Identifying Important Regions in EEG Epilepsy Brain Networks.

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Abstract— The human brain has been called the most complex object in the known universe and in many ways it constitutes the final frontier of science. Lately, the functional connectivity in human brain has been regarded and studied as a complex network using electroencephalography (EEG) signals. This means that the brain is studied as a connected system, where nodes represent different specialized brain regions and links or connections, represent communication pathways between the nodes. It is also fairly established that graph theory provides a variety of measures, methods and tools that can be useful to efficiently model, analyze and study an EEG network

In this article we study weighted and fully-connected brain networks, created from long-recorded EEG measurements that concern patients with focal and generalized epilepsy. Our goal is to identify important regions in EEG brain networks that will reveal the seed of the abnormal electrical activities of the human brain, which in our case are called seizures. Thus, we apply particular graph theory and statistical measures to our data and especially we focus on the use of the well-known eigenvector centrality measure, which shows the influence of a node in a network and also constitutes the basis of the famous Google's PageRank algorithm. Finally, we present and discuss the results and conclusions of our methodology, which demonstrates a standard EEG behavior in particular phases of the recording period, which are the following: pre-ictal, ictal, inter-ictal or post-ictal period.

Keywords—Brain networks, eigenvector centrality, epilepsy, graph theory.

I. INTRODUCTION

E PILEPSY is one of the most common neurological disorders of the human brain and affects people of all ages, regardless of gender or ethnic group. It is characterized by sudden and unpredictable seizures that can cause other health problems as well and/or affect any part of the human body [1]. The human brain is the source of human epilepsy, since all the electrical events that produce the symptoms occur in the brain.

It has also been found that almost one in four patients with epilepsy does not respond to medication and cannot be controlled by any anti-epileptic drugs or surgery [2], [3].

Consequently, anyone can understand that it is highly essential to study epileptic data in order to help patients avoid potentially endangering situations at the first place and of course to locate the regions of brain that are responsible for seizure's aberrant electrical activity and surgically remove the corresponding neurons.

Over the last few decades, several methods have been developed to detect seizures and perform predictions based on electroencephalographic (EEG) measurements, in order to characterize the transition from pre-ictal or inter-ictal to ictal state in quantitative terms [4], [5]. This happens because measurements of brain electrical activity with EEG have long been one of the most valuable sources of information for epilepsy research and diagnosis [6], since they carry a large amount of rich information that is useful to detect ongoing seizures.

The vast majority of the proposed methods include feature computation directly from the initial EEG time series, in order to detect changes immediately prior or after the onset of seizures [5]. All these studies strongly suggest that the information contained in EEG data relevant to seizure detection has not yet been fully exploited and thus, continued research and new approaches are needed. Also, individual patient-based detector training could be necessary to increase sensitivity and specificity [5].

For these reasons, during the last few years there has been a focus on studying EEG signals as graphs using complex network analysis – a methodology based on graph theory – in order to investigate the human brain [7], [8]. The graphs that have been derived from EEG signals are weighted, undirected and fully-connected. Some studies [9], [10] have already provided evidence that epileptic seizures are characterized by changes in functional network topology and features, but they came to these conclusions by truncating and binarizing the graphs and studying differences only between some parts of these (truncated) networks' topology before and after the seizure onset.

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In this paper we study weighted, fully-connected and undirected brain networks, created from real EEG long-recorded signals that concern patients with focal and generalized epilepsy. In all cases the recording period of the data that we study lasts more than 20 hours. We represent the brain networks as graphs and we introduce and evaluate the application of a commonly used graph theoretic measure, which is called *eigenvector centrality*. This measure shows the influence of a node in a network, by ranking higher the nodes which are connected to important neighbors. Consequently, a node has high value of eigenvector centrality either if it connected with many other nodes, or if it connected to nodes that themselves have high eigenvector centrality. The eigenvector centrality measure also constitutes the basis of the famous Google's PageRank algorithm [11].

A significant benefit of that measure is that it can be directly applied to weighted, undirected and fully-connected graphs, without cutting, binarizing or ignoring any values. In this way, we can explore and take advantage of the full structure of the connectivity weighting profile. Consequently, we calculate the eigenvector centrality score of every node in a set of consecutive graphs for long time periods (>20 hours). Thereby, we identify important nodes in the epileptic graph dataset and observe which brain regions mostly affect the occurrence of an epileptic episode.

The rest of the paper is organized as follows: After a short description of the data that we use in this study, section II presents our novel methodology and describes the adopted experimental procedure. Section III demonstrates the obtained results, while conclusions and future work are cited in section IV.

II. METHODOLOGY

A. Functional Connectivity Data

The data that are used in this study come from the Neurology Ward of the Cyprus Institute of Neurology and Genetics, where long-term EEG recordings were collected from 5 patients with epilepsy. Brain activity was recorded using twenty-one electrodes which were placed according to the 10-20 international system with two additional anterotemporal electrodes, as shown in Fig. 1. The data were recorded using the XLTEK system, at a sampling rate of 200Hz using a cephalic reference. A 50Hz Notch filter was applied to remove line noise and subsequently the signals were band-pass filtered between 1 and 45Hz.

Finally, the data were converted to the bipolar montage, where pairs of electrodes placed in nearby locations of the scalp, taken in straight lines from the front to the back of the head, were used to obtain the time-series by subtracting the corresponding measurements.

In this work, we analyzed long-duration data from five patients with epilepsy. Table I summarizes the duration of the recordings, as well as the number and type of seizures of each patient. Seizures were identified and marked by expert neurophysiologists (co-authors E.S.P. and S.S.P.).
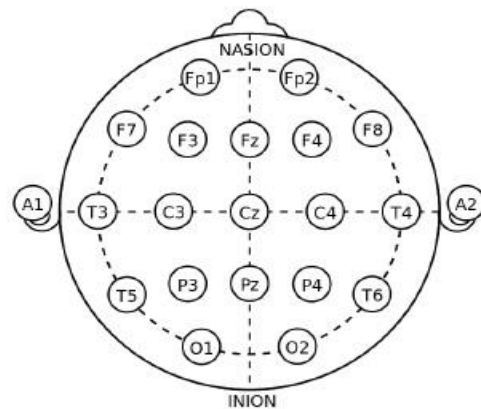

Fig. 1 The 21 electrodes placement according to the 10-20 international system.

The aforementioned data as well as the functional connectivity graph datasets were created as an intermediate result in a previous study [12] and hence a more detailed description can be found therein. The data were processed in consecutive non-overlapping windows of 5 seconds length and one functional network for each such window was constructed. All the derived graphs are weighted, undirected and fully connected and have size of 18x18. The topology of these graphs is depicted in Fig. 2.

TABLE I
EEG RECORDINGS

Patient	Length of Recording	Number of Seizures	Type of Epilepsy
1	47h	1	Focal
2	22h	2	Focal
3	68h	2	Focal
4	94h	1	Generalized
5	66h	1	Generalized

B. Feature Extraction

1) The Eigenvector centrality measure.

Eigenvector centrality is a self-referential measure of centrality because nodes have high eigenvector centrality if the other nodes that they are connected with, also have high eigenvector centrality [13]. The eigenvector centrality of a node i is equivalent to the ith element in the eigenvector corresponding to the largest eigenvalue of the adjacency matrix [14]:

Let $G = (V, E)$ be an undirected graph and A the adjacency matrix of the network G. The eigenvector centrality is the eigenvector C_{eiv} of the largest eigenvalue λ_{max} in absolute value such that $\lambda C_{eiv} = AC_{eiv}$. Formally, if A is the adjacency matrix of a network G with $V(G) = v_1, \ldots, v_n$ and $\rho(A) = max|\lambda|$, then the eigenvector centrality $C_{eiv}(v_i)$ of the node v_i is given by the ith coordinate x_i of a normalized eigenvector that satisfies the condition:
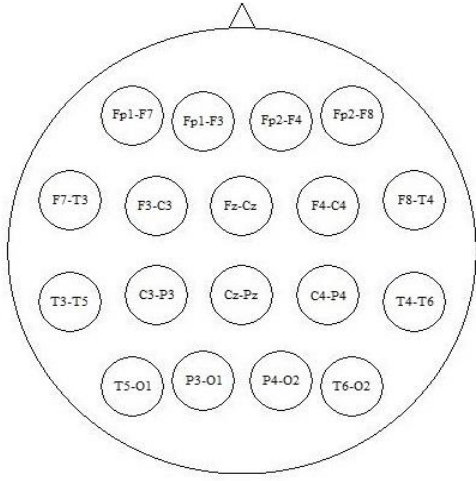
$$Ax = \rho(A)x \qquad (1)$$

Fig. 2 Representation of brain network, after the application of bipolar montage.

2) The Statistical Mean:

A measure of central tendency is a single value that attempts to describe a set of data by identifying the central position within that set of data. The mean (or average) is the most popular and well known measure of central tendency and it is defined as the sum of all the values in the data set divided by the number of elements of this data set [15]. So, if we have n elements in a data set and they have values $x_1, x_2, \ldots, x_n$, the statistical mean is:

$$\bar{x} = \sum_{i=1}^{n} \frac{x_i}{n} \qquad (2)$$

3) The Standard Deviation:

In statistics, the standard deviation σ is a measure that is used to quantify the amount of variation or dispersion of a set of data values [15]. A standard deviation close to 0 indicates that the data points tend to be very close to the mean of the set, while a high standard deviation indicates that the data points are spread out over a wider range of values. It is defined as follows:

$$\sigma = \sqrt{\frac{1}{n} \sum_{i=1}^{n} \left(x_i - \bar{x} \right)^2} \qquad (3)$$

C. Algorithm Description

At the first step we divide the datasets in time periods and more specifically we divide the datasets of patients 1, 4 and 5 in three periods which are the: Pre-ictal, Ictal and Post-Ictal period. Respectively we divide the datasets of patients 2 and 3, which both contain two epileptic seizures, in five time periods which are the: Pre-ictal, Ictal, Inter-ictal, Ictal and Post-ictal period. Next, we apply the eigenvector centrality measure to the entire dataset of each patient separately.

It is important to mention here that each person's seizures are unique, with a unique origin and a unique seizure network that the abnormal brain waves traverse, causing a unique seizure behavior for each one of them [16]. Therefore, this constitutes the reason why we choose to study each patient separately.

As a result for every dataset we have 18 vectors, one for each node, that contain the eigenvector centrality measure values for

all the duration of the recording time. After that, we calculate the mean and standard deviation values for every vector and finally we get pairs of values for each node individually that correspond to the aforementioned time periods. For example, for patients 1, 4 and 5 we get three sets of 18 pairs that contain the mean and standard deviation values and for patients 2 and 3 we get five sets of 18 pairs that also contain the mean and standard deviation values.

At the final step of our methodology, we examine which nodes have at the same time high mean values but low standard deviation rates of the eigenvector centrality measure. Consequently we aim at identifying which nodes serve as hubs and play an essential role in each brain network during the Pre-ictal, Ictal, Inter-ictal or Post-ictal period.

III. RESULTS

Five datasets of functional brain networks from patients with epilepsy were studied in total, as shown in Table I. The datasets were studied according to the procedure that was described in the previous section. In this paper, due to lack of space we only demonstrate results from the second patient, but it is important to mention that analogous results were obtained from the study of the other patients as well.

Fig. 3 demonstrates the mean eigenvector centrality values of two particular nodes for all the five time periods that were previously described. These two nodes represent the right and left temporal lobe of the human brain. It is obvious that the mean eigenvector centralities before each seizure onset (Pre-ictal and Inter-ictal period) are high while at the rest of the time periods the rates are lower. This means that these two nodes have an important influence in the network during these periods of time and play a significant role before the occurrence of each epileptic seizure. For this reason, these regions could also be examined for the prediction of epileptic seizures in that particular patient.

Fig. 4 also displays the mean eigenvector centrality values of another two nodes of the epileptic brain networks for all the five time periods. This time, we observe that the direction of the values is totally opposite. The two nodes, that represent the parietal and occipital lobe of the human brain, present higher mean eigenvector centrality values during the two seizures and lower rates during the Pre-ictal and Inter-ictal periods. This fact can imply that these two regions may constitute the seed of the abnormal electrical activity that the human brain presents during seizures. Also, in both of the aforementioned figures all the values of standard deviation are very close to zero.

IV. CONCLUSIONS

We demonstrated a new methodology for identifying important regions in long-recorded EEG epilepsy brain networks during different recording stages that refer to Pre-ictal, Ictal, Inter-ictal and Post-ictal periods. The most important advantage of our method is that it was directly applied to weighted and fully-connected networks, by taking advantage of the full exploitation of connectivity weights without truncating, binarizing or ignoring any edges of the graphs. In this context, we used the well-known eigenvector
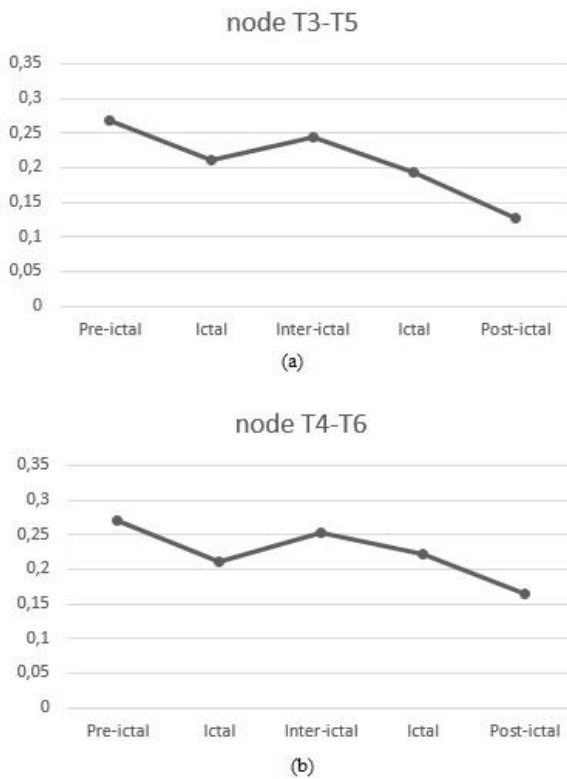
node T3-T5

(a)

node T4-T6

(b)

Fig. 3 Mean eigenvector centrality values for nodes that represent the temporal lobe.
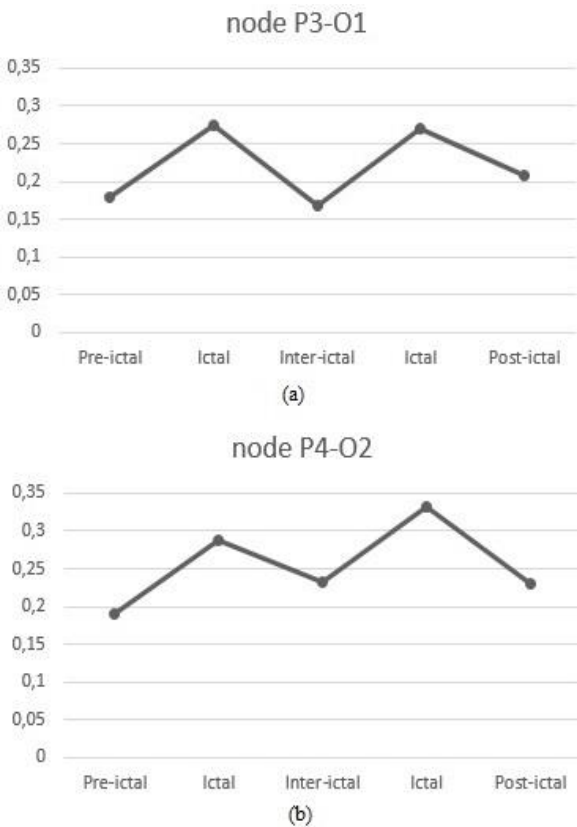

node P3-O1

(a)

node P4-O2

(b)

Fig. 4 Mean eigenvector centrality values for nodes that represent the parietal and occipital lobe.

centrality measure in order to assess the importance of each node at each time.

We studied each patient separately and presented an implementation of our proposed scheme in one of them with quite interesting results. As a future work, we are intending to apply the suggested methodology to a sufficient number of patients and also to perform statistical validation procedures in order to reaffirm and validate our results and conclusions.

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