Graph Theoretical Analysis of Cortical Networks based on Conscious Experience

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7 authors, including:

Minji Lee
Korea University

Benjamin Baird
University of Wisconsin–Madison

Olivia Gosseries
University of Liège

Jaakko O. Nieminen
Aalto University

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Minji Lee, Benjamin Baird, Olivia Gosseries, Jaakko O. Nieminen, Melanie Boly, Giulio Tononi, and Seong-Whan Lee

Abstract— **The aim of the study was to investigate differences in cortical networks based on the state of consciousness. Five subjects performed a serial-awakening paradigm with electroencephalography (EEG) recordings. We considered four states of consciousness: (1) non-rapid eye movement (NREM) sleep with no conscious experience, (2) NREM sleep with conscious experience, (3) rapid eye movement (REM) sleep with conscious experience, and (4) wakefulness. We applied graph theoretical analysis to explore the cortical connectivity and network properties in five frequency bands. Connectivity between EEG channels was evaluated with the weighted phase lag index (wPLI). The characteristic path length, transitivity, and clustering coefficient were computed to evaluate functional integration and segregation of the associated brain network. There were no significant differences in wPLI among the four states of consciousness. In the beta band, functional integration in wakefulness was higher than in NREM sleep. Regarding functional segregation, in the theta band, transitivity and clustering coefficient in NREM sleep with no conscious experience were stronger than in wakefulness or REM sleep, but clustering in the beta band showed an opposite effect. The observed differences may be related to cortical bistability and add to previously observed neural correlates of consciousness.**

I. Introduction

The neural correlates of consciousness are not fully understood [1]. Although dreaming has been traditionally thought to happen only in rapid eye movement (REM) sleep where people dream over 80% of the time [2], dreaming also happens in non-rapid eye movement (NREM) sleep, in the order of about 60% of the time [3-4]. Specifically, dreams in NREM sleep are less extraordinary in vividness, quantity, and emotion compared to those in REM sleep [5]. Therefore, in recent years, researchers have not considered NREM sleep as unconsciousness but focused on features with or without conscious experience during NREM sleep.

A serial-awakening paradigm is a way to characterize the conscious experience during sleep [6]. Recently, several studies have applied this method to investigate the neural correlates of consciousness. During NREM and REM sleep, reports of conscious experience have been related to local decreases in low-frequency activity as evaluated with electroencephalography (EEG) [3]. In contrast, reports of conscious experience have been associated with increased high-frequency activity compared to reports of no dream experience [3]. In addition, transcranial magnetic stimulation (TMS) evokes a smaller negative deflection and a longer phase-locked response in relation to reports of conscious experience during NREM sleep compared to reports of no conscious experience [4]. However, differences in connectivity between EEG channels based on conscious experience during sleep remain to be explored. In addition, it is not yet clear which spatial and spectral characteristics relate to consciousness. Some studies have focused on differences in the frontal region in the levels of consciousness [7], whereas other studies have highlighted consciousness-related differences in the parietal region [3-4, 8-9]. Despite the breakdown of brain connectivity during unconsciousness [10], connectivity in the delta band has been shown to increase during propofol-induced unconsciousness [9].

In this study, we investigated differences in cortical networks based on conscious experiences in NREM and REM sleep and wakefulness using TMS–EEG and graph theoretical analysis. This analysis can be used to study brain complexity by mathematically quantifying network properties and thus suits for characterizing changes in the connectivity of brain networks as observed by TMS–EEG [11].

II. Methods

A. Data Acquisition and Preprocessing

The TMS–EEG data are from a previous study [4]. Six healthy subjects participated in the original study, but in one subject, reports of conscious experience during REM sleep were hardly measured. Thus, we analyzed TMS–EEG data of only five subjects. The study was approved by the University of Wisconsin Human Subjects Committee and all subjects gave their written informed consent.

Subjects performed a serial-awakening paradigm [6] in the course of 4–5 overnight sessions. When a subject had been in a specific sleep stage for more than 3 min, the medial superior parietal cortex was stimulated with TMS. Subjects were awakened after each such TMS session to report whether they had had a conscious experience (dreaming). The sleep stages

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M. Lee and S.-W. Lee are with the Department of Brain and Cognitive Engineering, Korea University, 145, Anam-ro, Seongbuk-gu, Seoul 02841, Republic of Korea (corresponding author to provide e-mail: sw.lee@korea.ac.kr).

B. Baird, M. Boly, and G. Tononi are with the Department of Psychiatry, University of Wisconsin, Madison, Wisconsin 53719, USA.

O. Gosseries is with GIGA-Consciousness & Coma Science Group, University and University Hospital of Liege, Liege 4000, Belgium.

J. O. Nieminen is with the Department of Neuroscience and Biomedical Engineering, Aalto University School of Science, Espoo 02150, Finland.

TABLE I. NUMBER OF TRIALS FOR THE STATES OF CONSCIOUSNESS

Subject	State of Consciousness			
	NREM–NCE	***NREM–CE***	***REM–CE***	***WFN***
1	243	230	83	240
2	175	90	70	182
3	163	133	108	236
4	104	285	82	261
5	142	257	111	192

were scored in accordance with the AASM criteria [12]. We divided the data into four states of consciousness: (1) no conscious experience during NREM sleep (NREM–NCE), (2) conscious experience during NREM sleep (NREM–CE) (with or without the recall of contents), (3) conscious experience during REM sleep (REM–CE), (4) wakefulness (WFN). In our study, there were only a few awakenings with no conscious experience during REM sleep; thus, this state was excluded. Table I shows the individual number of trials after cleaning.

EEG was measured with a 60-channel TMS-compatible amplifier (Nexstim eXimia, Nexstim Plc; 1450-Hz sampling rate). The data were processed using MATLAB 2017a. TMS-induced artifacts were removed by interpolating the first 15 ms of the signals after TMS; other artifacts, e.g., those due to eye movements, were rejected. The data were bandpass filtered (1.5–50 Hz), down-sampled to 362.5 Hz, epoched to −400–400 ms, and baseline-corrected (from −400 to 0 ms). Also, the bad channels were interpolated and the EEG data were average-referenced.

We studied five frequency bands: delta (1.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–45 Hz). A frontal region was defined as 6 channels (Fp1, Fpz, Fp2, AF1, AFz, and AF2) and a parietal region as 7 channels (PO3, POz, PO4, O1, Oz, O2, and lz).

B. Connectivity Estimation

The weighted phase lag index (wPLI) [13] was used as a connectivity measure between pairs of channels. It was calculated as changes in phase-synchronization to reduce the impact of volume conduction and the number of artifacts:

$$\mathrm{wPLI} = \frac{|E\{\Im\{X\}\}|}{E\{|\Im\{X\}|\}} = \frac{|E\{|\Im\{X\}|\mathrm{sgn}(\Im\{X\})\}|}{E\{|\Im\{X\}|\}} \qquad (1)$$

where $\Im\{X\}$ indicates the imaginary component of the cross-spectrum $X = Z_i Z_j^*$ between channels i and j, Z_i is the complex-valued Fourier transform of the signal of channel i, Z_j^* is the complex conjugate of Z_j, and $E\{\cdot\}$ means the expected-value operator.

C. Graph Theoretical Analysis

Figure 1 shows the analytic flow. The wPLI matrices were calculated for the five frequency bands. The data were thresholded at the 0.3023 density to discard false positives and maintain strong connections. This density was computed by the maximum value of the difference between the global and local efficiency of 1000 random graphs with 60 nodes [14].

The network properties were calculated using the Brain Connectivity Toolbox [15]. We computed the characteristic path length (CPL), transitivity, and clustering coefficient (CC) for functional integration and segregation based on wPLI. We selected these properties because they are the most basic measures to quantify network complexity [15].

The CPL is the mean shortest path length between all pairs of nodes in a network and measures its integration:

$$\mathrm{CPL} = \frac{1}{N}\sum_{i\in N} L_i = \frac{1}{N}\sum_{i\in N}\frac{\sum_{j\in N, j\neq i} d_{ij}}{n-1} \qquad (2)$$

where d_{ij} is the shortest path length between nodes i and j, L_i the mean distance between node i and all other nodes [16], N the number of all nodes in the network, and n the number of individual nodes. Low CPL means that network integration is high in the sense that the path lengths are short.

The CC represents the fraction of triangles around a node. It indicates clustered connectivity around individual nodes:

$$\mathrm{CC} = \frac{1}{n}\sum_{i\in N} C_i = \frac{1}{N}\sum_{i\in N}\frac{2t_i}{k_i(k_i-1)} \qquad (3)$$

where t_i represents the number of triangles around node i, k_i is the number of connections linked to node i, and C_i is the clustering coefficient of node i.

The transitivity T can be interpreted as a measure of segregated or localized processing in all pairs of nodes as a classical variant of the CC. In other words, it represents the ratio of triangles to triplets to the total number of node triplets:

$$T = \frac{\sum_{i\in N} 2t_i}{\sum_{i\in N} k_i(k_i-1)} \qquad (4)$$

In contrast to the CC, transitivity is a global measure of a network [15]. High transitivity and clustering coefficient indicate active local processing and high segregation.

D. Statistical Analysis

We used a Kruskal–Wallis test (non-parametric analysis of variance) across the four states of consciousness. For post-hoc analysis, a non-parametric permutation test was used (r =

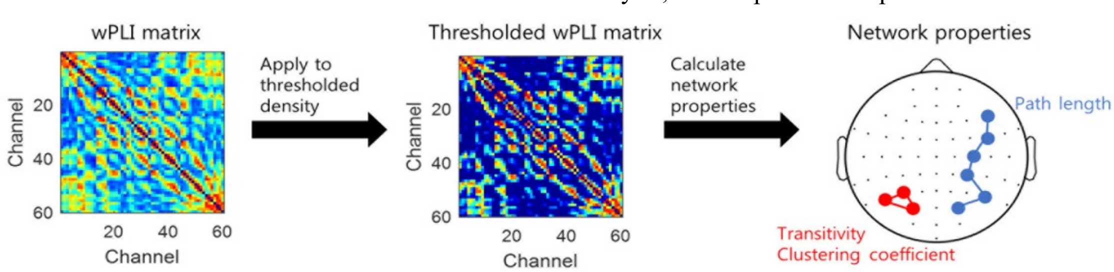

Figure 1. Pipeline in graph theoritical analysis. Based on wPLI matrix (connectivity estimator), network properties were calculated. The blue property in network represents the example path for measure of integration, whereas red property represents the example of node triplets for the measure of segregation.

1,000) between the states. In addition, Bonferroni correction was applied (five frequency bands). Results were considered statistically significant at the level α = 0.05.

III. Results

A. Connectivity based on wPLI

Table II summarizes the statistical results on the difference of wPLI for four conscious states (NREM–NCE, NREM–CE, REM–CE, and WFN) during sleep. Using Kruskal–Wallis test, the beta wPLI over the frontal and parietal regions significantly differed across the four states of consciousness, but there was no significance between the conscious states for the post-hoc analysis. In addition, no significant differences in wPLI between the states of consciousness in frontal or parietal regions were investigated at other frequency bands ($p > 0.05$ with Bonferroni correction).

B. Functional Integration and Segregation

In the CPL in the delta band, differences among the four conscious states were found, but there was no significant difference between two conscious states in a post-hoc test. The CPL in the beta band in WFN was higher than in NREM–NCE and NREM–CE when the frontal and parietal regions were analyzed together. In addition, the transitivity in NREM–NCE was higher than in REM–CE and WFN in the theta band.

TABLE II. Statistical Results of wPLI

Region	Statistical value	Frequency band				
		Delta	*Theta*	*Alpha*	*Beta*	*Gamma*
Frontal region	*F*-value	2.79	4.99	6.48	10.5	4.22
	P-value	0.42	0.17	0.09	0.01*	0.24
Parietal region	*F*-value	3.66	4.45	5.4	10.13	0.71
	P-value	0.30	0.21	0.14	0.02*	0.86

TABLE III. Statistical Results of Network Properties

Network property	Statistical value	Frequency band				
		Delta	*Theta*	*Alpha*	*Beta*	*Gamma*
CPL[a]	*F*-value	7.94	5.17	4.35	14.01	4.92
	P-value	0.047*	0.16	0.23	0.002*	0.18
Transitivity	*F*-value	3.23	11.23	4.83	4.14	4.92
	P-value	0.35	0.011*	0.18	0.27	0.18
CC[b]	*F*-value	6.93	5.97	5.22	2.66	7.71
	P-value	0.07	0.11	0.16	0.45	0.052

a. clustering path length, b. clustering coefficient

TABLE IV. Statistical Results of Clustering Coefficient in Frontal and Parietal Regions

Region	Statistical value	Frequency band				
		Delta	*Theta*	*Alpha*	*Beta*	*Gamma*
Frontal region	*F*-value	5.54	2.02	2.95	7.79	2.90
	P-value	0.14	0.57	0.40	0.052	0.42
Parietal region	*F*-value	4.27	9.15	0.10	10.53	0.62
	P-value	0.23	0.027*	0.99	0.014*	0.89

However, we found no significant interactions in CC among the four states of consciousness (Fig. 2 and Table III).

To investigate local processing in brain networks, we explored CC at the frontal and parietal regions, although there was no difference in CC in the whole region. There were no significant differences in the frontal region. However, in the theta band, CC in WFN was lower than in NREM–NCE and NREM–CE over the parietal region. In addition, the theta-band CC in NREM–NCE was higher than in REM–CE over the parietal region. There was lower beta-band CC in NREM–NCE compared to REM–CE and WFN over the

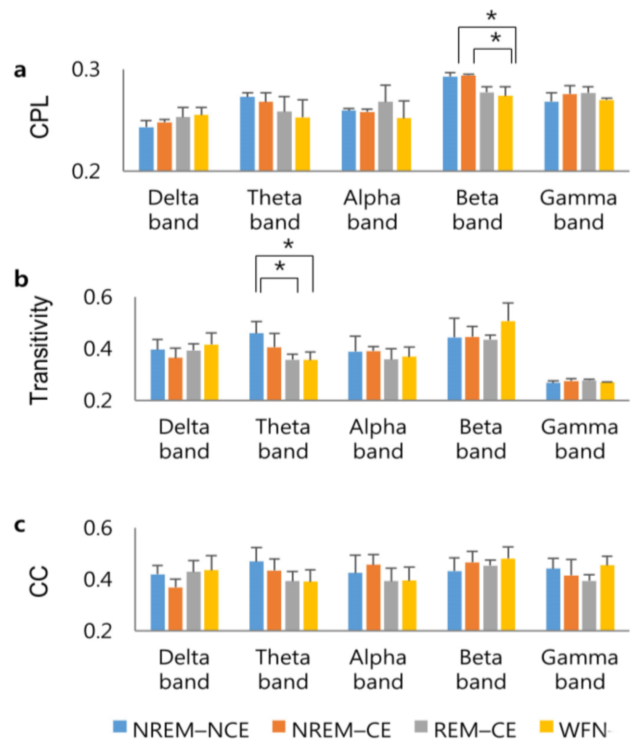

Figure 2. Network properties in the whole region. (a) characteristic path length, (b) transitivity, and (c) clustering coefficient. Error bars indicate standard deviation across subjects. * indicates a significant difference ($p < 0.05$) with Bonferroni correction.

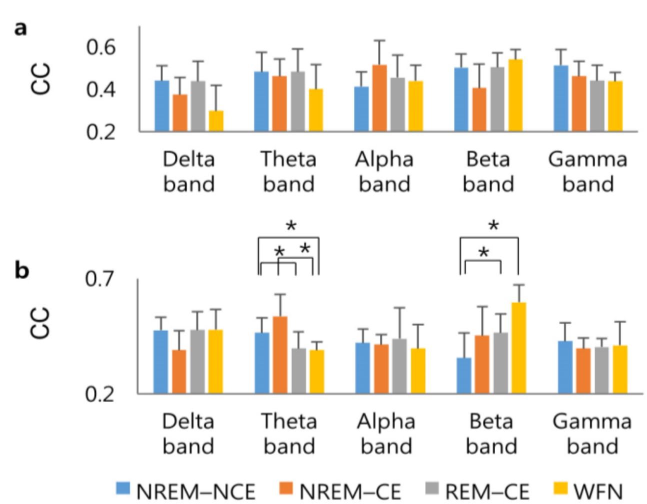

Figure 3. Clustering coefficient in the (a) frontal and (b) parietal region. Error bars indicate standard deviation across subjects. * indicates $p < 0.05$ with Bonferroni correction.

parietal region. Figure 3 and Table IV show these results.

IV. Discussion and Conclusion

We investigated cortical networks based on conscious experience during sleep and wakefulness. We found no significant differences in wPLI, but the network properties related to functional integration and segregation could distinguish four conscious states.

We observed that in the beta band CPL (measure of integration) in WFN was higher than in NREM–NCE or NREM–CE. Similar results were found in a study comparing only two conscious states (wakefulness vs. sleep) [16]. This increase in CPL in unconsciousness is possibly because the flow of information is not smooth due to the collapse of connections between regions. In line with the present findings, NREM sleep is associated with the breakdown of cortical connectivity and disconnection of brain networks [8-9]. In particular, a difference in the beta-band network may relate to conscious mentation [17]. This supports that the breakdown of connectivity in a high-frequency network may be evident during sleep. We also found a statistically significant difference in transitivity (a global indicator for measure of segregation) in the theta band. This network characteristics of low frequencies are likely caused by bistability, which is the occurrence of a down-state of cortical neurons [4]. This bistability is known to be important in consciousness; because it interferes with the efficiency of the recurrent process among cortical regions [3].

We investigated spatial differences through CC for local processing in the segregation of network. The difference between the states of consciousness in the parietal region was more evident than the difference in the frontal region. These results can be explained by the posterior hot zone associated with the neural correlates of consciousness [8]. Local processing in the theta network was more active in NREM–NCE compared with REM–CE and WFN, whereas in the beta-band network, local processing was more active in REM–CE and WFN compared to NREM–NCE over the parietal region. In addition, this result is consistent with a previous finding that the flow of information is higher in unconsciousness at low frequencies, but reversed at high frequencies [9].

Some studies claim that the delta network associated with slow wave activity in NREM sleep is a key indicator of consciousness [3, 9]. However, no significant differences for delta, alpha, or gamma band were observed in this study. In the future, it is necessary to explore the exact conscious mechanisms within the same physiological state to investigate delta, alpha, and gamma networks.

Our research has some limitations. The number of subjects is small. Therefore, our results are difficult to generalize. In addition, we did not classify the four conscious states based on network properties. Since the wPLI itself was an averaged measure of all trials in one subject, these features are not suitable for classification. Future studies should study EEG data of a larger population and investigate which of the network properties could be potential indicators for distinguishing (un)conscious states.

In conclusion, we distinguished functional networks across four conscious states. Our findings suggest that the network properties related to functional integration and segregation have the potential to distinguish the levels of consciousness.

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