Differences in EEG-based Brain Network Activity during Non-REM Sleep

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Abstract
Numerous studies have suggested that sleep spindle waves may play a role in the hippocampal-cortical transmission of information associated with memory enhancement. In previous research, the clustering coefficient increased significantly from wakefulness to sleep, indicating that the graph theory may be able to characterize brain network activity during sleep. However, previous studies have not investigated in detail the characteristics of the brain network in individual sleep stages; the brain network activity in the EEG at each sleep stage has not yet been clarified. In this study, we compared the characteristics of the network activity in various sleep stages by determining the functional connectivity from EEG in individual stages, constructing the networks and comparing the clustering coefficients and characteristic path lengths. We found a significant decrease in the characteristic path length in LowBeta band (13–15 Hz) from Stage 1 to later stages. However, there was no significant difference in the clustering coefficient. Our results are consistent with the concept that sleep spindles are related to memory consolidation. Therefore, the results suggest that the networks generated by the brain are more efficient in middle and deep sleep.

Keywords: EEG, sleep, functional connectivity, graph theory, sleep spindle.

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1. Introduction
Early research on the brain aimed at mapping the relationship between brain regions and brain functions. This has been studied from the perspective of functional localization, where a specific region of the brain has a specific function. Broca mentioned that damage to the inferior frontal gyrus (IFG: lower frontal lobe) is related to aphasia; Wernicke found that damage to the superior temporal gyrus (STS: upper temporal lobe) is related to language-based learning disabilities. These studies have provided evidence of the relationship between the brain region and its function in language ability [1].

However, as the task becomes more difficult, the brain no longer activates only one region. Several regions are activated together to solve complex tasks. IFG has been reported to be activated not only in language but also in many other cognitive tasks. STS shows activation in the perception of biological motion and is included as a part of the recognition network. Accordingly, IFG and STS have not only one but several functions, as they belong to more than one network. Therefore, there have been many studies on the relationship of networks between brain regions.

Numerous studies have been conducted on sleep and brain activity. In particular, sleep spindles, which are characteristic of Stage 2 sleep, have been suggested to play a role in the hippocampal-cortical transmission of information associated with memory enhancement [2]. Previous studies have proposed that non-REM (NREM) sleep preferentially facilitates declarative memory, whereas REM sleep preferentially facilitates non-declarative learning [3]. Sleep spindle density, which is related to NREM sleep, was enhanced after training the declarative memory task during night sleep [4].

In addition, increased sleep spindle waves correlated with overnight retention in a declarative word-to-associate task [5]. In contrast, Rasch et al. [6] observed a positive correlation between improved performance on a procedural finger-tapping task and spindle wave activity at night, when REM sleep was pharmacologically suppressed. However, whether this correlation is caused by
the implicit or explicit elements of this task remains unclear.

Sleep spindles are reported to be related to slow oscillations observed during Stages 3 and 4 [7]. Many studies of brain networks have used the functional connectivity method, which considers each single connectivity between brain regions. This method does not depend on how neurons connect to the brain region. Furthermore, this method depends on how the functions of each brain region are connected to one another. In a study using functional connectivity, phase synchronization of the alpha band is related to front-parietal network activity observed with fMRI. Many studies have been conducted to examine brain networks using brain information such as EEG [8–11]. Previous research also evaluated brain networks during sleep using graph theoretical analysis. The results revealed that clustering coefficients increased significantly from wakefulness to sleep, indicating that the graph theory may be able to characterize brain network activity during sleep [12]. However, the details of the brain network activity in each sleep stage remain unclear. In this study, we measured sleep EEG and then calculated the brain network activity using the graph theoretical method. We then compared the brain network properties in individual sleeping stages.

2. Methods

2.1 Participants and apparatus

In this study, EEG was measured in ten subjects (age: 22–24 years) during sleep at night using waveguard connect (eemagine Medical Imaging Solutions GmbH, Germany) and PolymateV (Miyuki Giken Co., Ltd., Japan). Nineteen Sn (tin) electrodes (Fp1, Fp2, F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, O1, O2) were attached to the head according to the international 10–20 method. The reference electrode was the CPz. The subjects were asked to wear an EEG cap, and the electrodes were subsequently placed on the cap. An experimenter was in charge of attaching the electrodes during EEG data measurement. Before recording the data, impedance of the electrodes was monitored and whether there was any noise in the waveform was checked. Measurement was started if there was no problem. This study was conducted in accordance with the ethical principles of Kyushu University (ID: 2021–14) and the Declaration of Helsinki. We first explained about the experiment to the subjects, and then obtained informed consent from them. The sampling frequency was 500 Hz. All electrodes were placed in such a way that the impedance was less than 10 KΩ. The subjects were asked to sleep in a bed in a simple shielded room at night. Then, the EEG was measured during sleep.

2.2 Sleep scoring

We identified the sleep stages by visually checking the EEG data during sleep, according to standard criteria [13]. The characteristics of each sleep stage are as follows.

Stage 1: Low amplitude alpha, theta, and beta waves appear, and vertex sharp waves emerge.

Stage 2: K-complex and sleep spindle (13–15 Hz) are observed.

Stage 3: Slow waves occupy 20–50% of the time in 30 seconds.

Stage 4: Slow waves occupy more than 50% of 30 seconds.

In order to discriminate between non-REM and REM sleep, we excluded from the analysis REM sleep in the range where slow waves suddenly disappeared from Stage 3–4 and high frequency signals such as alpha waves appeared, based on the sleep cycle period of 90 minutes. Then, we re-analyzed the data as Stage 1 (non-REM) when more than 90 minutes passed from the beginning of Stage 1 in the cycle. To discriminate between sleep and wakefulness, subjects were instructed prior to the start of the experiment to report when they were awake.

Considering the characteristics of sleep EEG, Stage 1 was classified as light sleep, Stage 2 as middle sleep, and Stages 3 and 4 as deep sleep.

In this study, EEG data of three out of ten patients could not be classified into sleep stages due to noise and other factors; they were excluded from the analysis.

2.3 EEG pre-process

The EEG data were analyzed using MATLAB (MathWorks Natick, USA) embedded with Brainstorm [14] and Brain Connectivity Toolbox [15]. The EEG data were visually classified into sleep Stages 1 to 4. For each sleep stage, characteristic waves were extracted for 5 seconds each to create 60 epochs. Hence, 60 epochs with a time window of 5 seconds were extracted from the EEG data of 300 seconds (5 minutes) in each stage, and analyzed. The epochs for each sleep stage were extracted according to the characteristics described in 2.2.

In order to analyze the effect of the presence or absence of sleep spindle waves, 60 epochs with a time window of 0.5 seconds each were extracted from EEGs with and without sleep spindle waves during Stage 2. Then, the effect of sleep spindle waves was analyzed from the data of 30 seconds under each condition, or a total of 60 seconds.

2.4 Brain network analysis

We analyzed EEG using the graph theory. In this method, a network is represented as a graph constructed from
nodes connected by edges. In this study, functional connectivity was used as an edge. Furthermore, we used the phase-locking value (PLV) as an edge, which is also a method of functional connectivity. At each stage, the average PLV for each epoch was calculated for several frequency bands. The frequencies were divided into the following bands: delta (2–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), LowBeta (13–15 Hz), UpperBeta (15–30 Hz), Gamma1 (30–58 Hz), and Gamma2 (62–90 Hz). Only the nodes in the top 30% of the average PLV in each stage were retained as functional networks (define as base network). Then, the clustering coefficient and characteristic path length were calculated using the Brain Connectivity Toolbox to compare the network between sleeping stages. Then, to calculate small-worldness, 100 random networks were generated from the network displayed by EEG during sleep (define as random network). Then, we calculated the clustering coefficient and characteristic path length in each random network. Furthermore, small-worldness was calculated from the clustering coefficient and characteristic path length of the random network.

2.5 Statistical analysis
To analyze the qualities of network properties in the sleeping stages for each frequency band, one-way ANOVA was used to compare four network indices (clustering coefficient, characteristic path length, ratio of clustering coefficient between random network and base network, and ratio of characteristic path length between random network and base network) between sleeping stages (Stage 1 to Stage 4) in each frequency band. Then, t-test was performed on each network index between sleeping stages. After Bonferroni adjustment, p level was set at 0.05/6 = 0.00833.

In order to compare spindle effects in Stage 2, we extracted EEGs with spindle and those without spindle from Stage 2 data. Then, we applied t-test to compare between the two spindle status.

3. Theory
3.1 Functional Connectivity
Functional connectivity is a method used to investigate the functional connections between two regions. This method does not focus on how two regions are connected through direct nerve coupling or connections between a plurality of regions. Rather, this method focuses on how the two regions share functional properties.

The premise of functional connectivity is that activities synchronized in time are seen in these areas if they are coordinated with the execution of tasks between regions; these activities will then correlate highly with respect to time change.

Therefore, statistical tests such as t-test and z-test are employed to compare the brain network activities to determine the level of significance. Functional connectivity was developed to provide a new indicator of brain region activity.

3.2 Phase locking value
The PLV is a method of examining the extent to which the phase of a signal is synchronized between two regions. The PLV equation is shown as follows (1) [16]:

$$PLV_i = \frac{1}{N} \sum_{n=1}^{N} \exp (j \theta(t,n))$$

where $N$ is the number of total trials; and $\theta(t,n)$ is the phase difference $|\phi_1(t,n) - \phi_2(t,n)|$ between two signals at time $t$.

If the phase difference between two signals is constant, PLV will be close to 1. if the phase difference between two signals is not constant, PLV will be close to 0.

3.3 Clustering coefficient
The clustering coefficient is a number calculated based on the number of triangles in a network; it is the simplest measure of functional separation in a network. Locally, the clustering coefficient is the percentage of neighbors that are connected to a particular contact point (a neighbor).

The clustering coefficient of the entire network is the average of the clustering coefficients of individual contacts. It can range from 0 to 1, with higher values indicating a more separated network. Furthermore, it can also be calculated using the following equations:

$$C^w_i = \frac{1}{n} \sum_{n \in N} \frac{2t^w_i}{k_i(k_i-1)}$$  \hspace{1cm} (2)

$$t^w_i = \frac{1}{2} \sum_{j \in N} \left( W_{ij}W_{ik}W_{jk} \right)^{\frac{1}{2}}$$  \hspace{1cm} (3)

$$k_i = \sum_{j \in N} a_{ij}$$  \hspace{1cm} (4)

where $N$ is the number of nodes in the network. In this study, $N$ is the number of electrodes; $t^w_i$ is the number of triangles around the node $i$; and $W_{ij}$ is the connection weight between nodes $i$ and $j$. Moreover, we used the PLV as the connection weight $k_i$ which is the degree of node $I$; and $a_{ij}$ is the connection status between nodes $i$ and $j$.

3.4 Characteristic path length
The characteristic path length is the average of the shortest path lengths of all contact combinations. It is often used as an indicator of the functional integration of a network, where a smaller value indicates a more integrated network. Functional integration is the ability to quickly combine specific information from widely distributed
brain regions. It is calculated using the following formula:

\[ L^W = \frac{1}{n} \sum_{i \in N} \sum_{j \in N} d^w_{ij} \frac{1}{n-1} \]  

(5)

\[ d^w_{ij} = \min_{i \neq j} \{ g_{w_{ij}} \} \]

(6)

where \( d^w_{ij} \) is the shortest weighted path length between nodes \( i \) and \( j \); \( f(W_{uv}) \) is a map from weight to length; and \( g_{w_{ij}} \) is the shortest path length between nodes \( i \) and \( j \).

3.5 Small-worldness

A small-world network is defined as a network that is predominantly clustered over a random network, yet maintains the same level of characteristic path length as a random network. Small-worldness is assessed from normalized clustering coefficient and normalized characteristic path length. These two factors are calculated using the following formulae:

\[ \text{Normalized CC} = \frac{C}{C_{\text{random}}} \]  

(7)

\[ \text{Normalized CPL} = \frac{L}{L_{\text{random}}} \]  

(8)

where \( C_{\text{random}} \) is the clustering coefficient calculated from a random network; \( L_{\text{random}} \) is the characteristic path length calculated using a random network. If the values of \( C/C_{\text{random}} \) and \( L/L_{\text{random}} \) are both close to 1, it is a random network. On the other hand, if the value of \( C/C_{\text{random}} \) is much higher than 1 and \( L/L_{\text{random}} \) is close to 1, it is a small-world network. If the values of \( C/C_{\text{random}} \) and \( L/L_{\text{random}} \) are both higher than 1, it is an ordered network.

4. Results

4.1 Subject parameters and behavior results

The mean age of the seven subjects analyzed in this study was 28.286 (SD: 0.951) years; the mean sleep duration of the seven subjects was 6.962 (SD: 1.185) h. The percentage of each sleep stage judged by visual inspection was 38.07 ± 10.91% for Stage 1, 44.61 ± 10.78% for Stage 2, 9.16 ± 3.41% for Stage 3, and 8.17 ± 6.15% for Stage 4.

4.2 Results of clustering coefficient

Figure 1 shows a plot of the mean clustering coefficients for various frequency bands. Statistical analysis by ANOVA showed that there was no significant difference among the four stages for each frequency band.

4.3 Results of characteristic path length

Figure 2 shows a plot of the mean characteristic path lengths for various frequency bands. Overall, the characteristic path length decreased in middle and deep sleep, especially in the LowBeta frequency band. The ANOVA results showed a significant difference between Stage 1 and the other stages (\( p \leq 0.00833 \)). In the UpperBeta band, ANOVA showed a significant difference between Stage 1 and Stage 2 or 3 (\( p \leq 0.00833 \)). In Stage 1, both LowBeta and UpperBeta showed the same level of characteristic path length; however, as sleep became deeper, a greater decrease in characteristic path length in LowBeta band was observed.

4.4 Analysis of small-worldness

Small-worldness is calculated from the ratio of the clustering coefficient and characteristic path length, which is calculated from the base and random networks generated by the network.

Figure 3 shows the ratios of the clustering coefficient of the base network to the clustering coefficient of the random network. Statistical analysis by ANOVA showed no significant difference among stages for each frequency band.

Figure 4 shows the ratios of the characteristic path length of the base network to that of the random network. The results showed a decrease in the ratio in Stages 2 to 4 when sleep became deeper, compared to Stage 1 when sleep was shallow, especially in the LowBeta band. Statistical analysis by ANOVA showed a significant difference (\( p \leq 0.00833 \)) in the ratio between Stage 1 and Stages 2 to 4 in LowBeta band.

4.5 Analysis of spindle effect

Figure 5 shows a plot of mean clustering coefficients...
when spindle was present and when spindle was absent. Statistical analysis by ANOVA showed significant differences in theta, LowBeta and UpperBeta frequency bands ($p \leq 0.05$). Clustering coefficient was higher in the absence of spindle than in its presence in theta band, while clustering coefficient was lower in the absence of spindle than in its presence in LowBeta and UpperBeta bands.

Figure 6 shows a plot of mean characteristic path lengths when spindle was present and when spindle was absent. Statistical analysis by ANOVA showed significant differences in LowBeta and UpperBeta bands ($p \leq 0.05$). Characteristic path length was higher in the absence of spindle than in its presence in LowBeta and UpperBeta bands.

Figure 7 compares the ratios of the clustering coefficient of the base network to the clustering coefficient of the random network between the presence and the absence of spindle. Statistical analysis by ANOVA showed significant differences in LowBeta and UpperBeta bands ($p \leq 0.05$). $C/C_{random}$ was much higher in the absence of spindle state than in its presence in LowBeta and UpperBeta bands.

Figure 8 compares the ratios of the characteristic path length of the base network to the characteristic path length of the random network between the presence and the absence of spindle. Statistical analysis by ANOVA showed significant differences in theta, LowBeta, and UpperBeta bands ($p \leq 0.05$). $L/L_{random}$ was much higher in the absence of spindle state than in its presence in theta, LowBeta, and UpperBeta bands.
et al. [23] reported a correlation between small-worldness and cognitive functions. Furthermore, Vecchio healthy subjects, which may indicate that the integration of impaired memory and cognitive functions compared to these results are contradictory, it has been reported that healthy subjects [19–22]. Although healthy subjects [17, 18]. On the contrary, other studies characteristic path lengths in AD patients compared to healthy subjects also seen in Stage 2 to Stage 4. Koenis et al. [26] reported that sleep deprivation affected C/Crandom and L/Lrandom during eyes-closed.

5. Discussion

In this study, we conducted a detailed network analysis in the four sleep stages. The results showed that the path length in LowBeta band (13–15 Hz) decreased as sleep became deeper. Moreover, Stage 2 is characterized by having the smallest path length and the appearance of spindles, which are waves around 14 Hz. Previous studies have suggested that sleep spindle waves are related to memory enhancement during sleep. Therefore, the results obtained in this study may reflect the functional integration of the network linked to any brain activity related to sleep spindle. In a previous study that calculated the clustering coefficient and characteristic path length during wakefulness, light sleep, and deep sleep, a decrease in the clustering coefficient and an increase in the characteristic path length from wakefulness to light and deep sleep were reported [17]. This result shows the opposite trend to that of our results. A possible reason for this is that in this study, the network was constructed with the top 30% of functional connectivity as nodes. The analysis was not focused on a specific frequency in previous research.

Several studies have compared the path lengths between healthy subjects and patients with Alzheimer’s disease (AD). Some of these studies revealed decreased characteristic path lengths in AD patients compared to healthy subjects [17, 18]. On the contrary, other studies showed increased characteristic path lengths in AD patients compared to healthy subjects [19–22]. Although these results are contradictory, it has been reported that changes in path lengths are observed in AD patients with impaired memory and cognitive functions compared to healthy subjects, which may indicate that the integration of brain networks is promoted or inhibited in relation to memory and cognitive functions. Furthermore, Vecchio et al. [23] reported a correlation between small-worldness and performance of short-term memory. They found a positive correlation between small-worldness in gamma band (30–45 Hz) and performance of digit span task both forward and backward. This result is consistent with other previous reports that oscillatory neural activity in gamma band (> 30 Hz) is involved in some cognitive functions including memory [24]. In another study, Dai et al. [25] investigated the EEG-based cortical brain network during working memory task (2-back task) and control task (0-back task) using graph theoretical analysis. They found that normalized characteristic path length in theta band (4–7 Hz) was significantly lower during working memory task than during control task, while clustering coefficient in alpha band (8–12 Hz) was significantly lower during working memory task than during control task. These findings suggested improvement of brain network efficiency for propagation of information on the network. Therefore, they demonstrated the potential of using brain network metrics as biomarker for predicting the task performance during working memory task. From these previous research, network metrics such as small-worldness and characteristic path length are useful for the analysis of brain network activity in memory process. Therefore, decreases in characteristic path lengths in LowBeta band during sleep may indicate that the consolidation of brain networks related to memory enhancement is based on the characteristics of the sleep spindle and the previous assumption. Ferri et al. [12] found that during sleep, the brain exhibits a small-world network-like structure. They used the following definitions. If the values of C/Crandom, L/Lrandom are both close to 1, it is a random network. On the other hand, if the value of C/Crandom is much higher than 1 and L/Lrandom is close to 1, it is a small-world network. If the values of C/Crandom, L/Lrandom are both higher than 1, it is an ordered network. They reported that the network calculated from slow-wave EEG during sleep constitutes a small-world network.

In the present study, in delta band, C/Crandom was higher in Stage 2 to Stage 4 than in Stage 1, although there was no significant difference. Moreover, L/Lrandom had similar values in all the stages. Therefore, in delta band, the deeper the sleep, the more the structure of the brain network becomes a small-world-like network. This result supports the results of a previous study showing that small-world networks are constructed during slow-wave sleep [12].

In LowBeta band, C/Crandom decreased from Stage 1 to Stages 2 – 4, but there were no significant differences. Decreases in L/Lrandom were also seen in Stage 2 to Stage 4, with significant differences between Stage 1 and Stages 2 to 4. Koenis et al. [26] reported that sleep deprivation affected C/Crandom and L/Lrandom during eyes-closed.
and eyed-open resting states, inducing a more random network in alpha band and a more ordered network in gamma band. This result suggests that sleep can affect $C/C_{random}$ and $L/L_{random}$ in the brain network. In our study, significant differences in $L/L_{random}$ between Stage 1 and Stages 2 to 4 were obtained. This result may suggest that the functional brain network in LowBeta band is more integrated during middle and deep sleep. Also, the network becomes a more small-world network in middle and deep sleep compared to light sleep. These results indicate the possibility that the depth of sleep affects the integration of brain networks. Also, in LowBeta and UpperBeta bands, significant differences in all the graph theoretical metrics were observed between the presence and absence of spindle in Stage 2. While sleep spindle appears, the brain is more segregated in function, building a more integrated network. Therefore, these results may suggest that the brain generates efficient brain network through sleep spindles in Stage 2. Considering the role of sleep spindle from previous studies and these results, the efficiency of the network in which the spindles appear is related to the roles of the spindles, such as memory enhancement, and the results in Stage 3 and Stage 4 may be due to similar activities.

However, in this study, tasks related to cognitive function and memory were not performed before and after sleep. Thus, whether the results of this study truly reflect changes in the network due to the functioning of memory and cognition during sleep cannot be discussed with certainty. Furthermore, in this study, we tried to extract non-REM sleep EEG from sleeping EEG upon considering 90 min as the duration of one sleep cycle. However, we did not measure EOG or EMG. Therefore, the lack of discrimination between non-REM and REM sleep using EOG and EMG, and the lack of reliability in the extraction of non-REM sleep are limitations of this study.

6. Conclusion

In this study, to clarify the brain network activity, we performed a detailed brain network analysis in the four sleep stages using EEG. In LowBeta band, which is the same frequency range as the sleep spindle associated with memory enhancement, there was a significant reduction in the characteristic path length in middle and deep sleep compared to light sleep. These results suggest that the brain network may be integrated in middle and deep sleep by sleep spindles, suggesting that graph theoretical analysis is useful for studying fine network activity during sleep, as seen on EEG. However, the relationship between memory consolidation and integration of the brain network remains unclear.

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Conflicts of interest

The authors have no conflicts of interest directly relevant to the content of this article.

References

1. Koshino H, Osaka M, Osaka N: Competition and cooperation among brain networks: Interactions between the default mode network and working memory network. Jpn Psychol Rev. 56(3), 376–391, 2013.
2. Rosanova M, Ulrich D: Pattern-specific associative long-term potentiation induced by a sleep spindle-related spike train. J Neurosci. 25(41), 9398–9405, 2005.
3. Pihlal W, Born J: Effects of early and late nocturnal sleep on priming and spatial memory. Psychophysiology. 36(5), 571–582, 1999.
4. Gais S, Mölle M, Helms K, Born J: Learning-dependent increases in sleep spindle density. J Neurosci. 22(15), 6830–6834, 2002.
5. Schabus M, Gruber G, Parapatics S, Sauter C, Klösch G, Anderer P, Klimesch W, Saletu B, Zeilhofer J: Sleep spindles and their significance for declarative memory consolidation. Sleep. 27(8), 1479–1485, 2004.
6. Rasch B, Pommer J, Dieckmann S, Born J: Pharmacological REM sleep suppression paradoxically improves rather than impairs skill memory. Nat Neurosci. 12(4), 396–397, 2009.
7. Klinzing JG, Mölle M, Weber F, Supp G, Hipp JF, Engel AK, Born J: Spindle activity phase-locked to sleep slow oscillations. Neuroimage. 134, 607–616, 2016.
8. Sadaghiani S, Scheeringa R, Leborgne K, Morillon B, Giraud A-L, D’Esposito M, Kleinschmidt A: Alpha-band phase synchrony is related to activity in the fronto-parietal adaptive control network. J Neurosci. 32(41), 14305–14310, 2012.
9. Wu L, Eichele T, Calhoun VD: Reactivity of hemodynamics responses and functional connectivity to different states of alpha synchrony: a concurrent EEG-fMRI study. Neuroimage. 52(4), 1252–1260, 2010.
10. Sasai S, Homae F, Watanabe H, Sasaki AT, Tanabe HC, Sadato N, Taga G: A NIRS-fMRI study of resting state network. Neuroimage. 63(1), 179–193, 2012.
11. Imperatori C, Della Marca G, Amoroso N, Maestos G, Valenti EM, Massullo C, Carbone GA, Contardi A, Farina B: Alpha/theta neurofeedback increases mentalization and default mode network connectivity in a non-clinical sample. Brain Topogr. 30(6), 822–831, 2017.
12. Ferri R, Rundo F, Bruni O, Terzano MG, Stam CJ: Small-world network organization of functional connectivity of EEG slow-wave activity during sleep. Clin Neurophysiol. 118(2), 449–456, 2007.
13. T. Hori, Y Sugita, E Koga, S Shirakawa, K Inoue, S Uchida, Kuwahara H, Kousaka M, Kobayashi T, Tsuji Y, Terashima M, Fukuda K, Fukuda N, Sleep Computing Committee of the Japanese Society of Sleep Research Society: Proposed supplements and amendments to ‘A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Sub-
jects’, the Rechtschaffen & Kales (1968) standard. Psychiatry Clin Neurosci. 55(3), 305–310, 2001.

14. Tadel F, Baillet S, Mosher JC, Pantazis D, Leahy RM: Brainstorm: A user-friendly application for MEG/EEG analysis. Comput Intell Neurosci. 2011, 879716, 2011.

15. Rubinov M, Sporns O: Complex network measures of brain connectivity: Uses and interpretations. Neuroimage. 52(3), 1059–1069, 2010.

16. Lachaux JP, Rodriguez E, Martinerie J, Varela FJ: Measuring phase synchrony in brain signals. Hum Brain Mapp. 8(4), 194–208, 1999.

17. Ferrer R, Rundo F, Bruni O, Terzano MG, Stam CJ: The functional connectivity of different EEG bands moves towards small-world network organization during sleep. Clin Neurophysiol. 119(9), 2026–2036, 2008.

18. Sanz-Arigita EJ, Schoonheim MM, Damoiseaux JS, Rombouts SAR, Maris E, Barkhof F, Philip S, Cornelis CJ: Loss of ‘small-world’ networks in Alzheimer’s disease: Graph analysis of fMRI resting-state functional connectivity. PLoS One. 5(11), e13788, 2010.

19. Tijms BM, Wink AM, de Haan W, van der Flier WM, Stam CJ, Scheltens P, Barkhof F: Alzheimer’s disease: connecting findings from graph theoretical studies of brain networks. Neurobiol Aging. 34(8), 2023–2036, 2013.

20. Stam CJ, Jones BF, Nolte G, Breakspear M, Scheltens P: Small-world networks and functional connectivity in Alzheimer’s disease. Cereb Cortex. 17(1), 92–99, 2007.

21. Stam CJ, De Haan W, Daffertshofer A, Jones BF, Manshanden I, van Cappellen Van Walsum AM, Montez T, De Munck JC, van Dijk BW, Berendse HW, Scheltens P: Graph theoretical analysis of magnetoencephalographic functional connectivity in Alzheimer’s disease. Brain. 132(1), 213–224, 2009.

22. He Y, Chen Z, Evans A: Structural insights into aberrant topological patterns of large-scale cortical networks in Alzheimer’s disease. J Neurosci. 28(18), 4756–4766, 2008.

23. Vecchio F, Miragliotta F, Quaranta Q, Granata G, Romanello R, Marra C, Bramanti P, Rossini PM: Cortical connectivity and memory performance in cognitive decline: A study via graph theory from EEG data. Neurosci. 316, 143–150, 2016.

24. Tallon-Baudry C, Bertrand O, Peronnet F, Pernier J: Induced $\gamma$-band activity during the delay of a visual short-term memory task in humans. J Neurosci. 18(11), 4244–4254, 1998.

25. Dai Z, Souza JD, Lim J, Ho PM, Chen Y, Li J, Thakor N, Bezerianos A, Sun Y: EEG cortical connectivity analysis of working memory reveals topological reorganization in theta and alpha bands. Front Hum Neurosci. 11, 1–13, 2017.

26. Koenis MMG, Romeijn N, Piantoni G, Verweij I, Van Der Werf YD, Van Someren EJW, Stam CJ: Does sleep restore the topology of functional brain networks? Hum Brain Mapp. 34(2), 487–500, 2013.

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