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OPEN ACCESS
IOP Publishing | Institute of Physics and Engineering in Medicine Physiological Measurement
Physiol. Meas. **38** (2017) 759–773 https://doi.org/10.1088/1361-6579/aa6b4c

Automated network analysis to measure brain effective connectivity estimated from EEG data of patients with alcoholism

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Received 20 September 2016, revised 17 March 2017
Accepted for publication 4 April 2017
Published 27 April 2017

Abstract

Objective. Detection and diagnosis based on extracting features and classification using electroencephalography (EEG) signals are being studied vigorously. A network analysis of time series EEG signal data is one of many techniques that could help study brain functions. In this study, we analyze EEG to diagnose alcoholism. *Approach.* We propose a novel methodology to estimate the differences in the status of the brain based on EEG data of normal subjects and data from alcoholics by computing many parameters stemming from effective network using Granger causality. *Main results.* Among many parameters, only ten parameters were chosen as final candidates. By the combination of ten graph-based parameters, our results demonstrate predictable differences between alcoholics and normal subjects. A support vector machine classifier with best performance had 90% accuracy with

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sensitivity of 95.3%, and specificity of 82.4% for differentiating between the two groups.

Keywords: support vector machine, granger causality, network analysis, electroencephalography, alcoholism

1. Introduction

Alcoholism is one of the most influential psychiatric disease resulting from social, environmental, clinical, behavioral and individual factors. This disease refers to a condition where individuals with symptoms are significantly affected to guarantee the diagnosis of alcohol use disorder and alcohol abuse (American Psychiatric Association 2013). About 1.5 million adults in the United States received treatment for alcoholism in 2014. Around 10 percent of the total adult population in the United States are diagnosed AS alcoholics IN OF treatment (United States Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality and Inter-university Consortium for Political and Social Research 2016). Due to these reasons, the ANNUAL cost of treating alcoholism is around $ 250 billion (Sacks *et al* 2015). Since alcoholism is a large burden on any modern society, there is a need to further the knowledge about alcoholism in both physiological and neurological terms in order to improve treatment.

Clinical studies on alcoholism have been performed using EEG, MEG, and fMRI. Such techniques have been applied to in order to understand the physiology behind alcoholism and to find neurological patterns associated with alcoholism. Brain wave patterns have been investigated extensively for several decades with regards to alcoholism. In particular, EEG is considered practical due to the fact that it possesses multiple advantages over other methods when studying the function of the brain. EEG provides data of high temporal resolution with low cost (Gevins 1993, Lee and Tan 2006). EEG is portable and requires no exposure to magnetic fields or x-rays (Ng and Chan 2005). Additionally, non-invasive and silent testing of reaction to stimulus could be conducted with EEG (Lin *et al* 2008, Knoll *et al* 2011). This is important when studying the reaction to a certain stimulus. Furthermore neurological disorders such as attention deficit hyperactivity disorder (ADHD), Alzheimer disease, epilepsy could be diagnosed by using clinical information and EEG (Lubar 1991, Besthorn *et al* 1997, Kannathal *et al* 2005). In the same manner, many studies have tried to find the signs or patterns of alcoholism in EEG data (Coger *et al* 1978, Pollock *et al* 1983, Acharya *et al* 2012).

Some previous studies proposed ways to detect particular patterns or features from alcoholic EEG (Subasi and Ismail Gursoy 2010). Although researches on cognitive impairments among individuals with alcoholism suggest that analysis in time series of each electrical node cannot completely explain the physiological process, most current works collect and analyze data based on signal processing of time series data of a particular electrode (Coger *et al* 1978, Subasi and Ismail Gursoy 2010). For example, several groups extracted linear and nonlinear features, and employed time series data to differentiate alcoholics and epileptic patients from normal people (Garrett *et al* 2003, Kannathal *et al* 2005, Acharya *et al* 2012). These studies concentrated on specific nodes without analyzing the relationship amongst the nodes. Such research focusing on an individual feature from one EEG electrode could overlook the relationship between different brain regions. To overcome this weakness, researchers have increasingly focused on understanding the integrity of the relationship among all EEG channels covering the whole head to determine the physiological difference between the brains of patients and the brains of normal subjects.

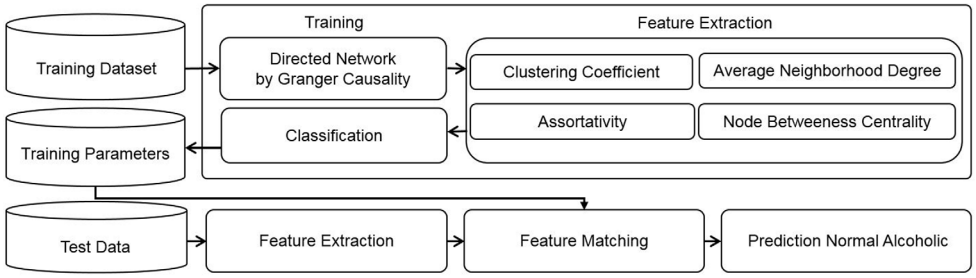

Figure 1. Block diagram of the proposed system for distinguishing between normal subjects and alcoholics. This data mining framework uses network properties, which are used to express the state of brains with the following parameters: clustering coefficient, assortativity, average neighborhood degree, and node between-ness centrality.

Graph theory has been used previously in a variety of manners to understand psychological diseases (de Haan *et al* 2009, Vecchio *et al* 2014). Along the same lines, there is a mathematically well-defined relation, called Granger causality which can be applied to a given brain region of interest from the time series of two EEG electrodes. Some of the work identifying the function of the brain have used Granger causality to define the relations between nodes (Hesse *et al* 2003). In addition, a number of studies have used graph theory to find the meanings behind these relationships to understand certain roles of the brain (de Haan *et al* 2009). To be specific, in one study, Alzheimer's disease was investigated by analyzing the topological changes in local and global functional brain network (de Haan *et al* 2009). In another study, functional brain networks during seizure revealed changes in certain Granger causality parameters (Ponten *et al* 2007). Furthermore, no studies have attempted to use network properties based on Granger causality to distinguish between alcoholics and normal subjects.

In this study, causal relationships among EEG electrodes was analyzed during a given task to differentiate between alcoholics and normal subjects. Based on these relationships, we calculated the parameters of network properties. After analyzing of the majority of the effective network properties, the parameters from the network properties that significantly influenced the discrimination between normal subjects and alcoholics were selected. A variety of classifiers were tested and trained based on the selected network properties. Finally, an alcoholism prediction system as illustrated as a block diagram in figure 1 is proposed. This figure presents the methodology to distinguish the status of the brain from normal and alcoholic EEG data. Lastly, combining multiple network properties is shown to improve the prediction performance.

2. Methods

2.1. Data description

The EEG data used in this study was acquired from the University of California, Irvine Knowledge Discovery in Database Archive (http://archive.ics.uci.edu/ml). The data was a time series EEG data from the 61 electrodes placed on the scalp and the 3 electrodes placed at the nose and both at the ears. An experimental dataset for a subject was 120 s long and contained the voltage levels from multiple electrodes recorded at 256 Hz (3.9 ms epoch). EEG from alcoholics and normal subjects were sampled. Each subject underwent two different experiments which consisted of one stimulus (S1) and two mixed stimuli (S1 and S2). The stimuli consisted of 90 pictures of objects chosen from the 1980 Snodgrass and Vanderwart

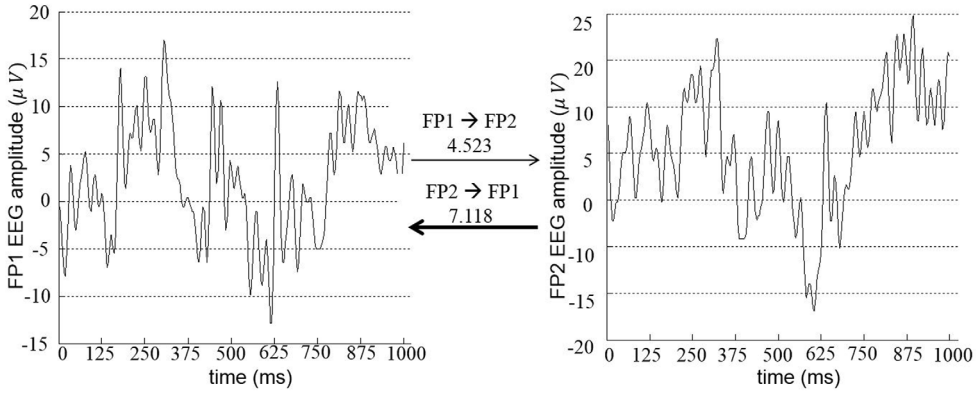

Figure 2. Time-series data acquired from the FP1 and FP2 nodes for 1 s in a NOMATCH condition. The Granger causality from FP1 to FP2 is 4.523 while that of FP2 to FP1 was 7.118.

picture set. The pictures shown to the subjects were presented in two different ways depending on whether S1 was identical to S2. If S1 is equal to S2, then the experiment is labelled as 'MATCH.' If S1 is not equal to S2, this experiment is labelled as 'NOMATCH.' If a single object is shown, we call the experiment 'OBJECT.' The description of database mentioned that there were 122 subjects, and each subject completed 120 trials in which three types of stimuli were shown. MATCH, NOMATCH, and OBJECT experiments contained pre-stimulus and post-stimulus EEG data. Each experiment was performed on each subject with a 61-lead electrode placed on scalp (ECI, Electrocap International, Eaton, OH, USA). The entire 10/20 International montage was employed along with 41 additional sites as followed: FPz, AFz, AF1, AF2, AF7, AF8, F1, F2, F5, F6, FCz, FC1, FC2, FC3, FC4, FC5, FC6, FC7, FC8, C1, C2, C5, C6, CPz, CP1, CP2, CP3, CP4, CP5, CP6, TP7, TP8, PI, P2, P5, P6, POz, POI, PO2, PO7, and PO8 (American Clinical Neurophysiology Society 2006).

Data from 60 subjects (37 alcoholics and 23 normal subjects) were used in this study. Three sets of experiments were conducted using the data from each subject. Appropriate data for the analysis were rearranged for the purpose of this study. For example, we deleted the relation between EEG time-series data if Granger causality were below statistically sufficient p-value between two channels. We also removed some subjects from the dataset if they belonged to both the alcoholics and the normal subjects group, or if sufficient data for calculating Granger causality was not available, and if a particular experiment was not performed on a subject. 23 controls and 37 alcoholics remained after the above elimination process. Figure 2 shows the time-series EEG data on channels FP1 and FP2 as an example. In this study, we calculated Granger causality from two pair time-series data and represented the magnitude of Granger causality using arrows as seen on figure 2 in between the two time series EEG data plots.

2.2. EEG analysis

The time series data (digitization rate of 256 Hz) from EEG channels were obtained from alcoholics and normal subjects. By extracting the average value from time series data of each channel, this time series applied a common average reference was derived (Ludwig *et al* 2009). Next, a Laplacian spatial filter for the highest signal-to-noise ratio based on the set of next-nearest neighbour electrodes was applied to the time series data (McFarland *et al* 1997, Nunez *et al* 1997). Time series data were temporally aligned by linear interpolation prior to

processing. Then, for each EEG channel, we derived the EEG time series data. The relationship between two sets of time series data from EEG channels were calculated using Granger causality to construct effective networks (described in section 2.2.1). After randomly selecting twenty subjects (13 alcoholics, 7 normal subjects), a large number of features including the global and local network parameters were obtained (described in section 2.2.2). All network properties from twenty subjects were evaluated by the use of Relief Algorithm rating the attribute importance. Ten features of time series network were selected by using importance score (described in section 2.2.3). The alcoholics and normal subjects were differentiated if elected features from the network had statistically significant differences between the two groups. The selected features were used to train the SVM classifier for the final classification step. Eventually, a 4-fold cross validation was conducted on the rest of forty subjects (24 alcoholics, 16 normal subjects). This validation was applied to each kernel to demonstrate the generalizability of each feature (as described in section 2.2.5).

2.2.1. Construction of an effective network. The first step of construction of an effective network is to build the relevant the causality amongst EEG channels. This method is to calculate Granger causality between EEG channels for each second and to take average several networks measured over 1 s. We computed Granger causality which was employed to configure the effective connectivity in different cognitive tasks to illustrate the information flow of one channel over another (McIntosh and Gonzalez-Lima 1994). Granger causality was applied to every 1 s of time-series with the reference of 0.125 s to obtain the effective network representation. Because we had 120 s data for each subject, we could acquire the averages of the networks measured over 1 s and analyze the result of changing networks. Effective network of transition from EEG was finally acquired. Further, extracting features of effective networks are established by the graph theory measurements. By regarding each channel as a node and using its time-series data as the observed output of the node, a linear model was constructed to represent nodes caused by other nodes as followed (Granger 1969):

$$X_1(t) = \sum_{j=1}^{p} A_{11,j} X_1(t-j) + \sum_{j=1}^{p} A_{12,j} X_2(t-j) + \varepsilon_1(t) \quad (1)$$

$$X_2(t) = \sum_{j=1}^{p} A_{21,j} X_1(t-j) + \sum_{j=1}^{p} A_{22,j} X_2(t-j) + \varepsilon_2(t) \quad (2)$$

where $X_2(t)$ causes $X_1(t)$, p represents the number of lagged observations and is used as a timing reference. In this study, we attempted to extend the time reference to 0.125. The above equations result to a simple causal model if $b_0 = c_0 = 0$. Otherwise, it will be an instantaneous causality model. Let U_t be a universe set of time series for 1 s from $t-1$ to t, and let $U_t - X_{2t}$ denote the set of all elements in U_t, which are not in the set X_{2t}. Granger suggested the definition of causality as: If X_2 is causing X_1, it is denoted by $X_{2t} \rightarrow X_{1t}$, $\sigma^2(X_1|U) < \sigma^2(X_1|\overline{U - X_2})$ where the bar indicates the boundary containing the set written below the bar. X_2 has greater causality on X_1 to extrapolate in the case in which variance increases in the absence of X_2 (Granger 1969). Using Granger causality equation, effective network was constructed as seen on the figure 3.

Figure 3(a) represents the employed EEG channels in this study. Figure 3(b) shows a constructed adjacent matrix, and each element filled with Granger causality value amongst the channels. The adjacency matrix for the weight- directed graphs indicating the presence of the corresponding edge were built. It is noteworthy that the adjacent matrix of the figure 3(b) identically represents the figure 3(c) which shows the sophisticated connectivity amongst the EEG

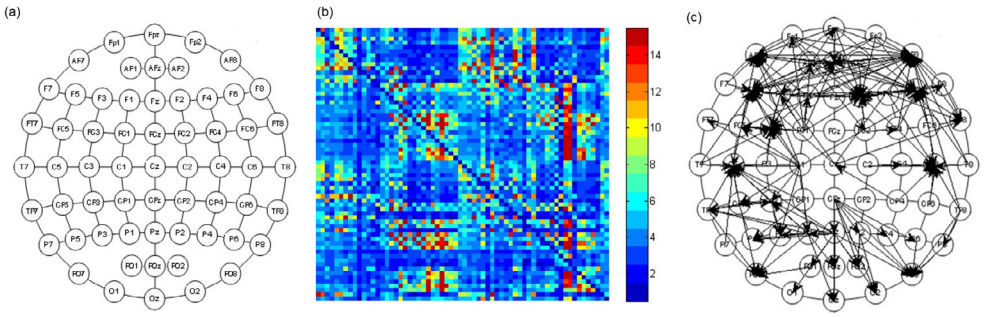

Figure 3. (a) The position of EEG electrodes used in this study. (b) An example of the 64 by 64 adjacent matrix was shown. Each element of the matrix represents a Granger causality value between EEG channels in a NOMATCH experiment. (c) Relations of Granger causality among EEG electrodes. The increasing degree of Granger causality among the nodes is expressed with the thickness of the arrows. Only edges having statistically significant p-value less than 0.05 is shown.

electrodes. Each arrow indicates Granger causality among the EEG channels. The only values of Granger causality greater than the average were employed in this study. In other words, we only considered the relations if they had Granger causality value greater than the average of all relations. In this study, a weighted network was defined as a set of values greater than the original mean value, and a binary network was defined as a weighted network with all values set to '1'. Using weighted networks and binary networks, features of network properties were calculated.

2.2.2. Computation of features. Our aim is to identify how those network properties changes between alcoholics and normal subjects; if each network property from the EEG time-series differs from that in another class, the degree of change is expected to be a marker of alcoholism. To address this question, the computation of the network properties in a given network should be conducted. Therefore, the next step of EEG analysis in this study following the construction of network representation is to compute meaningful parameters from the selected features. The development of mathematical concepts for computational techniques has made it possible to represent connectivity using features (Rubinov and Sporns 2010). Such network features describe the network properties of individual subjects. Computation of all network properties were performed using the brain connectivity tool box (Rubinov and Sporns 2010).

Through experimental analysis, it was found that employing binary/weighted and local parameters such as clustering coefficient, assortativity, average neighborhood degree, node between-ness enables the separation of the two groups of subjects. Those four concepts of parameters from the constructed complex network structure were examined and used to compare the two classes.

This section explains the definition of the selected features studies and their mathematical equations. The mathematical and statistical processing steps were performed on MATLAB® R2016a (Mathworks, Inc., Natick, MA, USA) with Windows® 7 PC. LIBSVM library (www.csie.ntu.edu.tw/~cjlin/libsvm/) was used for SVM classification process (Chang and Lin 2011).

2.2.2.1. Clustering coefficient. Clustering coefficient was defined for the extent to which nodes tend to cluster together. The binary clustering coefficient (bCC) of the network is defined by the ratio of the number of triangles around a node to that of triangles around a node's neighbours as followed:

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

where C_i is the clustering coefficient of node i, t_i is the number of triangles around node i, and k_i is the degree of node i (Watts and Strogatz 1998).

The weighted clustering coefficient (wCC) is computed as based on the definition of weighted and directed networks:

$$\mathrm{wCC} = \frac{1}{n}\sum_{i\in N} \frac{\overrightarrow{t_1}}{\left(k_i^{\mathrm{out}} + k_i^{\mathrm{in}}\right)\left(k_i^{\mathrm{out}} + k_i^{\mathrm{in}} - 1\right) - 2\sum_{j\in N} a_{ij}a_{ji}} \tag{4}$$

where $t \simeq 24M$ is the number of triangles around node i, k_i^{out} is the out degree of node i, and k_i^{in} is the in degree of node i (Fagiolo 2007).

2.2.2.2. Assortativity. The assortativity was described to say a correlation coefficient representing the preference of a network's node to other nodes. It is the correlation between two separate nodes of similar degrees. The assortativity coefficient of the network can be calculated as according to Newman and Leung. The binary and indirect assortativity coefficient (biA) of the network is:

$$\mathrm{biA}\,(k) = \frac{l^{-1}\sum_{(i,j)\in L} k_i^w k_j^w - \left[l^{-1}\sum_{(i,j)\in L} \frac{1}{2}\left(k_i^w + k_j^w\right)\right]^2}{l^{-1}\sum_{(i,j)\in L} \frac{1}{2}\left[k_i^2 + k_j^2\right] - \left[l^{-1}\sum_{(i,j)\in L} \frac{1}{2}\left(k_i^2 + k_j^2\right)\right]^2} \tag{5}$$

The weighted and directed assortativity coefficient (wdA) can be expressed by:

$$\mathrm{wdA}(k) = \frac{l^{-1}\sum_{(i,j)\in L} w_{ij}k_i^{\mathrm{out}}k_j^{\mathrm{in}} - \left[l^{-1}\sum_{(i,j)\in L} \frac{1}{2}w_{ij}\left(k_i^{\mathrm{out}} + k_j^{\mathrm{in}}\right)\right]^2}{l^{-1}\sum_{(i,j)\in L} \frac{1}{2}w_{ij}\left[\left(k_i^{\mathrm{out}}\right)^2 + \left(k_j^{\mathrm{in}}\right)^2\right] - \left[l^{-1}\sum_{(i,j)\in L} \frac{1}{2}\left(k_i^{\mathrm{out}} + k_j^{\mathrm{in}}\right)\right]^2} \tag{6}$$

where k is the average degree of neighbours of node i and L is the set of nodes (Foster *et al* 2010, Rubinov and Sporns 2010). There are four types of assortativity coefficients in weighted connectivity: i.e. out-degree/in-degree correlation ($k = 0$), in-degree/out-degree correlation ($k = 1$), out-degree/out-degree correlation ($k = 2$), and directed graph: in-degree/in-degree correlation ($k = 3$) (Newman 2002).

2.2.2.3. Average neighbourhood degree. Average neighbourhood degree is defined by the average closest neighbour degree of nodes with degree k and is termed degree centrality. This measurement can be described by the average number of links that come in or out for a given node. In this paper, the weighted average neighbourhood degree (wAND) was computed as:

For node i,

$$\mathrm{wAND} = \frac{1}{s_i}\sum_{j\in N(i)} w_{ij}k_j \tag{7}$$

where s_i is the weighted degree of node i, w_{ij} is the weight of the edge that links i and j, and $N(i)$ are the neighbors of node i. w_{ij} should be 1 for binary connectivity (Barrat *et al* 2004).

2.2.2.4. Node betweenness centrality. The meaning of node betweenness centrality implies the degree of participates in a large number of shortest paths. This weighted node betweenness centrality (wNBC) indicates the quantity of the shortest path that contains a node, and its value presents the number of bridges along between two other nodes.

For node i,

$$\text{wNBC} = \frac{1}{(n-1)(n-2)} \sum_{\substack{h,j \in N \\ h \neq i, h \neq j, i \neq j}} \frac{\rho_{hj}(i)}{\rho_{hj}} \tag{8}$$

where ρ_{hj} is the number of shortest paths between h and j, and $\rho_{hj}(i)$ is the number of shortest paths between hand j that pass through i (Kintali 2008).

2.2.3. Feature selection. The third step following the computation of network representation is feature selection. It is worth pointing out that dealing with parameters from network properties results in a large number of features. After every parameter which influenced the distinguishing between the two groups were found, feature selection was needed to reduce data redundancy. This feature selection process was executed using the Relief algorithm, which was applied for the dimensionality reduction as brevity of features space from the combination of features (Robnik-Šikonja and Kononenko 1997). Final feature selection and important score are shown in figure 4. Final ten features were chosen as using these features resulted in greater efficiency with no loss in performance as compared to using more ten features. Lastly, Welch's *t*-test was employed to verify the difference between the features of the alcoholic patients and the normal subjects. *p*-values less than 0.05 were considered statistically significant.

2.2.4. Surrogate data testing. After meaningful features have been selected, this third step of surrogate data testing is necessary to prove that the selected network features are non-linear properties and to control volume conduction artifacts for effective connectivity. Existence of nonlinearity and volume conduction effect could be tested by applying nonlinear time-series methods to quantify the network structure of the EEG. Surrogate data refer to time-series data that have the same mean, variance, and statistical properties such as the autocorrelation structure of a measured data set (Prichard and Theiler 1994). In this study, the surrogate data were generated using the phase shuffle method (Theiler *et al* 1992). The results show the value of the selected features from normal groups are higher than that of the surrogate data. Table 1 indicates the values of the normal group data and their surrogate data for the FP1 node parameter. The results show that the surrogate data and the experimental normal group data differed from each other by more than 38%. Similarly, the values of the alcoholic group data and their surrogated data for distinct node parameters had similar difference as shown in the table 1. Therefore, the calculated parameters are considered nonlinear in nature and these parameters do not contain volume conduction effects.

2.2.5. Classifier. Lastly, support vector machine (SVM) was used to distinguish between alcoholics and normal subjects. SVM is a common learning model associated with mathematical algorithms that interpret and recognize a pattern. SVM classifier has been discovered to use nonlinear data with several features and to investigate the performance of features in an automated pattern recognition system. This classifier can also generalize properties, which facilitates training and testing. In this study, SVM classifier was used to select network properties and classify the normal and alcoholic groups with several kernel such as linear kernel, polynomial third order kernel, and radial basis function kernel. Among selected features, the

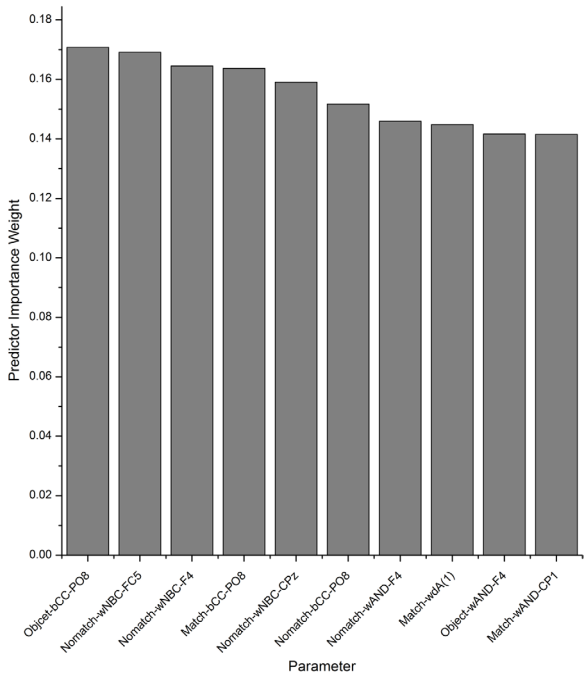

Figure 4. Graphs of computing importance score using relief algorithms. The selected feature is represented as experiment-parameter-node. The parameters were abbreviated to bCC (binary clustering coefficient), wNBC (weighted node betweenness centrality), wAND (weighted average neighborhood degree), wdA (1) (weighted and directed assortativity).

features having statistically significant were employed from the training samples based on Welch's *t*-test. Such features were applied to test samples to differentiate between normal individual from alcoholics. The selected features of SVM classifier were validated using 4 fold cross validations.

3. Results

Our results demonstrate that each parameter may be able to distinguish the alcoholics from the normal subjects. Table 2 represents the *p*-values for the bCC, wdA(1), wAND, and wNBC. Each of these parameters were obtained from each node. Further, table 2 shows a clear difference in all non-linear parameters. Specifically, in the case of MATCH experiment, the wdA(1) had a *p*-value less than 0.001. *p*-values less than 0.05 were calculated for bCC at node PO8 and for wAND at node CP1. In the NOMATCH experiment, the *p*-values of bCC of node PO8, wAND of node F4, and wNBC of node X, node TP7, and CPz were less than 0.05. Similarly, in the OBJECT experiment, bCC of node PO8 and wAND of node F4 had *p*-values less than 0.05. Therefore, bCC, wdA(1), AND, and NBC values differed markedly between the alcoholics and the normal subject. Although it was difficult to identify the physiological reason behind the differences in parameters between the two groups, the bCC, wAND, and wNBC values of the alcoholics were lower than those of the normal subject. These results suggest that the brain state in alcoholics at the time of the measurement was different from that in normal subject.

Table 1. Mean values of each parameter obtained from the effective network using EEG signals in the normal group and the surrogate data. This table shows the non-linearity in the case of NOMATCH experiments given a time reference of 0.125 s.

Parameter	Name of node	Normal	Surrogate data	Difference (%)
bCC	FP1	0.470	0.288	38.7
wCC	FP1	3.73	2.29	38.6
wdA(1)		0.005 88	0.001 50	74.5
wAND	FP1	4.82	2.91	39.9
wNBC	FP1	28.1	15.1	46.3

bCC—binary clustering coefficient; wCC—weighted clustering coefficient; wdA(1)—weighted and directed assortativity (in-degree/out-degree correlation); wAND—weighted average neighborhood degree; wNBC—weighted node betweenness centrality.

Table 2. Range (mean and standard deviation) of nonlinear features extracted from the graph using EEG signals in the normal subjects and the alcoholics with the time reference of 0.125 s. Welch's *t*-test was used for obtaining *p*-values <0.05 are shown, these data were obtained sequentially from (1) MATCH, (2) NOMATCH, and (3) OBJECT experiments.

			Normal		Alcoholic		
Nonlinear parameter		Name of node	Average	Standard deviation	Average	Standard deviation	*p*-value
(1)	bCC	PO8	0.633	0.119	0.542	0.101	<0.05
	wdA(1)		0.0159	1.41×10^{-17}	0.0437	3.57×10^{-18}	<0.001
	wAND	CP1	3.78	0.726	3.28	0.714	<0.05
(2)	bCC	PO8	0.632	0.0964	0.553	0.102	<0.01
	wAND	F4	4.59	1.51	3.62	0.877	<0.05
	wNBC	X	17.0	3.11	2.11	0.333	<0.05
	wNBC	TP7	10.1	1.91	2.83	0.995	<0.05
	wNBC	CPz	17.2	3.61	2.61	0.434	<0.05
(3)	bCC	PO8	0.626	0.0976	0.541	0.137	<0.05
	wAND	F4	4.80	1.30	4.14	0.955	<0.05

bCC—binary clustering coefficient; wdA(1)—weighted and directed assortativity (in-degree/out-degree correlation); wAND—weighted average neighborhood degree; wNBC—weighted Node Betweenness Centrality.

Table 3 shows the classification results for the SVM classifier. The maximum accuracy of classification was 90.0% for a polynomial order 3 classifier. The sensitivity and specificity of the polynomial order 3 classifier were 95.3% and 82.4%, respectively. The highest accuracy value for the linear classifier was 85.0% and sensitivity and specificity of the linear classifier were 85.7% and 83.3%, respectively. High sensitivity, specificity, and average accuracy were obtained using support vector machine for all classifier types.

4. Discussion

We have introduced fundamentally distinct features of network properties based on Granger causality and successfully designed a support vector machine using the selected features to distinguish between alcoholics and normal subjects. The support vector machine was trained and

Table 3. Classification results obtained by the each SVM classifier having the best performance. The results shown are averaged over 5-fold cross validations.

SVM	TN	FN	TP	FP	Acc (%)	Sn (%)	Sp (%)
Linear kernel	15	6	36	3	85.0	85.7	83.3
Polynomial order 3	14	2	41	3	90.0	95.3	82.4

TN—true negative; FN—false negative; TP—true positive; FP—false positive; Acc—accuracy; Sn—sensitivity; Sp—specificity.

tested based on traditional graphical theory once the network was constructed using Granger causality. Granger causality was applied as a first step to determine meaningful parameters for distinguishing alcoholism. This approach to distinguish alcoholics from normal subjects is helpful in understanding the physiological processes in the brains of alcoholics that distinguish them from normal subjects.

Several studies analyzed the physiology behind the relationships between different brain regions of interest. Seth *et al* explained the theoretical basis and the computational implementation of Granger causality analysis in neurophysiology. They reported a device for monitoring the depth of anesthesia during surgery using Granger causality-based features. In addition, they identified a feature of the brain activity that was different between subjects who were awake and those who were anesthetized (Seth *et al* 2015). Likewise, we proposed a novel identification algorithm for alcoholism using features of effective network based on Granger causality.

Similar attempts with our study have been made for several decades to understand the non-linear network properties of EEG channels from the brain (Ehlers *et al* 1998, Garrett *et al* 2003). Previous attempts have been made to distinguish the EEG signal patterns of alcoholics to those of normal subjects. To be specific, studies have analyzed chaotic features such as entropy, largest Lyapunov exponent, and higher order spectrum (Acharya *et al* 2012). The performance measurements of these methods were comparable to that of our study. Therefore, the present study is meaningful due to the use of graph analysis to obtain similar accuracy.

Although a number of EEG studies investigated the brain physiology (Ehlers *et al* 1998, Garrett *et al* 2003, Acharya *et al* 2012, Seth *et al* 2015), the effects of volume conduction could not neglect statistical interdependencies in any EEG experiment (Guevara *et al* 2005). This study of the constructed connectivity based on Granger causality also include the volume conduction effects. However, this problem can be solved by the proposed method, applying a Laplacian filter defined by next-nearest-neighbor electrodes while the use of a Laplacian filter may be dangerous for meaningful information to disappear (McFarland *et al* 1997, Nunez *et al* 1997). In order to ensure that our finding did not contain the effect of volume conduction, we conducted the surrogate data experiment. According to the difference between the parameter value of original and surrogate data, it may have additional information besides the volume conduction effect (Shahbazi *et al* 2010). Moreover, the features used in this study were obtained in the transition of the brain networks. The constructed model was not a conventional physiological model but it could be a representation of the brain state. Although the network obtained from scalp EEG has the limitation of expressing the physiological network, proposing significant features makes our EEG technique valuable and promising. Discrimination between the two groups was successful even in effective-transitional networks.

When applying network theory, there is the difficulty in understanding the underlying empirical process related to characteristic findings of a typical network derived from a big data set (Snijders *et al* 2012). In the present study, we found that most parameters in normal groups are greater than in alcoholics except for wdA(1). It should be stressed that these value in

normal subjects are more likely to have higher value of network properties than alcoholics. All experiments showed that binary clustering coefficient and weighted average neighbourhood degree in effective networks enables us to differentiate alcoholics from normal subjects. This result is similar to results published in another research (Sakkalis *et al* 2010). Here, each node of weighted node betweenness centrality was compared between normal subjects and alcoholics, showing significant difference. Weighted assortativity in alcoholics increased than in normal subjects, which meant that alcoholics tended to have more preference for a network's nodes to attach to others that are similar in degree. Within the framework of the effective networks, the network architecture in alcoholic group is closer to less condensed networks.

As finding features of the networks and classifying the groups using machine learning can be conducted in several ways, additional research on these parameters is needed. In this study, attempts to understand of the physiological processes of the human brain was conducted by the computation of feature based on Granger causality among the EEG recordings. We successfully trained and tested ten features for designing SVM classification. The ten parameters such as clustering coefficient, assortativity, AND, and NBC were successful in distinguishing alcoholics from normal subjects. Therefore, works to find more features of the networks in several conditions with various diseases are needed, finding features in EEG networks may further help to understand the status of the brain through EEG analysis.

Our results are consistent with many previous studies in that brain networks invoked by alcoholics are different as compared to the ones invoked by normal subjects. One study concluded that connectivity between the left posterior cingulate seed and left cerebellar regions differentiates alcoholics from normal subjects (Chanraud *et al* 2011). Another study found that the causality between the nodes in the limbic channels is higher than the one found in between the nodes of the hippocampus in case of alcohol addiction (Guerrero *et al* 2014). Furthermore, clustering coefficient have been found to be lower in alcoholics (Sakkalis *et al* 2007). Likewise, the ability of network properties such as clustering coefficient, assortativity, average neighborhood degree, and node betweenness centrality to separate alcoholics from normal subjects were confirmed in this study.

This suggested experiments from the proposed techniques had several advantages. First, our data-mining framework had a high success rate in distinguishing normal subjects from alcoholics. Second, only ten parameters are needed to acquire high robustness and accuracy. This study had limitations in terms of practicality. Although the proposed method is able to train itself automatically based on the testing data and exhibits high sensitivity, specificity, and accuracy, the experiment involved only a single ethnic group. These experimental data are not universally applicable because the study was carried out in only one institution. In addition, brain signals might exhibit inconsistencies because no information regarding subject's gender, and age were available. Furthermore, we cannot guarantee that alcoholics and normal individuals whom the data were recorded from did not have additional diseases or conditions which may have influenced the EEG signals.

In this study, given a database containing a large number of normal subjects and alcoholics, our proposed system will assist physicians in distinguishing between the two groups. We demonstrated that an automated analysis of short-term EEG recordings is feasible. Furthermore, we demonstrated the feasibility of quantifying network parameters for distinguishing the brain activity of alcoholics from that of normal subjects. Our findings also support the use of network properties from the effective connectivity to differentiate between EEG recordings of alcoholics and of normal subjects. In future studies, we believe our method may be applicable to other disorders. We believe that the proposed method for assessing the network measurements help to understand physiological characteristics of patients with diverse psychiatric or neurological diseases and help to distinguish the alcoholics from the normal subjects.

Additionally, the proposed EEG analysis technique using Granger causality and SVM may be useful in both brain computer interface (BCI) applications and cognitive studies.

5. Conclusions

EEG analysis using relationships amongst the EEG nodes is used to classify alcoholics from normal subjects. We identified possible parameters for use in graph theory, and attempted to provide physiological meanings in a Granger causality effective network. Alcoholics were successfully distinguished from normal subjects with our prediction system. The results suggest that the brain state of alcoholics shows patterns that are unlikely to be random, and that significant difference in neural processing in response to external stimuli was found between the alcoholics and the normal subjects.

Acknowledgments

This study was supported by the Korean Health Technology R&D Project, Ministry of Health & Welfare (HI14C0746, HI14C0559 and HI13C1468) and by the Education and Research Encouragement Fund of Seoul National University Hospital.

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