar{d}$ of a graph G with n nodes is defined as:

$$\bar{d} = \sum_{j=1}^{n} d_j \quad (2)$$

Clustering coefficient (*c*) is another typical property of complex network. The coefficient index C_i of node V_i is the number of existing edges between the nodes' neighbours divided by all their possible edges. The average *c* of a graph which includes n nodes is defined as:

$$\bar{c} = \frac{1}{n}\sum_{i=1}^{n} c_i \quad (3)$$

Numerous brain function connectivity, transport networks or internet have been exhibited a power-law distributions or exponential-law distributions [13, 18-20]. Current research believes that the degree distribution of EEG signals in sleep satisfy the power-law distributions [16, 21], which can be expressed as follows :

$$p(x) = \beta x^{-k} \quad (4)$$

where x is a number of degree, and β is a constant of proportionality and k is the scaling exponent. In this paper, p(x) is the distribution of the C over the respectively degree x as shown in Fig. 1. A graph having power-law degree distributions is named a scale-free network. A new node attached a scale-free network has high possibility to connect to a large degree node or be isolated.

In general, shortest paths play an important role in the transport and communication within a graph. The average path length (L) is defined by the average of geodesic lengths l_{ij} over all pairs of nodes.

$$\bar{l} = \frac{1}{n}\sum_{i=1}^{n} l_{ij} \quad (5)$$

where l_{ij} is the length of the shortest path from time point j to time point i in this study.

2.5 Small-world index

Most of complex brain networks are claimed as small-world networks [2, 4, 6, 11, 22, 23]. To measure whether a network satisfies small-world properties, a popular method is to compare the proposal networks with the random graphs [4, 22, 23]. However, an DVG is constructed from a time series, thus we define the relative path length l_r and the relative clustering coefficient c_r in DVG which are normalized from a random signals.

$$\sigma = \frac{\frac{c}{c_r}}{\frac{l}{l_r}} = \frac{c l_r}{c_r l} \quad (6)$$

This definition requires comparison the DVG of an ECG signals with those of a same length of random signal. Similar existed criteria for small-worldness of SCN, the small-world property from DVGs can be hold with the following condition.

$$\sigma \gg 1 \quad (7)$$

2.6 Pre-procession of Sleep databases

Before ECG analysis, the database individual variation is studied. There is no significant age difference between two sleep databases (results shown in Table 1).

Table 1 Two databases information (only male subjects)

Databases	Young		Old	
	Subjects	Ages	Subjects	Ages
UCDDB	4	33.8±4.2	17	51.8±4.4
Slpdb	7	36.5±2.9	8	47.3±5.4

Before two database ECG signals were transferred into graphs, the sleep scores in both databases were transferred into the Awa, LS, DS, REM, where the LS includes sleep stages 1 to 2 and the DS includes stages 3 and 4. Both hypnogram were in 30s, the ECG points in each epoch are either 3840 or 7500 based on the sampling rate of 128Hz and 250Hz respectively. The sampling rate difference was solved by taking an average point of each two adjacent numbers for the 250Hz sampling rate time series. Fig. 2 shows five epochs: 25th, 30rd, 245th , and 300th in four stages of sleep ECG signals from a subject slp03 in the Slpdb. The recordings in two databases were also divided into two groups according to the ages based on the previous study of the age effect on sleep stages and disorder [27]: younger group (age<=40) and older group (age>40) as shown in Table 1. The subject detail information can be found from supplied Tables 1 and 2.

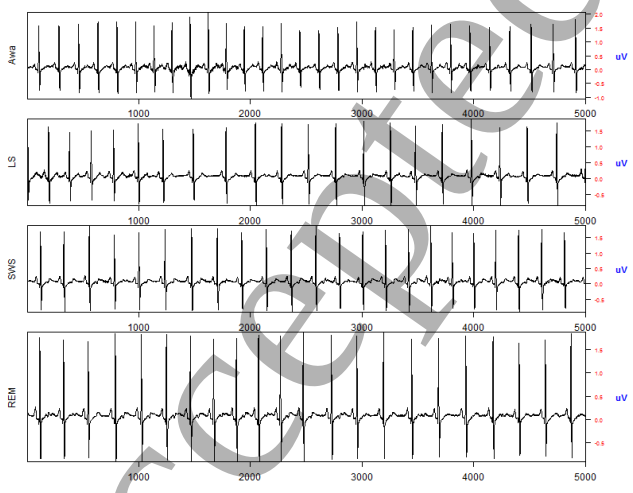

Fig.2 the ECG signal from foure different sleep stages including the W, LS, DS, REM.

3. Results

3.1 Scale-free network properties

To evaluate the network topology changes between two age groups among four sleep stages, experiment was conducted and the results consist of the analysis of mean degree, the clustering coefficient with its distributions and the average shortest path length. The feature extracted tool was implemented with C programming language, which can be download from http://uadi.project.uq.edu.au/UADI/sleep/.

3.1.1 Mean degree of the DVG in sleep ECG

The mean degree $\bar{d}$ of the DVG in four sleep stages from two sleep ECG datasets are shown in Fig 3. Generally, the $\bar{d}$ of the UCDDB database has a higher value than that of the Slpdb database. The wakeful stages of both age groups prone to have the lowest $\bar{d}$ which is significantly lower than the DS stage (Wilcoxon rank-sum test, p-values are shown in Table 2). In Table 2, where "W<D" means in wilcoxon test, the alternative hypothesis 'mean degree of Wake is less than that of DS'. "R<>L" means in wilcoxon test, the alternative hypothesis 'mean degree of REM is not equal to that of LS', and others are so on.

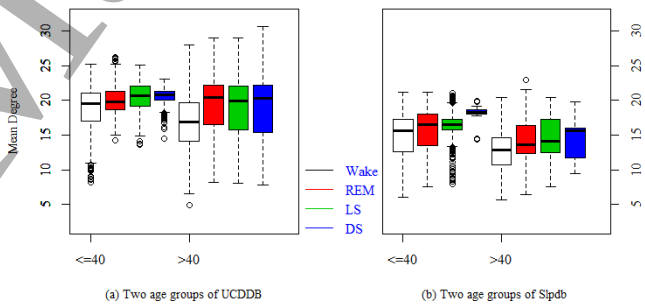

Fig. 3 Aged-related degree from two databases across four sleep stages

One difficulty for analysing EEG signal by visual inspection is to distinguish the REM stage and the LS stage[24]. Our results showed that there is significant difference (Wilcoxon rank-sum test, p-values are shown in Table 2) in $\bar{d}$ between the REM stage and the LS stage though in the younger group which could also be potentially used for age classification. Similar to degree features from the LS and the REM stages of the EEG signals in our previous study [16], only with the $\bar{d}$ information of the ECG is not enough for separating the REM from the LS because the significance only exists in the younger group.

Table 2 The degree $\bar{d}$ analysis between the Wake (W) vs DS (D) and the REM (R) vs LS (L) stages

	UCDDB				Slpdb			
Age	Young		Old		Young		Old	
Stage	W<D	R<L	W<D	R<>L	W<D	R<L	W<D	R<>L
p-value	<2.2e-16	0.009	<2.2e-16	6.23e-6	2.06e-6	0.0002	2.54e-11	0.0007

3.1.2 Mean local cluster coefficient of the DVG in sleep ECG

The mean local cluster coefficient $\bar{c}$ of the DVG of four sleep stages from two sleep ECG datasets are shown in Fig 4. Similar with the mean degree $\bar{d}$ of the DVG, the $\bar{c}$ of the DVG shows a significant increasing from wakefulness to the DS stage in both age groups (p-value shown in Table 3). However, the comparison between the REM stage and LS stage from these two databases is not consistent. Therefore, the $\bar{c}$ of the DVG is not an optimal candidate for the REM and LS stages classification.

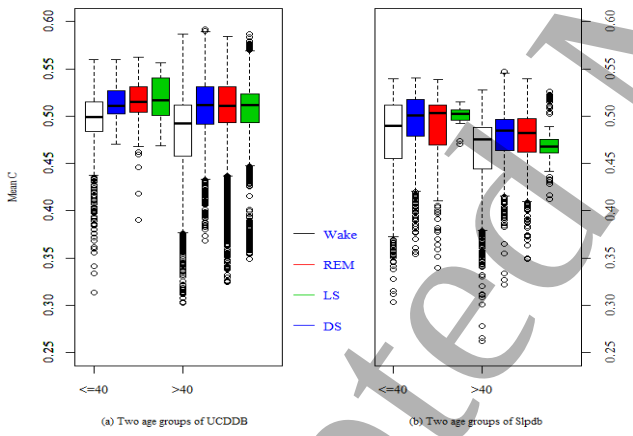

Fig. 4 Aged-related clustering coefficient from two databases across four sleep stages

We also compared the $\bar{c}$ of the younger group with the older group. Results show that the younger group has higher $\bar{c}$ than the older group in both the wakeful stage (*p=0.0001* in UCDDB and *p=5.72e-07* in Slpdb) and the DS stage(*p=2.25e-11* in UCDDB and *p=3.05e-10* in Slpdb). These agree with previous study that health subjects have higher $\bar{c}$ of the ECG in than those of Apnea patients [25].

Table 3 The clustering coefficient $\bar{c}$ analysis between the Wake (W) vs DS (D) and the REM (R) vs LS (L) stages

	UCDDB				Slpdb			
Age	Young		Old		Young		Old	
Stage	W<D	R<L	W<D	R<>L	W<D	R<>L	W<D	R<>L
p-value	<2.2e-16	0.015	<2.2e-16	0.809	2.06e-5	0.881	0.0007	0.334

Fig. 5 demonstrates the clustering coefficient distribution of the ECG signals in different sleep stages of two age groups from two sleep databases. Different colour lines represent different sleep stages and age groups.

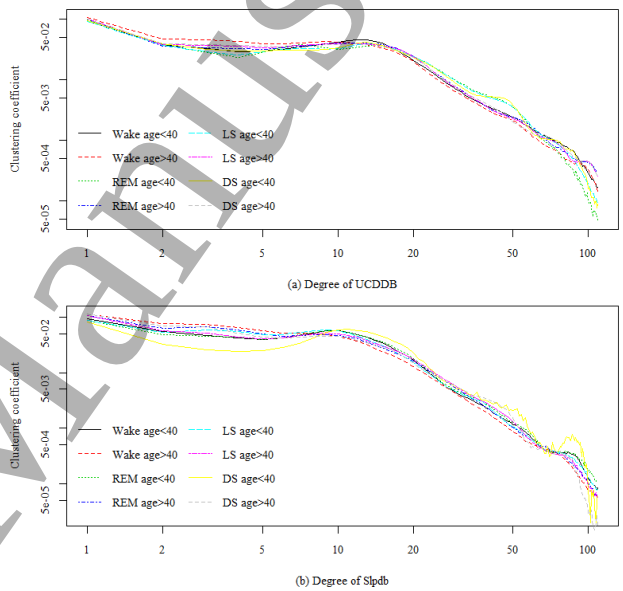

Fig.5 Distribution of c in Sleep ECGs from two databases

Among all the sleep stages and all the age groups, the $\bar{c}$ exhibits power-law distributions. Most slopes (k) of scale-free networks has $2 \le k \le 3$ [26]. In our results, the slope of the wakeful stage in the younger group is smaller than 2 while the slope of the DS stage is above 2, indicating that the network brain tends to form a more stable status when healthy young people fall into the deep sleep stage. Unlike the younger group, the older group shows more abnormal slopes. The pattern changes from the wakeful stage to the DS stage from two databases are not consistent. To be more specific, the k value shows decreasing form the wakeful stage to the DS stage in UCDDB database while it is the opposite in the Slpdb database which indicates that the brain function of the older

people are quite chaotic. Table 4 shows the slope of the distribution in details.

Table 4 The slope (*k*) of clustering coefficient distribution

	UCDDB				Slpdb			
Age	Young		Old		Young		Old	
Stage	Wake	DS	Wake	DS	Wake	DS	Wake	DS
k	1.994	2.248	1.917	1.765	1.911	2.05	1.562	2.196
KS.p	0.982	0.924	0.937	0.812	0.980	0.999	0.555	0.933

3.1.3 Mean average path of the DVG in sleep ECG

The average shortest path length $\bar{l}$ of the DVG of four sleep stages from two sleep ECG datasets are shown in Fig. 6.

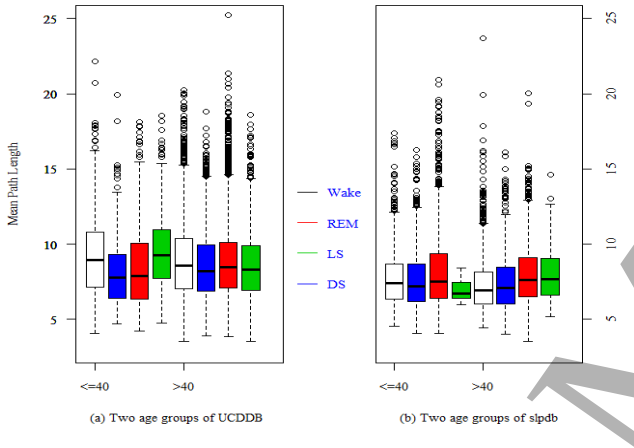

Fig. 6 Aged-related average path from two databases across four sleep stages

Generally, the $\bar{l}$ in the UCDDB is longer than those in the Slpdb which we believe that could be caused by the difference in sampling rate. Similarly, the $\bar{l}$ of the DVG showed significant difference from the wakeful stage to the DS stage in younger group and the trend of the $\bar{l}$ of the DVG prone to have larger value in the wakeful stage which suggesting the connectivity distance of the ECG signal networks is higher in the wakeful stage. On the other hand, the changing tendency of the $\bar{l}$ in the older group seems to be chaotic. However, the $\bar{l}$ difference is only significant in the older group when it comes to the comparison of the REM and LS stages. And in the older group, the $\bar{l}$ in the LS stage is higher than that in the REM stage. Therefore, the $\bar{l}$ is more applicable in REM and LS stages classificaiton in the older group.

Table 5 The path length $\bar{l}$ analysis between the Wake (W) vs DS (D) and the REM (R) vs LS (L) stages

	UCDDB				Slpdb			
Age	Young		Old		Young		Old	
Stage	W>R	R<>L	W>R	R<L	W>R	R<L	W<R	R<L
p-value	<2.2e-16	0.2528	<2.2e-16	0.00058	0.0095	3.77e-09	0.015	4.38e-05

3.2 Small-world network properties

Regarding to the SWN criteria, the topologies in general graphs are always compared with the random graphs. In this study, we compared the networks of the sleep ECG signals in the general graphs and random graphs.

From Fig 7, we can see that small-world index σ across all sleep stages are large than 200, which satisfies the equation (7) σ≫1. Thus the brain function always exhibits a SWN in both the wakeful and the sleep status.

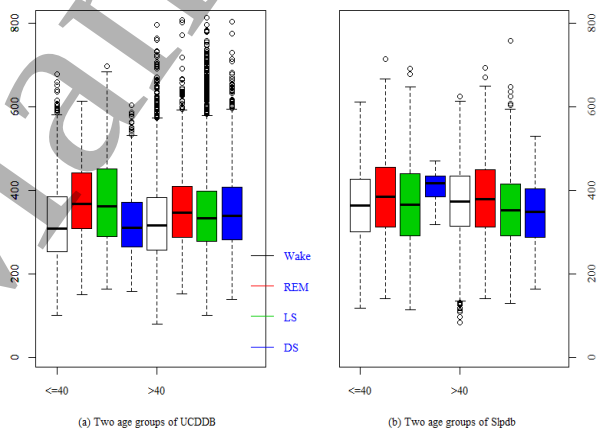

Fig. 7 Aged-related small-world index from two databases across four sleep stages

SWN has been studied in light sleep stages [6, 8]. Studies has shown that the $\bar{l}$ significantly increased in sleep stage 1 compared with the wakeful state, while $\bar{c}$ has no significant difference [6]. However, the authors in [6] cannot reveal the changes in sleep stage 2, REM and DS because they used the fMRI signals in which the subjects cannot generate long-term sleep.

Our results confirm that the $\bar{l}$ in the light sleep stage is shorter than the wakeful stage only in the younger group as shown in Table 5. However, this may not be the case for the older group. In addition, the study can show that the $\bar{c}$ actually has significant difference between the wakeful stage and the LS stage of ECG signals.

There are studies showing that the small-world index decreased with age in the wakeful state [22]. Our results in Table 6 compare σ across different sleep stages between younger and older groups. The comparison results show that the small-world index decreased with age only in the REM and the LS stages. It suggests the brain function in the REM and LS stages forming a small-world networks only in younger subjects but not in the elderly and chronical apnea patients.

Table 6 the small-world index $\bar{\sigma}$ analysis between the younger and older groups

	UCDDB				Slpdb			
Stage	Wake	REM	LS	DS	Wake	REM	LS	DS
p-value	0.736	0.4.35e-05	4.51e-14	0.999	0.986	0.0439	0.0006	0.001

4. Discussion

In this paper, we explored the sleep ECG signal's network topologies of the scale-free and the small-world properties in different age groups. The sleep stage is further divided into four distinctive stages and has a comparison of younger and older. We found that the younger subjects and older subjects showed distinctive feature patterns of the ECG signal across sleep stages.

For the scale-free networks, our results show that the distribution of clustering coefficient of the ECG signals are power-law tails in both the younger and older groups across wakeful and sleep status, which exhibits the similar results as existing brain networks of EEG [20] or fMRI [23].

Uehara et al. [6] have studied whether the decreased shortest path is only specific feature to classify from the wakeful stage to the sleep stage 1 or if the decay also occurs in deep NREM sleep. According to Fig.6 and Table 5, we have found that, the decreased shortest path pattern only appeared in the REM stage in the younger group but not happened in the older group.

The clustering coefficient distribution exponent of the younger group in the wakeful stage is significantly lower than that in the deep sleep stage. More specific, the exponent of distribution increased from about 1.9 of the wakeful stage to about 2.1 to 2.2 of the deep sleep in the younger group, which implies that the sleep ECG signals are less random and more robust in the DS stage than during the wakefulness. In the future, further exploration of relationship among the light sheep, deep sleep and age will be undertaken to investigate the reasons of the network differences between the EEG and ECG signals.

In addition, this is the first time to investigate the small-world property of the sleep ECG signal as far as we know. Similar to most existing results based on fMRI [6] or multi-channel EEG signals [2], the networks of the sleep ECG signal tend to show small-world properties across all sleep stages among different ages. On the other hand, there is a decreasing trend of the small-world index with age is only occurring in light sleep stage and REM but not during the wakefulness or deep sleep. It suggests the brain function in the REM and LS stages forming a small-world networks only in younger subjects but not in the older and chronical apnea patients.

Over all, this paper used the sleep ECG signal as the source for sleep stage analysis and classification which provide another accessible approach with high accuracy. Also it takes the age factor into consideration for the network topologies study and the results showed the distinctive patterns among different which shed light on the diagnosis and treatment of the aged-related sleep disorder.

Acknowledgements

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