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Statistical network analysis for epilepsy MEG data

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Abstract

Brain network analysis has attracted the interest of neuroscience researchers in studying brain diseases. Magnetoencephalography (MEG) is especially proper for analyzing functional connectivity due to high temporal and spatial resolution. The application of graph theory for functional connectivity analysis has been studied widely, but research on network modeling for MEG still needs more. Temporal exponential random graph model (TERGM) considers temporal dependencies of networks. We performed the brain network analysis, including static/temporal network statistics, on two groups of epilepsy patients who removed the left (LT) or right (RT) part of the brain and healthy controls. We investigate network differences using Multiset canonical correlation analysis (MCCA) and TERGM between epilepsy patients and healthy controls (HC). The brain network of healthy controls had fewer temporal changes than patient groups. As a result of TERGM, on the simulation networks, LT and RT had less stable state than HC in the network connectivity structure. HC had a stable state of the brain network.

Keywords: brain network, epilepsy, MCCA, MEG, TERGM

1. Introduction

The brain is an essential organ in our body that controls brain activities such as emotion and memory. The brain maintains human life activities by constructing a complex neural network between neurons and communicating with the brain electrical signals. The graph theory of neuroscience can provide valuable insights into the structural and functional organization of neural networks. Due to the brain's structural and functional systems as complex networks, the quantitative analysis of complex networks, based largely on graph theory, has been rapidly increasingly translated to studies of brain network organization as a characteristic of brain disease (Bullmore and Sporns, 2009). Magnetoencephalography (MEG) is a non-invasive method that records neuronal activity with several sensors (Mandal *et al.*, 2018). Especially considering the high spatial-temporal resolution, MEG is also used to diagnose epilepsy, including detecting and forecasting seizures.

The brain works cooperatively by connecting different areas through interaction with brain electrical signals. Therefore, analyzing brain connectivity is important for investigating brain activities. The definition of connection or edges based on empirical data is a key issue for brain connectivity. Weighted connection estimates from inherently noisy data might provide false positive connections

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in the network. Furthermore, comparing networks with differences in mean connection weights introduces possible bias since thresholding influences graph measurements such as clustering coefficient (van Wijk *et al.*, 2010).

For estimating functional connectivity (FC), Jin *et al.* (2015) use mutual information, and van Dellen *et al.* (2012) use the phase lag index to estimate functional connectivity. Coherence and phase locking value (PLV) are also suggested for FC (Mandal *et al.*, 2018). Coherence is the frequency domain function mathematically equivalent to the time domain cross-correlation. We can analyze functional brain connectivity by network analysis since the connections between brain regions can be regarded as a network. MEG has high temporal and spatial resolution and is measured simultaneously on multiple channels over time, so it is suitable for brain connectivity analysis (Zhang *et al.*, 2014).

Network statistics provide information about network status and dynamics. Hub nodes selected by comparing betweenness centrality are compared between patients and healthy controls (Jin *et al.*, 2015). Network measures such as clustering coefficient and path length are compared between patient groups with different glioma grades (van Dellen *et al.*, 2012). Mandal *et al.* (2018) suggested using network statistics such as eigenvector centrality, clustering coefficient, and path length to get information related to in-depth brain functioning. Thompson *et al.* (2017) incorporated temporal network statistics such as temporal network centrality, fluctuability, and volatility to analyze functional brain connectivity.

Network modeling is also an active research topic including minimum-spanning tree (van Dellen *et al.*, 2014), and temporal exponential random graph models (Simpson *et al.*, 2013). There are more dynamic network models. Separable temporal ERGM (STERGM) is an extension of ERGM for discrete-time dynamic networks consisting of two models: Formation network and dissolution network (Krivitsky and Handcock, 2014). Varying coefficient ERGM (VCERGM) is the model that more efficiently characterizes the effects of temporal heterogeneity and subgraph properties (Lee *et al.*, 2020). Relation event model (REM) can handle time-clustered dynamic networks (Fritz *et al.*, 2020). Such models can be used for modeling dynamic networks.

MEG is used for basic and diagnostic research on brain diseases through network comparison and connectivity analysis between patients and healthy controls (van Straaten and Stam, 2013). However, there is not much research on temporal network modeling for MEG, and there still needs to be more studied, incorporating space-time factors. The motivation of the study is to provide temporal MEG connectivity models for epilepsy group comparison that can help identify groups and diagnostic biomarkers for epilepsy. In this study, We compare three groups via MEG brain networks by static/temporal network statistics, multiset canonical correlation analysis (MCCA) to get a representative of each group, and temporal exponential random graph models (TERGM).

2. Materials and methods

2.1. Materials

2.1.1. Epilepsy MEG data

The MEG data came from Seoul national university hospital. The dataset contained data from 44 mesial temporal lobe epilepsy (mTLE) with hippocampal sclerosis (HS) patients who underwent epilepsy surgery between 2005 and 2011 and 46 health controls (HC). The mTLE patients have post-surgical seizure freedom, patient population homogeneity is obtained in terms of the main pathology and surgical outcome (Jin *et al.*, 2015). Twenty-two patients removed the left part of the brain (LT), and the other removed the right part of the brain (RT). Forty-six age-matched right-handed healthy controls voluntarily participated in the study. Table 1 provides patient demographic data.

Table 1: Frequency table of subjects per group

	LT (n = 22)	RT (n = 22)	HC (n = 46)
Male	10	7	19
Female	12	15	27
Mean age	31	32	29
Duration of epilepsy (year)	21	18	n.a.

n.a. : not applicable

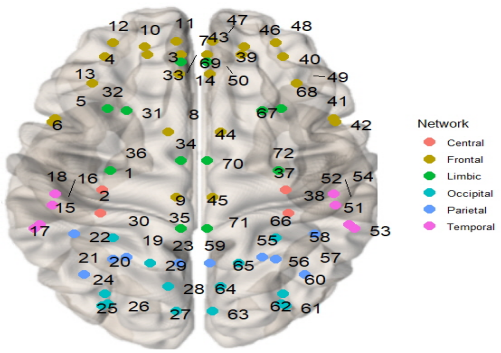

Figure 1: *Location of ROI nodes.*

For MEG recordings, a 306-channel whole-head system was used with MEG sensors arranged to consist of two orthogonal planar gradiometers and one magnetometer (Jin *et al.*, 2015). MEG recordings were obtained in a magnetically shielded room at a sampling frequency of 600.615 Hz. For records of twenty-six people sampled at 1,200 Hz, only odd time-points are extracted and used for analysis. All records were collected while subjects were lying or sitting with the resting-state signals. Each subject was instructed to remain relaxed and asked to avoid thinking about anything during the recording.

2.1.2. Network analysis

Epilepsy is commonly considered an archetypical network disease affecting structural and functional connectivity with seizures and interactions consistently generated and spreading in networks involving one or both hemispheres. The predefined 72 nodes (36 nodes in each hemisphere) comprise a set of 2 central, 12 frontal, 4 temporal, 5 parietal, 7 occipital, and 6 limbic regions in each hemisphere. These nodes were selected from the automated anatomic labeling (AAL) atlas. The location of the nodes is in Figure 1. The AAL atlas is used for anatomical parcellation of the brain (Tzourio-Mazoyer *et al.*, 2002). and has been used and defined brain network nodes with fMRI (He *et al.*, 2009; Liao *et al.*, 2010) and MEG (Jin *et al.*, 2015). Reconstruction of source waveforms at 72 nodes was performed with programs such as BESA 2000 software (MEGIS Software, Gräfelfing, Germany).

For our analysis, the data is divided into six accumulated parts according to time. The accumulated time-points of every data except 5 data are considered at 5,000, 10,000, 15,000, 20,000, 25,000, and 30,000.

2.2. Methods

2.2.1. Functional connectivity

The brain has a complexly connected structure of different neurons. Thus, the brain's connectivity plays a role in determining brain network characteristics. Functional connectivity analysis can reveal the patterns of brain connectivity in certain diseases such as epilepsy (van Diessen *et al.*, 2013). To construct a brain network, estimating the brain's connectivity is required.

Functional connectivity is defined as a statistically significant temporal correlation between neurophysiological signals of different spatially separated nerve cells (Friston *et al.*, 1993; Kim, 2022). Functional connectivity can be estimated through the Pearson correlation coefficient, partial correlation coefficient, coherence function, and mutual information (Simpson *et al.*, 2013). In this work, Pearson correlation coefficients for data are used as functional connectivity to consider the time-dependent changes in connections between neurons.

2.2.2. Basic network measures

Brain networks deal with the modular and hierarchical nature of brain activities with the hub regions of the brain (Bassett and Bullmore, 2009; Bullmore and Sporns, 2009). Graph and modern network theory applied to FC values of connectivity matrix has been used to find out the framework of brain topology. In order to capture the most significant connections within a graph, the application of statistical thresholding schemes and selection of appropriate filtering for meaningful topologies is a critical step in brain connectivity analysis. Common measures like degree, centrality, and clustering coefficient intramodular connectivity can be utilized for MEG based network analysis. "Hub" is defined as a network node (brain region of interest) that plays an important role with the specific property of having a high centrality.

The degree of a node, a basic measure of the network, is the number of edges. Nodes with a high degree can be regarded as important nodes in the network.

Centrality represents how central each node is to the entire network. Betweenness centrality measures how much one node acts as a bridge to another. If the betweenness centrality of the node is high, the node acts as a bridge to another node.

Eigenvector centrality measures centrality with weights using the adjacency matrix's eigenvector. It is useful for finding the most powerful node in the network.

Density indicates the degree of connections between nodes. It has a value between 0 and 1. If the density is close to 1, the network has many connections between nodes. It can compute by dividing actual degrees by the number of all connectable edges.

The participation coefficient measures the distribution of edges among the clusters in the graph. If the node's edges are only in its cluster, the participation coefficient is 0. The node with high participation coefficient is called the "connector" hub (Power *et al.*, 2013), which connects clusters.

2.2.3. Temporal network measures

Temporal network measures can be defined by extending the definitions and logic of static network theory (Thompson *et al.*, 2017). The temporal network graph is defined with nodes, edges, and an additional dimension of time information such as

$$G = (V, E, D)\,, \tag{2.1}$$

where G is a graph, V is a set of n nodes, E is a set of edges and D is a set of additional dimension of graph. In a temporal network, D is a set of time-points. Time-varying brain functional connectivity is

an inherently temporal network involving dynamic fluctuation. The connectivity matrix at each time-point t is referred to as a graphlet or a snapshot representation (Thompson and Fransson, 2015). Each t-graphlet is a part with temporal information of the entire network. Once the t-graphlets are derived, various temporal network measures can be implemented for the characteristics of the temporal flow of information through the network.

To derive the temporal properties at the global level, we consider global measures such as fluctuability, volatility, and temporal efficiency. As a global state of a temporal network, fluctuability can quantify the temporal variability of connectivity and the temporal diversity of edges providing how connectivity patterns within the network fluctuate across time. The lower the fluctuability, the less the edge changes across time. As a possible measure of temporal order, volatility indicates how volatile the temporal network is over time. Temporal efficiency measures the efficiency of temporal information exchange as the inverse of the average shortest path of all nodes. We referred to Thompson *et al.* (2017) temporal network statistics.

2.2.4. MCCA

Canonical correlation analysis (CCA) is a powerful multivariate tool to jointly investigate relationships among multiple data sets. CCA can identify the source of common statistical variations among multiple modalities and link multiple modal data without assuming any particular form which suits neuroscience applications. Multiset canonical correlation analysis (MCCA), the extension of CCA, is a method that finds linear relationships between more than two groups of variables. In neuroscience research, MCCA is used to combine multiple brain imaging data and combine multiple subjects' data (Zhuang *et al.*, 2020).

Sparse-MCCA finds canonical vectors by penalized matrix decomposition (PMD). PMD is a method for estimating penalized canonical vectors through computing an approximation. Let $\mathbf{X}$ be a $n \times p$ matrix with rank k. Then approximation of $\mathbf{X}$ is as follows (Witten *et al.*, 2009):

$$\hat{\mathbf{X}} = \sum_{i=1}^{k} d_i \mathbf{u}_i \mathbf{v}_i^{\top}, \tag{2.2}$$

where $\mathbf{u}_i \in R^n$ and $\mathbf{v}_i \in R^p$, and d_i are nonnegative constants. Using PMD, we can estimate $\mathbf{u}_i$ and $\mathbf{v}_i$.

Sparse MCCA can be formulated to optimization the problem as follows. Let $\mathbf{X}$ be $n \times p$ matrix composed of the first set of variables and $\mathbf{Y}$ denote $n \times q$ matrix composed of the remaining set of variables. $\mathbf{X}$ and $\mathbf{Y}$ are centered and scaled.

$$\begin{aligned} &\arg\max_{\mathbf{u},\mathbf{v}} \mathbf{u}^{\top}\mathbf{X}^{\top}\mathbf{Y}\mathbf{v} \quad \text{subject to} \\ &\mathbf{u}^{\top}\mathbf{u} \le 1, \quad \mathbf{v}^{\top}\mathbf{v} \le 1, \quad P_1(\mathbf{u}) \le c_1, \quad P_2(\mathbf{v}) \le c_2, \quad d \ge 0. \end{aligned} \tag{2.3}$$

Here $P_1(\mathbf{u}), P_2(\mathbf{v})$ are convex penalty function, and $\top$ notes transpose, and c_1, c_2 are upper bound constant of penalty function. Solving the optimization problem (2.3) using PMD, we can obtain canonical vectors $\mathbf{u}$ and $\mathbf{v}$. Sparse-MCCA is good for analyzing more than two modalities and removing noninformative features (Zhuang *et al*., 2020). We use sparse MCCA to remove noninformative features and to combine MEG data across multiple subjects in each group.

2.2.5. TERGM

Exponential random graph model (ERGM) (Robinson *et al.*, 2007) is a representative statistical model that can analyze variables affecting the connection between nodes in the network. Variables in ERGM

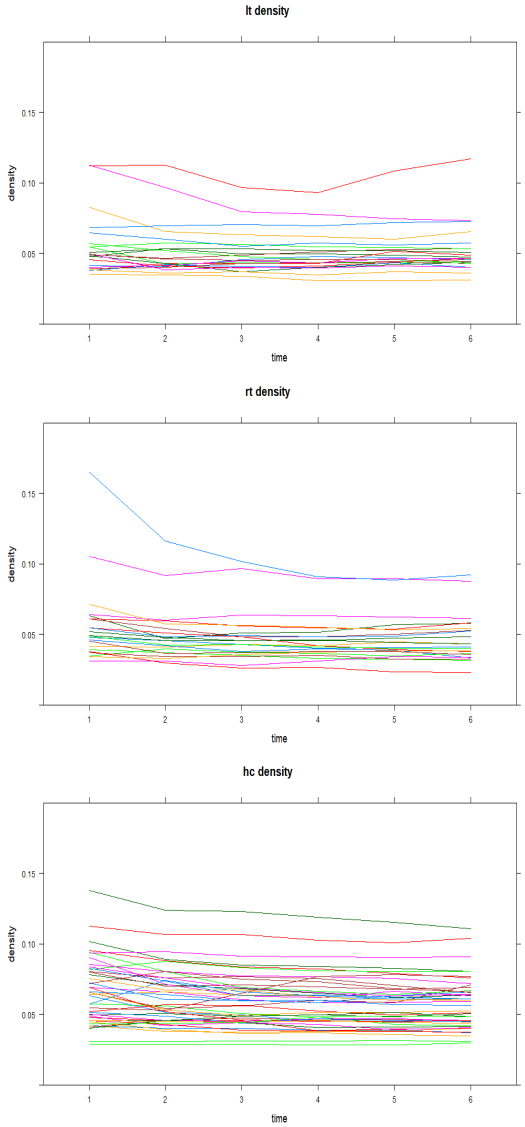

Figure 2: *Density changes over time in group LT (upper), RT (middle), HC (lower).*

include not only network structural characteristics but also exogenous factors. ERGM has the following form (Leifeld *et al.*, 2018):

$$P(N, \boldsymbol{\theta}) = \frac{\exp(\boldsymbol{\theta}^{\top}\mathbf{g}(N))}{c(\boldsymbol{\theta})}, \tag{2.4}$$

where N is an adjacency matrix, $\boldsymbol{\theta}$ is the vector of model coefficients, $\mathbf{g}(N)$ is the vector of statistics such as gwesp (geometrically weighted edgewise shared partnerships), edges, etc., and $c(\boldsymbol{\theta})$ is the normalizing factor. We can compute the maximum pseudo-likelihood estimator or maximum likelihood

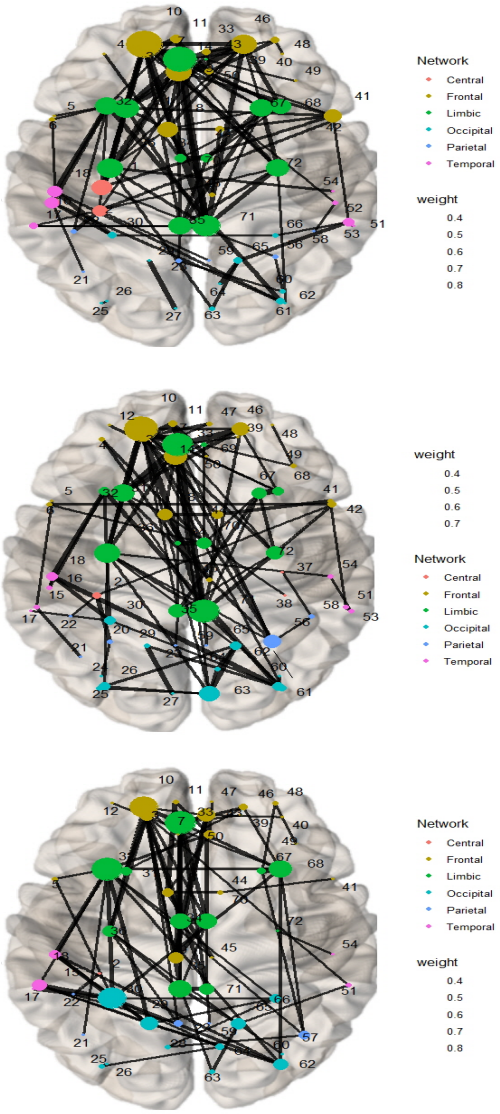

Figure 3: *Network example of LT (upper), RT (middle), HC (lower) at* $t = 30,000$.

estimator using the Markov chain Monte Carlo (MCMC) method to estimate parameters.

TERGM (Hanneke *et al.*, 2010) is the extension of ERGM designed to consider temporal dependence. The model with lag K can be formulated as follows (Leifeld *et al.*, 2018):

$$P\left(N^t \mid N^{t-K}, \ldots, N^{t-1}, \boldsymbol{\theta}\right) = \frac{\exp\left(\boldsymbol{\theta}^\top \mathbf{g}\left(N^t, N^{t-1}, \ldots, N^{t-K}\right)\right)}{c(\boldsymbol{\theta})}, \tag{2.5}$$

where $K \in \{0, \ldots, T-1\}$, N^t is the adjacency matrix at time t, $\boldsymbol{\theta}$ is the vector of model coefficients, $\mathbf{g}(N^t, N^{t-1}, \ldots, N^{t-K})$ is the vector of statistics and $c(\boldsymbol{\theta})$ is the normalizing factor. To contain temporal

Table 2: The static network statistics and Kruskal-Wallis test result

	LT	RT	HC	test stat	p-value	Tukey grouping
Degree	3.69	3.33	4.08	7.7434	0.02082	(LT,RT)/HC
Betweenness centrality	77.42	66.19	58.49	13.187	0.00137	LT/(RT,HC)
Eigenvector centrality	0.14	0.13	0.15	17.522	0.00015	(LT,RT)/HC
Density	0.052	0.047	0.057	7.7434	0.02083	(LT,RT)/HC

Table 3: Hub nodes of groups

Group	LT	RT	HC
Hub node	11,31,71,8	11,71	68,33,3

dependencies, statistics $\mathbf{g}$ can include memory terms related to time.

3. Results

3.1. Static network analysis

Functional connectivity is estimated as a network by a correlation matrix of 72 nodes. We determine to retain the edges which has a strength bigger than a threshold. A threshold can be selected differently depending on the situation, but an inappropriate threshold can obscure the differences in the network. There is no gold standard to select the proper threshold, so studies about edge filtering are required.

In this work, we chose the threshold value 0.3 by referring to some literature (Fransson *et al.*, 2011; Luppi and Stamatakis, 2021) and comparing a temporal measure. The networks of one example subject per group are shown in Figure 3. The node color indicates the brain regions, the node size reflects the degree of the corresponding node, and the edge weight reflects the connection strength by edge thickness.

To identify the network characteristics, we analyzed the connections in each subject. We found that most nodes had a low degree of 1 or 2, and some had a high degree. We compared the groupwise network statistics in Table 2 and found hub nodes based on the centrality and participation coefficient in Table 3.

Since the network characteristic statistics do not satisfy the normality, we compared degree, betweenness centrality (BC), eigenvector centrality (EC), and density by the Kruskal-Wallis (K-W) test and Tukey multiple comparison tests. The K-W test results provide that the groupwise difference of each network measures are significant at 0.05 significance level.

The degree of HC was significantly bigger than the degree of patient groups, and the betweenness centrality of LT was bigger than the other. The healthy control group (HC) also has bigger eigenvector centrality and density than the patient groups.

Hub nodes are selected by comparing BC, EC, and participation coefficient (PC). BC and EC were standardized by conversion to a z_score, and nodes with z_score $>$ 2sd (standard deviation) are considered as hub nodes. Since a node with a high PC (close to 1) is considered as a "connector hub" which links nodes across the different clusters (Rubinov and Sporns, 2010; Power *et al.*, 2013), we selected the nodes with PC $>$ 0.5 to hub nodes. Moreover, we considered the variability of statistics across time to select hub nodes.

Nodes 3, 8, and 11 are located in the frontal, nodes 31 and 68 are in the temporal pole of the limbic, and nodes 33 and 71 are located in the limbic. According to the selected hub nodes, nodes 11 and 71 were commonly selected as hub nodes in the two patient groups, unlike healthy controls. We plot the individual density of each network according to the six time-points in Figure 2. In Figure 2,

Table 4: The global statistics for temporal network and Kruskal-Wallis test result

	LT	RT	HC	test stat	p-value	Tukey grouping
Fluctuability	0.223	0.230	0.216	6.7643	0.03397	(LT,RT)/HC
Volatility	47.036	44.363	42.4	0.53436	0.07655	.
Temporal efficiency	0.00055	0.00051	0.00060	4.8845	0.08697	.

Table 5: The mean of temporal centrality per group and Kruskal-Wallis test result

	LT	RT	HC	test stat	p-value	Tukey grouping
Temporal betweenness centrality	0.0121	0.0107	0.0116	1.7404	0.4189	.
Temporal degree centrality	0.0625	0.0591	0.0722	9.4835	0.008723	(LT,RT)/HC

each line represents each subject's density change in each group.

3.2. Temporal network analysis

Adjacency matrices are made binary for dynamic network statistics calculation. The K-W test is performed to compare groupwise differences in temporal network statistics (Table 4). Fluctuability, volatility, and temporal efficiency are calculated to compare and investigate the groupwise global network characteristics. The means of fluctuability and volatility of the HC group has the smallest value, so the HC has less network change than the patient group (LT & RT). In the K-W test, only the fluctuability was significant.

To analyze nodal information, we performed the K-W test for temporal degree centrality and temporal betweenness centrality (Table 5). As a result, the temporal degree centrality was significant in that HC was bigger than the others. Figure 4 is the boxplot of the node's temporal betweenness centrality of each group. Although the group difference is not in temporal betweenness centrality, in Figure 4, we could find the temporal betweenness centralities of hub nodes are higher than the other nodes.

3.3. MCCA and TERGM

Before fitting the TERGM, in order to find the group representative, we combined the subject information at each time-point in each group by sparse-MCCA with the lasso penalty function. For combining subjects we excluded five subjects with less than 30,000 time-points observed. We fitted TERGM with the group representatives for LT, RT, and HC resulting estimates in Table 6.

Edges, gwesp, nodecov, nodefactor, nodematch, memory terms are used to fit final TERGM. Edges and gwesp terms are for network structure. Gwesp means geometrically weighted edgewise shared partnerships. Gwesp term can identify transitivities of triangular structure that occur between three nodes. If the coefficient of gwesp is positive, the networks tend to cluster statistically. Transitivity means if the connection of nodes A and B exists, and nodes B and C are connected, then A and C will be connected. Thus, Gwesp can evaluate network clustering through triangular structures between three nodes. Gwesp can be formulated as follows (Dichio and Fallani, 2022):

$$w = e^{\alpha} \sum_{i=1}^{n-2} \left\{ 1 - (1 - e^{-\alpha})^{i} \right\} p_i, \tag{3.1}$$

where α is decay parameter, p_i is number of pairs with i shared partners. In this work, we used $\alpha = 0.25$ as a decay parameter.

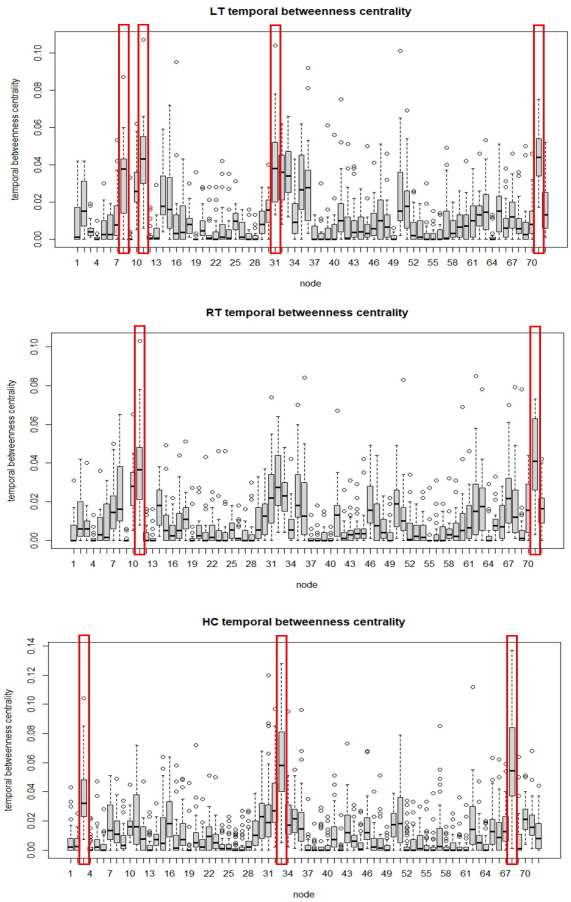

Figure 4: *Boxplot of node's temporal betweenness centrality for LT (upper), RT (middle), HC (lower).*

Nodecov, nodefactor, nodematch terms are used as terms of exogenous factors. Nodecov can identify the effect of numerical variables, and we use the square root of the degree of each node as nodecov. Nodefactor is for investigating the effect of categorical variables. Nodefactor is contained to verify the effect on brain regions. Nodematch is the dyadic covariate that measures homophily in a network based on a categorical variable. We can investigate the effect of a connection between regions of the same brain region using nodematch.

Also, the stability term of memory term is used to consider the changes across time. The stability term means whether the previous edge is maintained at the following time-point. The stability term h_m is defined as follows (Leifeld *et al.*, 2018; Obando Forero, 2018):

$$h_m = \sum_{i \neq j} N_{ij}^t N_{ij}^{t-1} + \left(1 - N_{ij}^t\right)\left(1 - N_{ij}^{t-1}\right). \tag{3.2}$$

We consider the lag of the memory term as 1 to identify whether the network at time t is affected by the network at the previous time. To fit TERGM, we use temporal bootstrap with 100 replication and maximum pseudo-likelihood. The TERGM parameter estimation result is shown in Table 6.

Table 6: Fitted TERGMs in each group after MCCA applied

Variable		LT	RT	HC
		Estimate	Estimate	Estimate
Edges		−6.51*	−10.78*	−9.41*
Gwesp		0.94*	0.85*	0.50*
Nodal covariate (nodefactor, nodecov)	Nodecov	0.53*	0.59*	0.52*
	Frontal	−0.64*	1.33	1.04
	Limbic	0.48*	2.37*	1.39*
	Occipital	−0.80*	1.82	−0.49
	Parietal	0.10	2.18*	0.06
	Temporal	−0.12	1.87*	−0.11
Dyadic covariate (nodematch)	Central	3.90*	8.76*	3.70*
	Frontal	1.48*	1.60*	0.22*
	Limbic	−0.92*	−0.56*	−0.15
	Occipital	3.49*	2.93*	4.34*
	Parietal	−11.65*	1.97*	1.26*
	Temporal	2.43*	3.06*	2.88*
Time covariate (memory)	Stability	1.00*	1.14*	0.38*

* : term is significant at significance level 0.05.

As a result of fitting TERGM, edges, gwesp, and nodecov terms are significant in all three groups. Because the coefficients of edges are negative, it is estimated that the network's density is low. Also the gwesp is significant and has positive coefficients in all group. Therefore clusters tend to be formed within the network. Considering the nodecov term, the degree in LT and RT has more significant effect on the connection between nodes than HC.

However, for the regions of the brain where nodes are located, in LT, connections between the same regions influenced the formation of connections between nodes. However, the effects of the parietal and temporal were not significant. In the case of RT, the term for the connection between the same regions was significant in all region, but the frontal and occipital effect were not significant. In the case of HC, the connection within the limbic was not significant, and the frontal, occipital, parietal, and temporal effects were also not significant. Moreover, using the "btergm" package to estimate TERGM can have degeneracy problems. Thus, we checked degeneracy and found no problems in the three models. Also, we assessed the goodness-of-fit (GOF) of the model for within-sample. The GOF method compares the simulated networks to the observed networks. The model fits better when the medians of the box plots are close to the line which plots the actual value of the statistics in the observed network (Leifeld *et al.*, 2018). Figure 5 represents the GOF of the three fitted models. Each GOF graph is good enough to be accepted for the model.

The simulated networks of each group based on the fitted models are shown in Figure 6. The model that produces better out-of-sample predictive fit is doing a better job of capturing the data generating process in the group nature. The node size represents each node's degree, and the node color indicates the region of the brain. Some specific node size is large in patient groups LT and RT, and this indicates that the large nodes play a significant role. From the simulated brain network plot of HC, most nodes are of similar size and most edges are distributed centrally.

4. Conclusion

In this paper, we analyzed and found the difference between networks of epilepsy patients and healthy controls by statistical network analysis. We calculated the temporal network statistics by considering

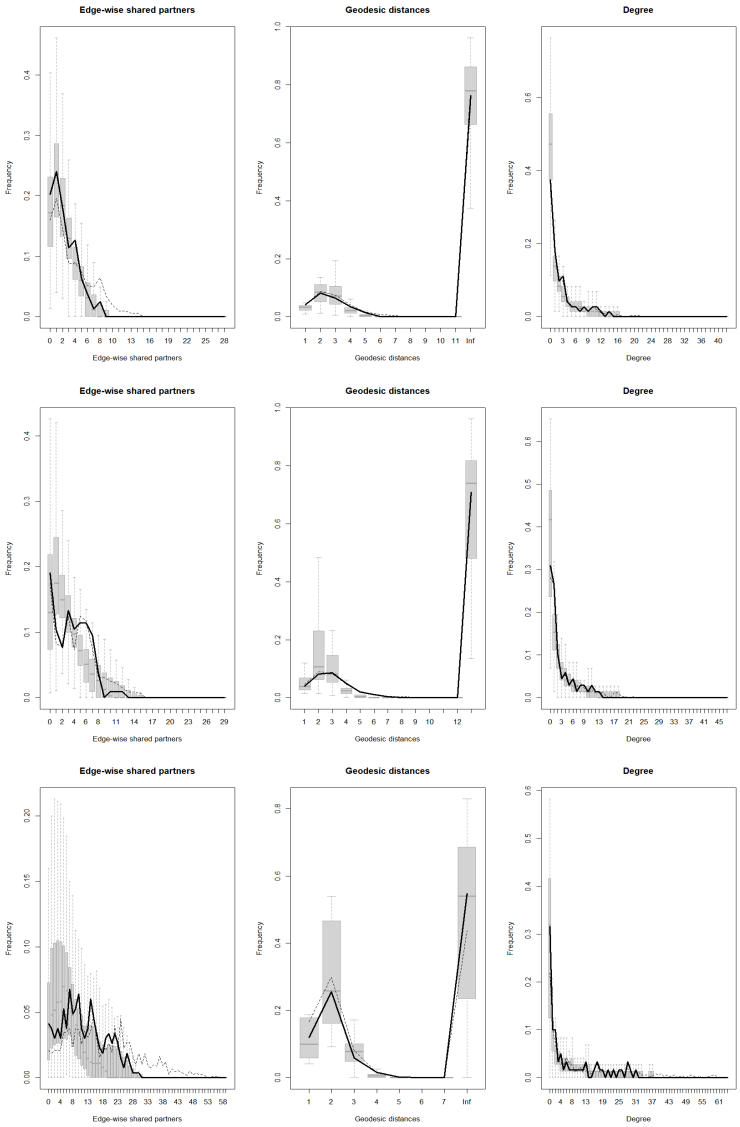

Figure 5: *Goodness-of-fit plots of TERGM in LT (upper), RT (middle), HC (lower).*

the temporal evolution. We fitted the TERGM after MCCA is applied to find a group representative using real neuroimaging MEG data. Specifically, we found that the HC has less network change than the patient groups. And the results of TERGM, a simulated network using fitted TERGM of HC has more edges distributed centrally than the patient groups.

However, we can also consider the other dynamic network model. Thus, studies for dynamic network modeling, such as STERGM and VCERGM using brain networks, are required. Furthermore, there is a limitation in that deciding the time-points may affect the result and considering temporal models not including patients' information affecting the disease status. And our analysis has informa-

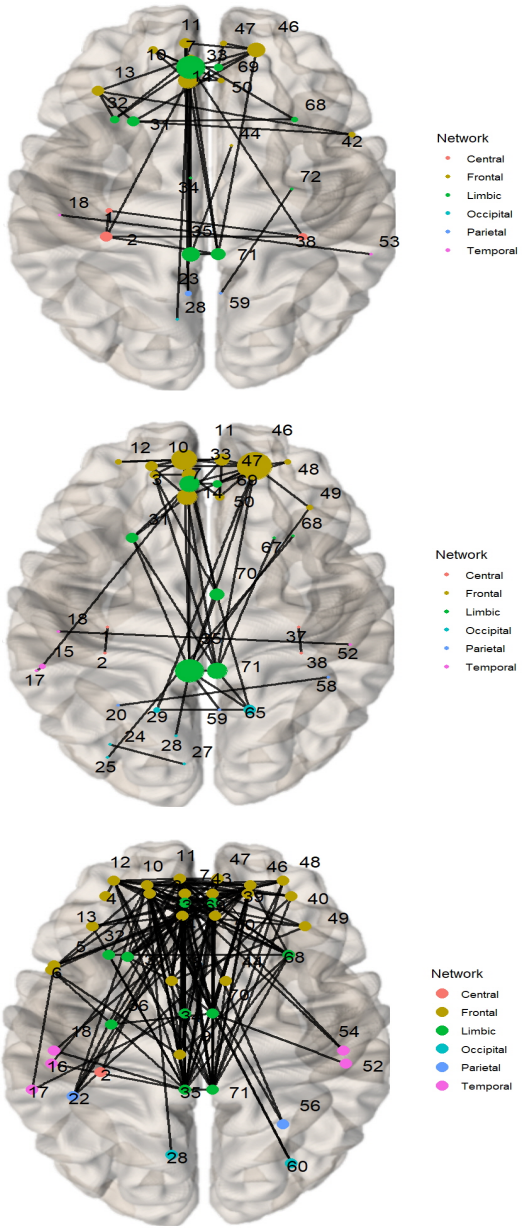

Figure 6: *Simulation networks of LT (upper), RT (middle), HC (lower) using TERGM.*

tion only about nodal information. We can also combine data from different neuroimaging modalities such as fMRI and MEG or investigate information given by edges to utilize more information about brain networks, which is the next topic. These studies and our methods can be helpful for basic research and diagnosis of patients with brain diseases.

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