Computers in Biology and Medicine 46 (2014) 11–21

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

Connectivity analysis of multichannel EEG signals using recurrence based phase synchronization technique

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ARTICLE INFO

Article history:
Received 22 October 2012
Accepted 26 October 2013

Keywords:
Brain connectivity
EEG signals
Recurrence quantification analysis
Phase synchronization
Correlation between probabilities of recurrence
Linear correlation
Epileptic seizure
Brain headmap

ABSTRACT

Real world biological systems such as the human brain are inherently nonlinear and difficult to model. However, most of the previous studies have either employed linear models or parametric nonlinear models for investigating brain function. In this paper, a novel application of a nonlinear measure of phase synchronization based on recurrences, correlation between probabilities of recurrence (CPR), to study connectivity in the brain has been proposed. Being non-parametric, this method makes very few assumptions, making it suitable for investigating brain function in a data-driven way. CPR's utility with application to multichannel electroencephalographic (EEG) signals has been demonstrated. Brain connectivity obtained using thresholded CPR matrix of multichannel EEG signals showed clear differences in the number and pattern of connections in brain connectivity between (a) epileptic seizure and pre-seizure and (b) eyes open and eyes closed states. Corresponding brain headmaps provide meaningful insights about synchronization in the brain in those states. K-means clustering of connectivity parameters of CPR and linear correlation obtained from global epileptic seizure and pre-seizure showed significantly larger cluster centroid distances for CPR as opposed to linear correlation, thereby demonstrating the superior ability of CPR for discriminating seizure from pre-seizure. The headmap in the case of focal epilepsy clearly enables us to identify the focus of the epilepsy which provides certain diagnostic value.

1. Introduction

Studies on human brain have taken two directions. On one hand, various brain regions have different functionality. On the other hand, functionally different regions are connected as a network acting together. There has been substantial progress in the area of brain connectivity [1]. In particular, electroencephalographic (EEG) signals are found to be very effective signals in inferring functional connectivity. EEG provides a more direct measure with high temporal resolution. Functional connectivity helps us to understand brain activity and to explore brain's functional networks. Many studies have shown that functional connectivity helps understand neural data and also how the brain works as a connected network [1].

This paper emphasizes the use of nonlinear techniques for studying connectivity in the brain. This seems logical since many real world biological systems, including brain, are inherently nonlinear in nature. Nonlinear neural time series analysis has been motivated by the fact that many crucial neural processes have nonlinear characteristics. Many nonlinear methods have been applied to analyze EEG signals obtained under various experimental conditions. In particular, measures based on nonlinear dynamical systems and chaos theory such as correlation dimension and Lyapunov exponents [2] have been used to describe the complex EEG signal. In order to compute invariants from the reconstructed attractors, chaos based approaches make certain general assumptions such as: (a) the signal possesses a non-evolving low-dimensional attractor and (b) signal is long, stationary and noiseless. To relax these assumptions, the non-parametric method of recurrence plot (RP) has been employed in the literature to visualize the behavior of trajectories of dynamical systems in phase space [3]. Unlike many approaches in nonlinear dynamical signal analysis, RPs have an apparent simplicity of implementation and interpretation, and do not require an understanding of system's dynamical behavior. This is not only a visualization technique but also provides quantification measures for the local rate of divergence, even for signals of short lengths [4]. In view of these facts, a recurrence based phase synchronization technique, which is both nonlinear and non-parametric, has been employed in this paper.

Recurrence based techniques have been greatly facilitated by the introduction of recurrence quantification analysis (RQA). It has been suggested that RQA may provide meaningful results even if the observation period is shorter than the characteristic time of dynamics in question [5]. Furthermore, RQA measures have been proposed to quantify systematically the different structures found in RP [5]. RQA has become very popular and has found numerous applications in diverse fields such as physiology [6], geology [7],

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http://dx.doi.org/10.1016/j.compbiomed.2013.10.025

and physics [8]. RQA has been used to study various biological systems including neuronal spike trains [9], electromyographic data [10], electroencephalogram [11] and tachogram data [12]. Since RQA can deal directly with the signal without the need for system identification and also quantifies the activity of a system irrespective of its dynamical nature, application of RQA to quantify dynamics of EEG appears to be a promising choice.

In recent years there have been extensive studies on phase synchronization(PS) [13,14]. PS has been applied to both natural [15] and engineering [16] systems with success. The importance of PS in the study of neuronal systems has also been recognized [17]. PS is of interest in neuroscience studies since many biological systems exhibits PS. The importance of phase synchronization for chaotic oscillators has been recognized [18,19] and synchronization of chaotic systems has been studied by many researchers [14,20]. Numerous applications of this phenomenon to magneto encephalography [21] and natural systems such as neuronal systems [15,17], cardio respiratory systems [22], ecological systems [23] and laser systems [16] have been reported in literature. Many techniques for studying brain connectivity have been discussed but most of the previous studies have either employed linear models or parametric nonlinear models for brain connectivity studies [24]. However, it appears that no attempt has been made to apply recurrence based phase synchronization measure for studying connectivity in the brain. In this work an attempt has been made in this direction. It should be noted that this method, being non-parametric, makes very few assumptions, making it suitable for investigating brain function in a data-driven way.

It may be noted that many of the brain connectivity studies are based on linear correlation which has rather limited interpretability in the broader context of biological interaction, which is based on synchronization. Specifically, it has been recognized that phase synchronization in the brain plays an important role in distributed information processing necessary to sustain many higher order brain processes such as consciousness [25]. While zero-lag first order phase synchronization can be detected by linear correlation, higher order and lagged synchronization cannot be detected by it [25,34]. Therefore, linear correlation may not be suitable for characterizing certain interactions in the brain. The use of CPR for characterizing phase synchronization in brain networks alleviates the above issues with linear correlation-based methods. This fact has been validated in this paper by showing that the nonlinear correlation measure CPR is superior in performance to the linear correlation measure. Here a novel use of a nonlinear and non-parametric recurrence based phase synchronization measure has been made for connectivity analysis of multichannel EEG signals.

In this paper we present a novel application of CPR for making connectivity studies. Connectivity analysis is a post-processing technique applied on CPR matrix to obtain insights into the interdependency of the different regions of the brain. Here, brain connectivity using EEG signals by making use of the concept of significance matrix has been studied. The study has been made on EEG signals recorded under various experimental conditions and a comparative study with the linear correlation measure has been made to establish that the nonlinear measure CPR outperforms the linear correlation.

2. Methods

2.1. Recurrence plot

EEG signals are recorded from the brain and the phase space trajectory is constructed from the signal. According to Takens [26], the procedure for mapping of a discrete signal x into phase space is as follows. Given a signal with N terms, $x_1, x_2, x_3, \ldots x_i, \ldots x_{N_s}$ vectors $\boldsymbol{y}_i$ of dimension D with lag (delay) d are defined as follows:

$$\boldsymbol{y}_i = \begin{bmatrix} x_k \\ x_{k+d} \\ x_{k+2d} \\ \vdots \\ x_{k+(D-1)d} \end{bmatrix} \quad D \geq 1,\ d \geq 1,\ i = 1 \text{ to } N_s,\ k = i \bmod N-(D-1)d$$

This is referred to as embedding the signal in phase space of dimension D with lag d. The variable $\boldsymbol{y}$ gives the trajectory of the signal in phase space of dimension D. Takens's theorem states that phase space completely represents the original state space topologically, preserving all its properties. When two points $\boldsymbol{y_i}$ and $\boldsymbol{y_j}$ in phase space, corresponding to time instants i and j, are close to each other based on a certain pre-defined norm, a recurrence is said to have occurred. Recurrence is a topological property of state space and hence is preserved by phase space.

A plot called recurrence plot (RP) is obtained from such recurrences as follows: The RP is formed by comparing all points of the trajectory, $\boldsymbol{y}$, pair-wise, and assigning a recurrence when the distance between two vectors is below some chosen threshold, ε. This leads to a representation of a higher dimensional trajectory in a two-dimensional space. In other words, an $N \times N$ matrix is calculated as follows:

$$R_{i,j} = \Theta(\varepsilon - \|\boldsymbol{y}_i - \boldsymbol{y}_j\|)$$

where $\|\cdot\|$ is a norm, ε is the recurrence threshold and $\Theta(\ )$ is the Heaviside step function forcing $R(i,j)$ to be either 0 or 1. Throughout this paper Euclidean norm has been used.

2.1.1. Choice of D, d and ε

There appears to be no universal method available for optimum selection of D. Ideally the embedding dimension D must be the same as the dimensionality of the underlying system generating the signal. Since this dimensionality is not known, a suitable choice has to be made for D. There is a need to select a value that is sufficiently high so as to capture all state variables. But one must be aware that an excessively large value would increase the computation time. D can be determined experimentally on a case by case basis depending on the signal. Methods previously employed [27–29] are used to obtain the value of D.

There are various methods available in literature to obtain the delay time, d [30]. One method is based on the normalized autocorrelation function of the signal (ACF), where d is the time at which ACF falls down to $(1-e^{-1})$ of its maximum. For a rapidly time varying signal, d will be small, whereas it will be large for a slowly varying signal. In the literature, specific values for specific types of signals (ex. EEG) have already been found experimentally [27–29] which has been used in this paper.

The value of threshold, ε, cannot be chosen to be too low as no recurring points would be found, and also cannot be chosen to be too high that every point is a recurring point. As a way of determining an appropriate value, calculations are performed at the smallest ε, say 0.1, and then increased in steps of, say, 0.1, repeating the calculations for every ε. A plot of number of recurrences versus ε is drawn. The threshold is selected as that value where the percentage of recurring points begins to rise sharply off the noise floor. In this work, I have experimented as described above for EEG signal under consideration and used the obtained value.

2.1.2. Recurrence quantification analysis (RQA)

The main advantage of RP is its graphical appeal. However, RP often contains subtle patterns that are not easily distinguished by visual inspection, and thus, qualitative analysis alone is insufficient in practical applications. To solve this problem, Zbilut and Webber [31] introduced the concept of recurrence quantification analysis

(RQA) to quantify RPs. Other researchers have proposed additional measures thereafter [32].

Like RQA, cross recurrence quantification analysis (CRQA) is another set of measures to quantify recurrence plots. Here, two signals are simultaneously considered for the computation of CRQA measures, and hence are suitable for multichannel signals. In this section, a CRQA measure which quantifies phase synchronization is presented. The concept of phase synchronization is then extended to multichannel signals.

2.2. Probability of recurrence (PR)

Based on the definition of recurrence, when $j=i+\tau$, and $R(i,j)=1$ then it can be said that the trajectory returns to the neighborhood of i after a delay τ. If the number of such recurrences for all $(i, i+\tau)$ is considered, relative to the total number $N-\tau$, an estimate of the probability $P(\tau)$ of the system returning to a pre-defined state after a delay τ is obtained. Then the probability $P(\tau)$ that each sample in the trajectory returns to its neighborhood after a delay of τ samples is given by the equation:

$$P(\tau)=\frac{1}{N-\tau}\sum_{i=1}^{N-\tau}R_{i,i+\tau}=\frac{1}{N-\tau}\sum_{i=1}^{N-\tau}\Theta(\epsilon-||\vec{y}_i-\vec{y}_{i+\tau}||)$$

Since $\boldsymbol{y}$ has a dimensionality D, $P(\tau)$ describes higher order correlations between the points of the trajectory with time delay τ [18,21]. $P(\tau)$ has found applications in estimating dynamical invariants [33] and geophysics [7].

In the case of periodic systems it can be shown that $P(\tau)$ is equal to 1 for values of τ which are integral multiples of period k of the signal, and 0 otherwise. Integral multiples of the mean period show local maxima in $P(\tau)$. An ideal scenario describing this mathematically would be: $\boldsymbol{y}(i+k)-\boldsymbol{y}(i)=\mathbf{0}$. However, perfect recurrences are not characteristic of natural systems. As a result a modified requirement as obtained follows: $\|\boldsymbol{y}(i+k)-\boldsymbol{y}(i)\|\sim\mathbf{0}$, or equivalently: $\|\boldsymbol{y}(i+k)-\boldsymbol{y}(i)\|<\varepsilon$, where ε is a threshold; which implies that a recurrence $R(i, i+k)=1$ can be interpreted as an indicator of approximate periodicity in the trajectory at point i with period k. Then, $P(\tau)$ can be viewed as the probability with which the trajectory has a period k.

2.3. Correlation between probabilities of recurrence (CPR) for two signals

Two sinusoids are phase synchronized when their corresponding frequencies and phases are locked. Phase synchronization is different from generalized synchronization in that it does not consider relative amplitude variations into consideration. Using the probability of recurrence, $P(\tau)$ of two signals, it is possible to detect phase synchronization (PS) between any two signals [18]. Looking at the coincidence of the positions of the maxima of $P(\tau)$ for both signals, it is possible to quantify the degree of phase synchronization by a measure called Correlation coefficient between Probabilities of Recurrence (CPR) [34]. It is calculated using the relation:

$$\mathrm{CPR}=\frac{\sum_{\tau=\tau_e}^{\tau_m-1}\{P_1(\tau)-m_1\}\{P_2(\tau)-m_2\}}{\sigma_1\sigma_2}$$

where m_1 and m_2 are the mean, and σ_1 and σ_2 are the standard deviations of $P_1(\tau)$ and $P_2(\tau)$, respectively. τ ranges from τ_e to τ_m; since $P(\tau)$ always has a value of 1 for $\tau=0$, CPR is computed only over the segment starting when $P(\tau)$ falls below $1/e$. τ_e is the value of τ for which $P(\tau)=1/e$. The value of τ_m is usually chosen to be half the length of the longer signal.

CPR gives the degree of phase synchronization between two signals. If two signals are in perfect PS, the probability of recurrences has peaks for some delay, τ_1, and CPR$\sim$1. On the other hand, if the signals are not synchronized then the peaks of $P(\tau)$ do not coincide; in which case CPR will have a low value.

2.3.1. Phase synchronization in multichannel EEG signals

In this paper, the definition of CPR has been extended to study the overall synchrony of multichannel signals. EEG is recorded simultaneously using electrodes placed at various locations on scalp to obtain a multichannel signal (16 channels in this paper). CPR is calculated between all pairs of 16 channels, thus, obtaining a 16×16 matrix, $\mathrm{CPR}_{N\times N}$:

$$\mathrm{CPR}_{N\times N}=\begin{bmatrix}\mathrm{CPR}_{1,1} & \cdots & \mathrm{CPR}_{1,N}\\ \vdots & \ddots & \vdots\\ \mathrm{CPR}_{N,1} & \cdots & \mathrm{CPR}_{N,N}\end{bmatrix},$$

$\mathrm{CPR}_{i,j}=$ CPR between signals of channels i and j

The overall synchronicity of the brain is represented by mean value of all the 240 elements of the matrix (excluding principal diagonal elements). Application of CPR for the case of multichannel EEG signals has been discussed in this paper using EEG signals recorded under various conditions.

2.4. Connectivity analysis of multichannel signals using CPR

Connectivity analysis is a class of post-processing technique applied on CPR matrix. Elements of CPR matrix give the local picture of synchrony between two signals whereas connectivity gives the global picture through the degree and location of synchronicity over larger regions. To obtain connectivity, an approach that makes use of the concept of significance matrix is used in this paper, which is employed to analyze multichannel EEG signals.

A comparative study of the use of CPR and linear correlation for connectivity analysis has been performed and the results interpreted. In this paper, linear correlation corresponds to the evaluation of Pearson's cross correlation coefficient [35]. It is arguably the most widely used measure of linear correlation, and is also an indicator of phase synchronization since it takes only relative phases between the signals into consideration and not the amplitudes. In this paper, Pearson's cross correlation coefficient is used and is throughout referred to as "linear correlation" or even just "correlation".

2.4.1. Brain connectivity using significance matrix

Here a multichannel case is presented, where the 16×16 CPR matrix $\mathrm{CPR}_{i,j}$ is obtained. A significance matrix $\boldsymbol{S}$ is a thresholded CPR matrix, whose (i,j)th element is set to 0 when $\mathrm{CPR}_{i,j}<\tau_s$, else it is set to 1 where τ_s is an appropriately chosen threshold. When $S_{ij}=1$ it is said that there is a connectivity between i and j. Brain connectivity graph is obtained using S_{ij}, which shows network-level characterization of the brain. Brain headmap is obtained from the connectivity graph, which gives a visualization of connectivity across the brain. Headmaps are obtained using EEG topographic scalp mapping. It is generated as a mapping of the second order curve fit using the significance matrix obtained from the CPR matrix. The significance matrix elements are mapped onto the positions of electrodes placed on the scalp during data acquisition (which in this case is the International 10–20 system of electrode placement). This particular code had been designed with the help of EEG Matlab Toolbox (General Public License).

A study on brain network connectivity using records of multichannel EEG signals is presented in this paper. A comparative study of brain network connectivity using CPR and linear correlation is also performed and the results are interpreted.

3. Results and discussion

3.1. Multichannel EEG database

Multichannel EEG signals are used in this work. Sixteen channel EEG is recorded at a sampling frequency of 128 Hz for about 45 s for each subject, with electrodes placed on the scalp based on the international 10–20 system of electrode placement. The 16 channels are (in order from 1 to 16): Fp1, Fp2, F7, F3, F4, F8, T3, C3, C4, T4, T5, P3, P4, T6, O1 and O2. The recording is obtained for 16 neurological patients affected by epilepsy, and contains pre-seizure and seizure segments. Ethical clearance was obtained prior to data collection.

Focal epilepsy data is obtained from a patient already diagnosed with abnormalities in the somatosensory and motor cortex. Sixteen channel EEG data for eyes open and eyes closed (EO–EC) conditions is recorded at a sampling frequency of 128 Hz for about 10 min. For the first 5 min, the subject is asked to keep his eyes open. For the next 5 min he is asked to keep the eyes closed. The subject is found to be healthy and free of major psychological problems. Electrode placement for signal recording is same as that for epilepsy signal mentioned above.

RP is obtained using the following parameters: $D=8$, $d=10$, $\varepsilon=0.5$. These values of D and d are popularly used in the literature [29]. ε is derived experimentally in this paper.

3.2. Brain connectivity analysis using multichannel EEG signals

Connectivity study is performed on EEG recorded under different experimental conditions: (1) eyes open and eyes closed (EO–EC) experiment, (2) seizure EEG recorded from neurological patients with general epilepsy, and (3) seizure EEG of a patient with focal epilepsy.

3.2.1. Brain connectivity in EO–EC case

The database used for EEG is same as the one described above. A 16×16 CPR matrix is computed for each of the cases EO and EC as explained before.

The brain connectivity graph shows the number and location of connections between channels based on synchronicity. Using the brain connectivity graph, brain headmap is obtained, which shows the regions of the brain that are synchronized. Obtaining the brain headmap involves obtaining the topographic scalp map [36] using certain interpolation methods on the adjacency matrix. A similar analysis is carried out with linear correlation, instead of CPR, for comparison.

Fig. 1 shows the pictorial representation of significance matrices (black=1, white=0), which are obtained by thresholding the CPR and correlation matrices with a threshold of 0.85, chosen experimentally.

Figs. 2 and 3 show the brain connectivity graphs obtained for the two cases and the two methods of CPR and correlation, respectively. It is evident that the brain connectivity graph shows very few connections during eyes open (low synchronization) compared to eyes closed. This result is summarized in Table 1.

The ratio of the number of connections for EC to EO is 18 for CPR based method whereas that ratio is only 4.33 for correlation based method. CPR is closer to the physiologically established fact that there are significantly more number of connections in EC case.

3.2.2. Brain headmap

Figs. 4 and 5 show the brain headmaps. The brain headmap is obtained from the significance matrices and brain connectivity graphs, using the knowledge of the location of electrodes placed on the scalp during the recording of the 16 channel EEG data using the 10–20 system of electrode placement. It shows the relative magnitudes and locations of synchronization over the brain.

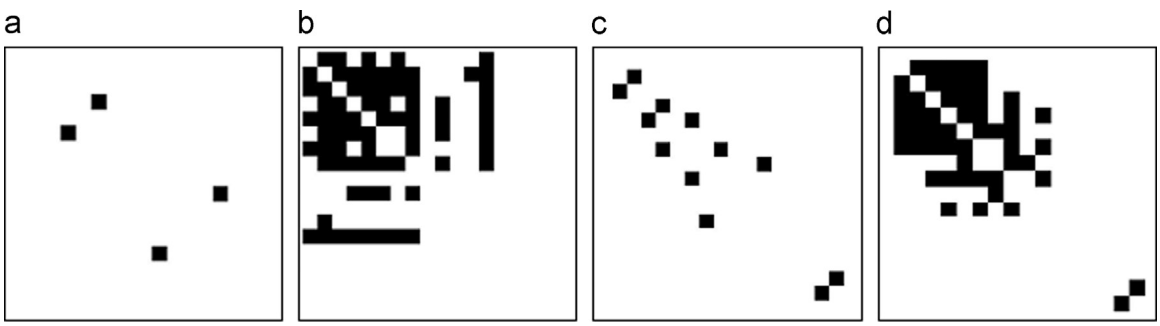

Fig. 1. Pictorial representation of significance matrices obtained using (a) CPR: eyes open, (b) CPR: eyes closed, (c) correlation: eyes open, and (d) correlation: eyes closed.

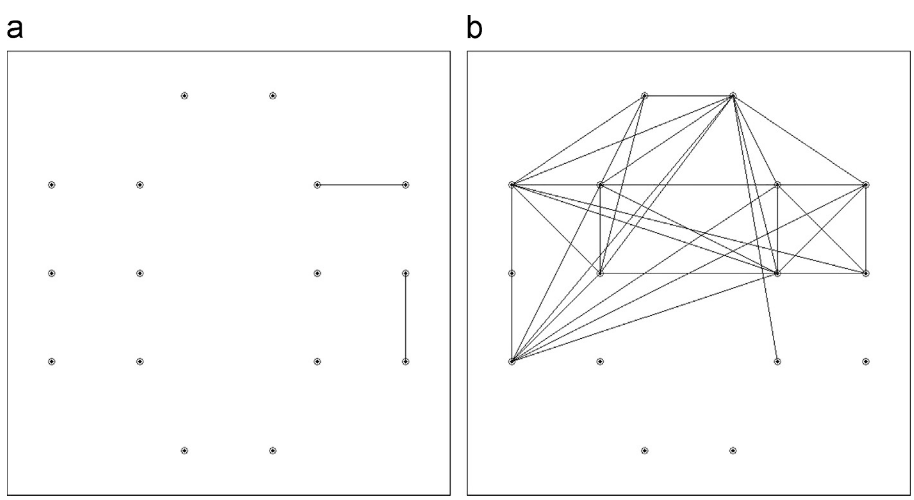

Fig. 2. Brain connectivity graph using CPR during: (a) eyes open and (b) eyes closed.

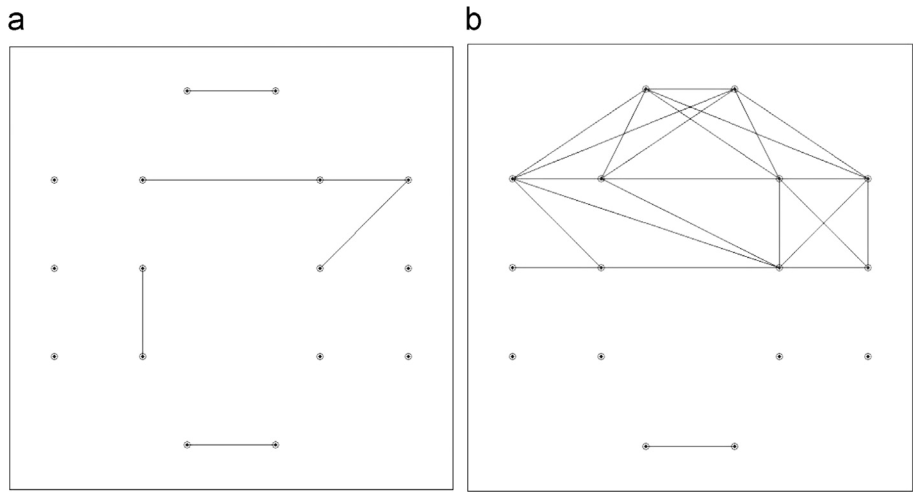

Fig. 3. Brain connectivity graph using Correlation during: (a) eyes open and (b) eyes closed.

Table 1
Number of connections in the brain connectivity graphs for CPR and correlation during eyes open and eyes closed states.

	Number of connections (CPR)	Number of connections (correlation)
Eyes open	2	6
Eyes closed	36	26

Fig. 4 clearly shows that brain is much more synchronized during eyes closed compared to eyes open for the CPR based method. Moreover the synchronization is distributed throughout the brain. However, from Fig. 5 it is evident that brain headmap is not showing a clear distinction between eyes open and eyes closed states for the correlation based method. It shows several synchronized locations when eyes are open (which is unexpected). Also during eyes closed it is showing synchronization only in the frontal areas (which is also unexpected). So, CPR based method appears to be closer to physiologically known facts [37].

3.3. Brain connectivity in global epilepsy case

The earlier used procedure (EO–EC case) is applied to the large database of 16 channel EEG recordings obtained for neurological patients with global epilepsy. The database consists of recordings made on 16 subjects. The threshold, τ is taken as the average of ($\text{mean}_{\text{pre-seizure}}+\text{std}_{\text{pre-seizure}}$) and ($\text{mean}_{\text{seizure}}-\text{std}_{\text{seizure}}$). In our experiment the value of τ is obtained as 0.7664. Significance matrices are obtained using this τ for pre-seizure and seizure conditions for all 16 subjects, which is then used in obtaining corresponding brain connectivity graphs.

As an illustration, average of CPR matrices of all 16 subjects is taken to obtain one CPR matrix (CPR_A). Then analysis is performed on this matrix similar to what was done on other 16×16 CPR matrices. Figs. 6 and 7 show the contour plots for the case of CPR and correlation, respectively. Figs. 8 and 9 show the brain connectivity graphs and Figs. 10 and 11 show the brain head maps using CPR and correlation, respectively, during pre-seizure and seizure states. It may be noted that the brain headmap before seizure using CPR is blank since no connections were found in the corresponding brain connectivity graph.

These figures contain statistically averaged information from all 16 subjects. Contour plots clearly show the statistical consistency of CPR and also its conformity to physiological facts. However, contour plots of correlation show negligible difference between the states, as well as an inconsistency in the pattern. It is also clear from the brain connectivity graphs that CPR is showing globally spread and uniform connectivity pattern, which is expected in case of epilepsy. However, correlation shows fewer concentrated connections which are uncharacteristic of global seizures. Brain headmaps visually reiterate the same.

3.3.1. *Number of connections for pre-seizure and during seizure for all 16 subjects*

The number of connections present in the brain connectivity graph are computed for all the 16 subjects. Number of connections is calculated for both pre-seizure and seizure states using CPR and the results are given in Table 2. The same procedure is repeated for correlation and time-lagged maximum cross correlation coefficient, which are presented in Tables 3 and 4, respectively.

The following inferences can be made from the above tables:

- CPR based case: There is a large difference between the mean values in the number of connections for pre-seizure (1.6875) and seizure (95.5625) states, with relatively small standard deviations of 2.1516 and 9.7705, respectively.
- Correlation based case: There is a relatively smaller difference between the mean values for pre-seizure (5.6250) and seizure (33.3750) states, with relatively larger standard deviations of 4.5443 and 20.2842, respectively.

The values obtained in the above tables are plotted. Fig. 12 shows the number of connections for all subjects in the case of CPR, while Fig. 13 shows them in the case of correlation.

These figures show clear evidence that CPR has provided better distinction than correlation. K-means clustering of CPR and linear correlation is obtained for the values in Tables 2 and 3, which showed significantly larger cluster centroid distances for CPR as opposed to linear correlation (Table 4), thereby demonstrating the efficacy of CPR.

Also, as in earlier cases, brain headmaps have been obtained for the two cases for all the 16 subjects. The contrast between

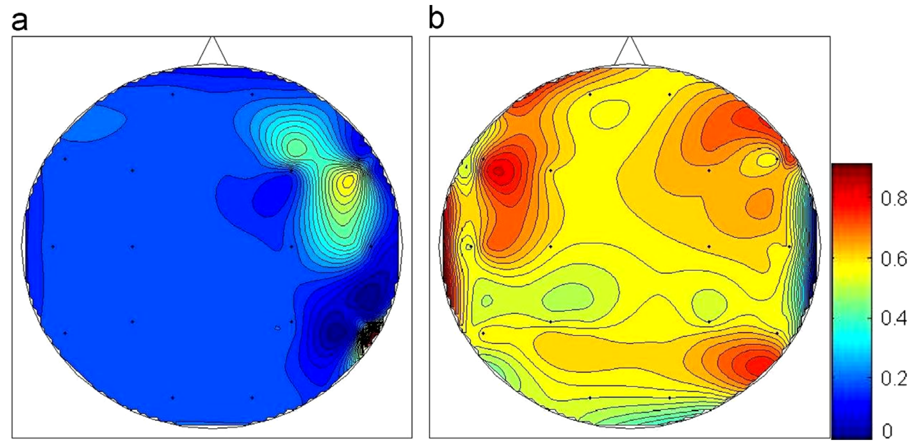

Fig. 4. Brain headmap using CPR based method for: (a) eyes open and (b) eyes closed.

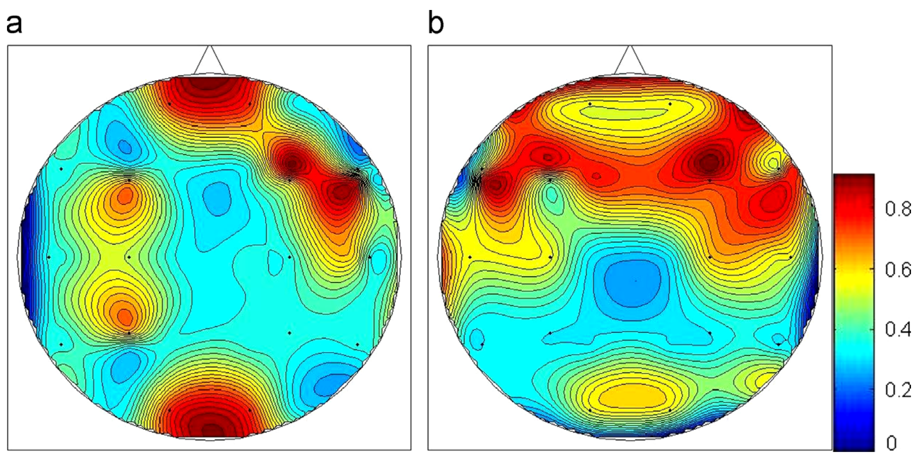

Fig. 5. Brain headmap using Correlation based method for: (a) eyes open and (b) eyes closed.

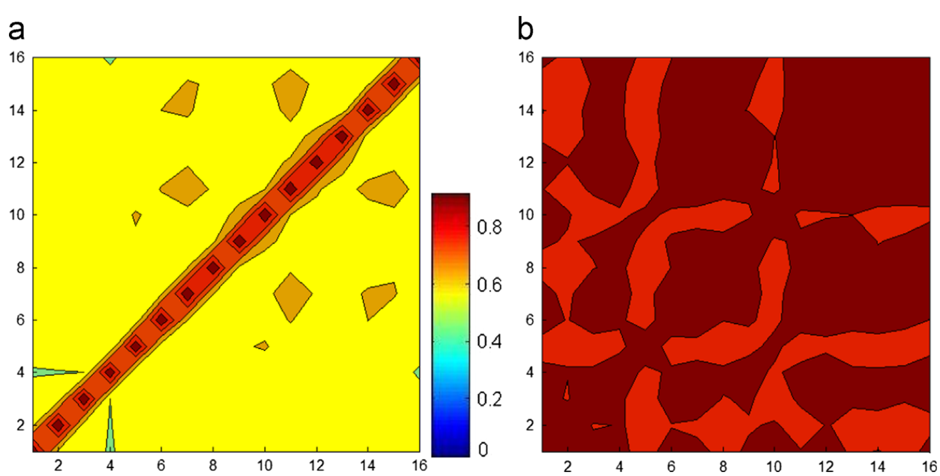

Fig. 6. Contour plots obtained using averaged CPR matrix of 16 subjects for (a) before seizure and (b) during seizure.

pre-seizure and seizure has been clearly observed in these cases also and it is seen to be closer to physiologically known facts in case of CPR based maps compared to correlation based maps.

These results also establish that the CPR based method gives a more reliable measure compared to correlation based method in analyzing the synchronicity in EEG signals. These results give a good insight about phase synchronicity in the brain during various experiments and across various states.

3.4. Brain connectivity in focal epilepsy case

Ten channel EEG signal is considered here, which is recorded during seizure in a patient with focal epilepsy. 16×16 CPR matrix is obtained and connectivity analysis is done as before. The brain connectivity graph and brain headmap are obtained using the significance matrix. Similar analysis is carried out using linear correlation in place of CPR.

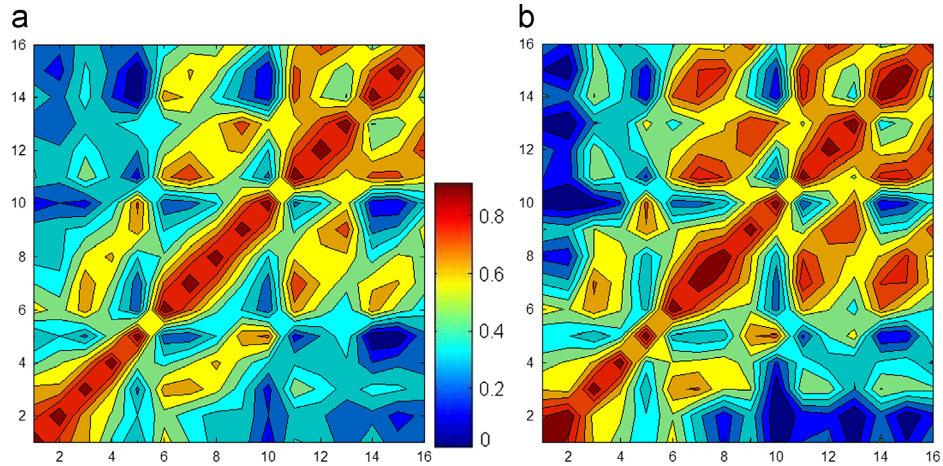

Fig. 7. Contour plots obtained using averaged correlation matrix of 16 subjects for (a) before seizure and (b) during seizure.

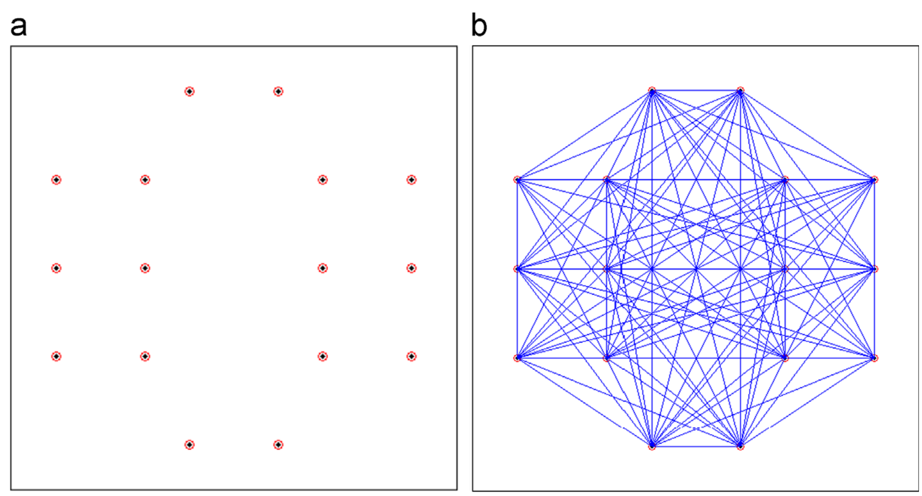

Fig. 8. Brain connectivity graph using CPR: (a) before seizure and (b) during seizure.

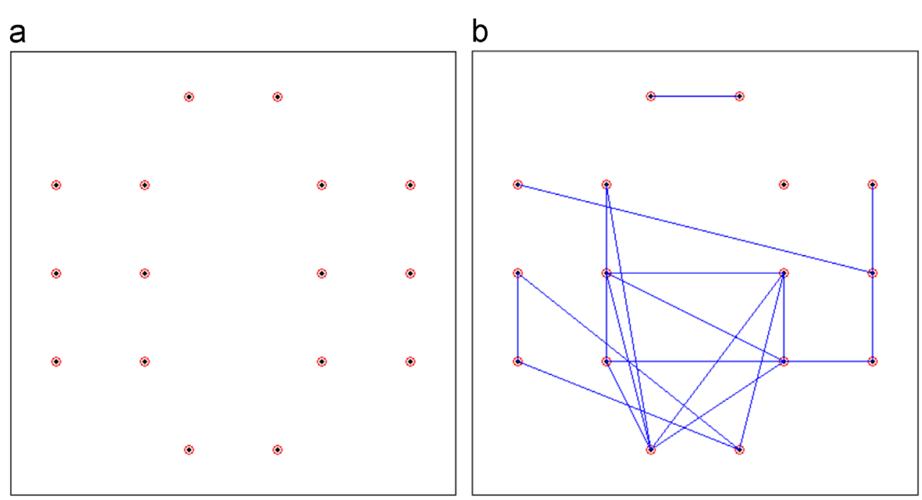

Fig. 9. Brain connectivity graph using correlation: (a) before seizure and (b) during seizure.

Fig. 14 shows the brain connectivity graphs obtained based on CPR and correlation. Fig. 15 shows the brain headmaps obtained based on CPR and correlation.

The brain connectivity graph for CPR case shows connections corresponding to the focus of epilepsy. These locations are also corroborated by the diagnosis done for the subject. However, the brain connectivity graph for correlation case shows no connections, indicating that correlation has not picked the focus of epilepsy.

The brain headmap for CPR shows clear information about the location of focus of epilepsy. The focus appears in the parietal lobe near the sensor motor area. This is the best that can be concluded with the available resolution of 10 channels in this recording.

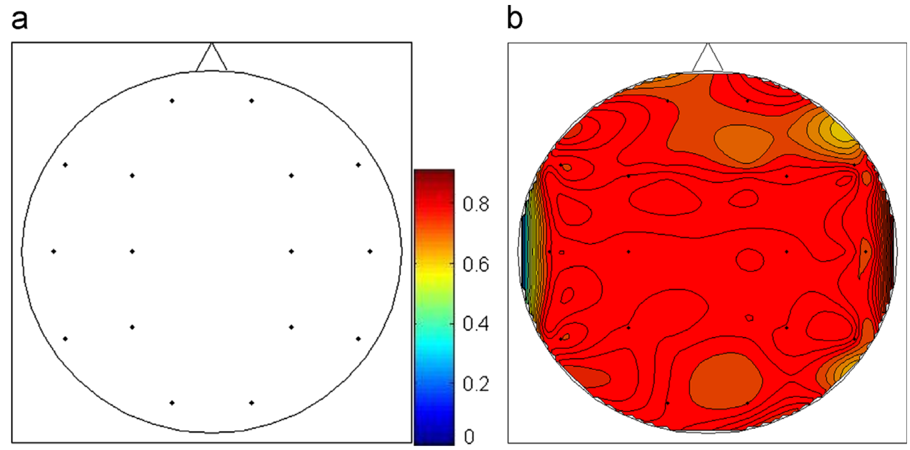

Fig. 10. Brain headmap using CPR: (a) before seizure and (b) during seizure.

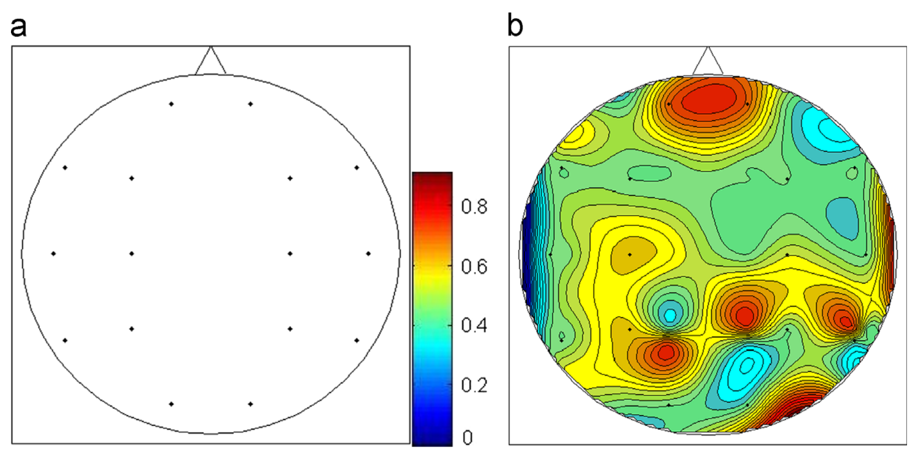

Fig. 11. Brain headmap using correlation: (a) before seizure and (b) during seizure.

Table 2
Number of connections in brain connectivity graph obtained using CPR.

No. of connections	Pre-seizure	During seizure
Subject-1	0	107
Subject-2	4	84
Subject-3	0	103
Subject-4	0	81
Subject-5	6	105
Subject-6	0	84
Subject-7	3	102
Subject-8	2	109
Subject-9	0	83
Subject-10	0	86
Subject-11	0	105
Subject-12	5	95
Subject-13	4	97
Subject-14	0	89
Subject-15	0	95
Subject-16	3	104
Mean	**1.6875**	**95.5625**
Standard deviation	**2.1516**	**9.7705**

Table 3
Number of connections in brain connectivity graph obtained using correlation.

No. of connections	Pre-seizure	During seizure
Subject-1	5	20
Subject-2	7	4
Subject-3	2	53
Subject-4	0	16
Subject-5	11	54
Subject-6	5	49
Subject-7	5	41
Subject-8	2	12
Subject-9	9	47
Subject-10	10	53
Subject-11	4	13
Subject-12	3	10
Subject-13	1	21
Subject-14	10	61
Subject-15	0	21
Subject-16	16	59
Mean	**5.6250**	**33.3750**
Standard deviation	**4.5443**	**20.2842**

These results show that CPR can be effectively used to infer about the focus of epilepsy in affected patients.

The brain headmap for correlation has no information about focus. These results show that CPR provides certain information which correlation fails to do, especially in the case of sophisticated biomedical signals.

Table 4
K-means distance between cluster centroids obtained using CPR and correlation.

	Using CPR	Using correlation
K-means cluster centroid distance	130.42	45.21

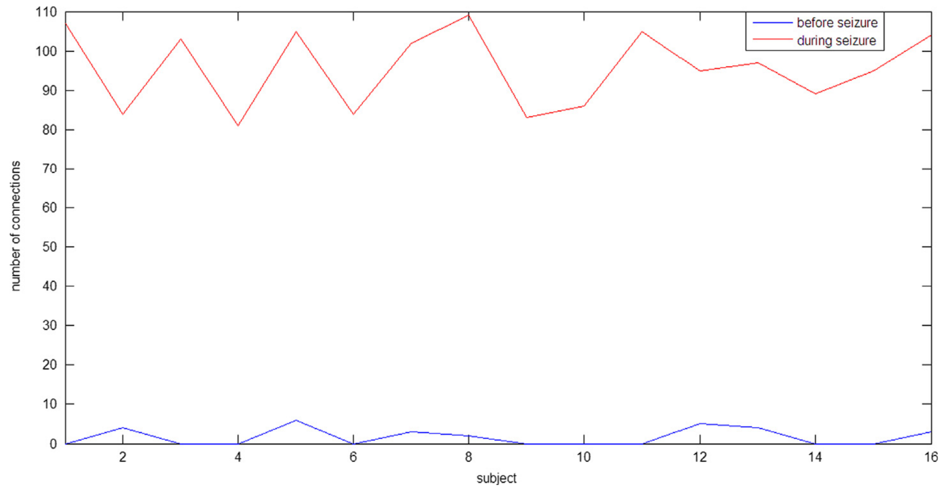

Fig. 12. Number of connections in brain connectivity graph for all subjects using CPR.

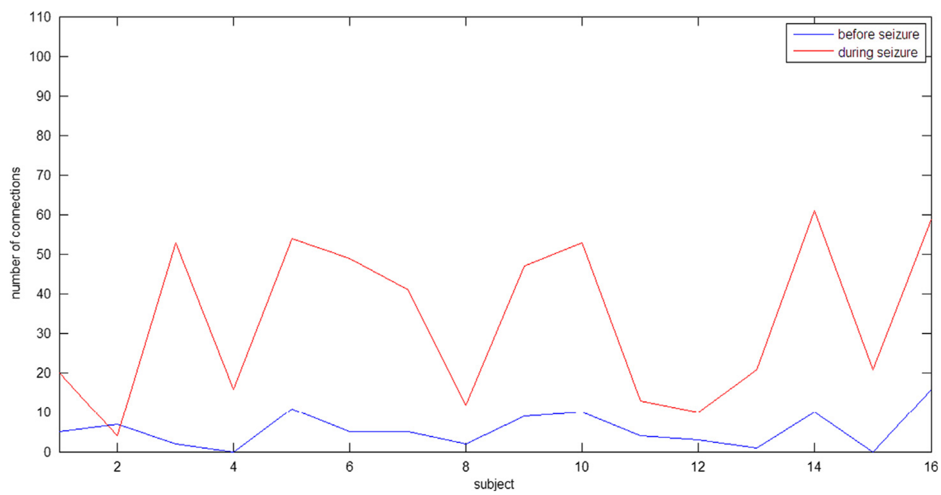

Fig. 13. Number of connections in brain connectivity graph for all subjects using correlation.

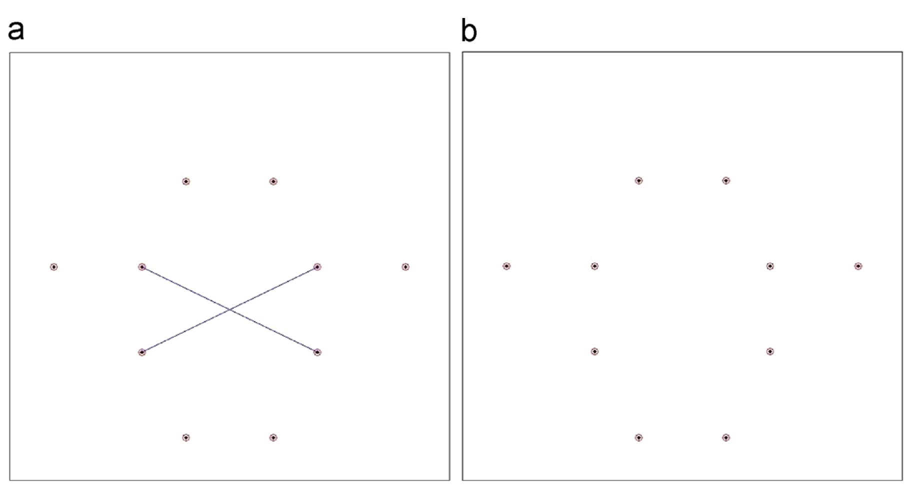

Fig. 14. Brain connectivity graph during focal seizure based on (a) CPR and (b) correlation.

4. Conclusions

Phase synchronization is known to occur for chaotic attractors that have comparatively simpler oscillatory patterns and distinguishable power spectral peaks. However, for attractors with a rather broadband power spectrum, an indirect method of quantifying PS based on recurrence plots needs to be employed. In this paper, a recurrence based PS measure has been employed for functional connectivity analysis of multichannel EEG signals. This study is important since functional connectivity plays an important role in understanding how brain works as a concerted network. It is also important since it employs a nonlinear technique which is eminently

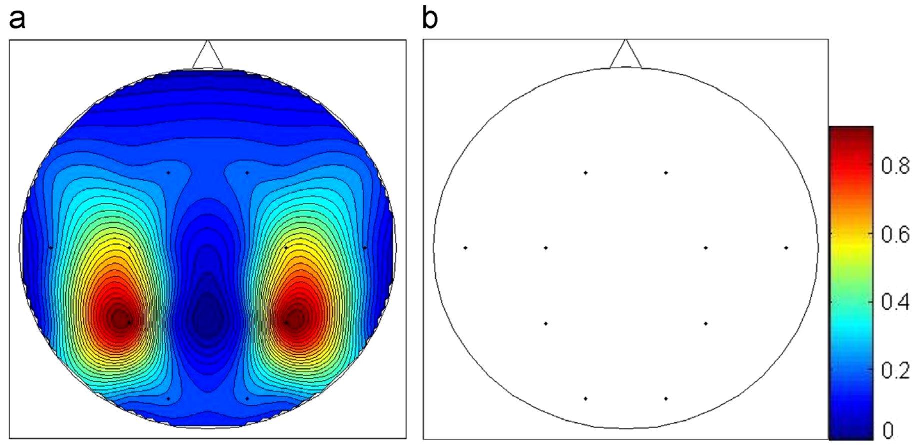

Fig. 15. Brain headmap during focal seizure based on (a) CPR and (b) correlation.

suitable for an inherently nonlinear system such as brain. Being non-parametric, this method makes very few assumptions, making it suitable for investigating brain function in a data-driven way. The importance of using a nonlinear recurrence based phase synchronization measure for brain connectivity studies has been validated by the results of this paper. Since not much effort appears to have been put in studying phase synchronization of EEG signals using recurrence based techniques, it is hoped that this work will trigger interest in this direction of study. The paper has effectively demonstrated the applicability of recurrence based phased synchronization analysis for brain connectivity studies for several multichannel EEG data acquired under various experimental conditions. The utility of the present study particularly for epilepsy cases – both global and focal epilepsy – has been clearly demonstrated and its potential diagnostic value is obvious. However, it is to be noted that EEG signals can be obtained under many other experimental conditions as well and then studied by the technique proposed in this paper to further show the utility of the technique for many other practical applications. It is also hoped that the paper will trigger interest in studying the applicability of many other nonlinear based connectivity analysis techniques in understanding inherently nonlinear brain function.

Summary

This paper is concerned with the novel use of a nonlinear recurrence plot based phase synchronization measure for the study of connectivity in the brain. Here a study of novel use of the nonlinear measure CPR to an altogether different application of connectivity analysis has been made, to obtain insights into the interdependency of the different brain regions under different experimental conditions. Being non-parametric, this method makes very few assumptions, making it suitable for investigating brain function in a data-driven way. The concept of significance matrix has been used and applied in a novel way to EEG signals in studying synchronization in brain networks. Multichannel EEG data recorded under eyes open–eyes closed (EO–EC) condition and also multichannel seizure signals recorded for the cases of global epilepsy and focal epilepsy has been used for this purpose. It has been shown that the synchronization measure could distinguish between eyes open and eyes closed states as also pre-seizure and seizure states in terms of number of connections in the brain connectivity graph, and also in the brain headmap. Effective visualization techniques provide a network-level characterization of the brain using CPR. The brain headmap for CPR shows clear information about the location of focus of epilepsy whereas the brain headmap for correlation has no information about focus. Similar results have been obtained using brain connectivity graph also. These results show that CPR provides certain information which correlation fails to do, especially in the case of sophisticated biomedical signals. Comparative study with correlation showed that CPR provides plausible results which correlation fails to do.

It is to be noted that most of the connectivity studies are made using linear correlation whose applicability is limited for an inherently nonlinear biological interactions taking place in the brain. Keeping this in mind, a nonlinear metric CPR using recurrence based technique has been effectively used in this paper. The results obtained in this paper have corroborated the above observations with the nonlinear measure CPR providing certain information which correlation fails to do. Results using 16 subjects on global epilepsy data show that there is a large difference between mean values in the number of connections for pre-seizure and seizure states for the CPR based case whereas there is relatively smaller difference for the corresponding linear correlation case. The brain connectivity graph and the headmap for the focal epilepsy case also show that the nonlinear CPR based measure clearly scores over the linear correlation. Also CPR based method provides results for the EO-EC case which are closer to the physiologically known facts compared to the linear correlation method. All these results establish the superiority of the proposed use of CPR measure over the conventional linear correlation for brain connectivity studies.

It should be noted that real world biological systems such as the human brain are inherently nonlinear and difficult to model. However, most of the previous studies have either employed linear models or parametric nonlinear models for investigating brain function. In this paper, a novel application of a nonlinear measure of phase synchronization based on recurrences to study connectivity in the brain has been proposed. Being non-parametric, this method makes very few assumptions, thus, making it suitable for brain connectivity studies in a data-driven way.

The main findings of this paper are: (i) Number of connections in the brain connectivity graph could clearly distinguish between pre-seizure and seizure states. (ii) Effective visualization techniques provide a network-level characterization of the brain using CPR. (iii) The headmap in the case of focal epilepsy clearly enables us to identify the focus of the epilepsy which has diagnostic value. (iv) Comparative study between CPR and linear correlation has shown that CPR clearly performs better than linear correlation.

Conflict of interest statement

None declared.

Acknowledgments

The author would like to thank Prof. N. Pradhan from NIMHANS, Bangalore for providing him with some of the data used in this work.

The author would also like to thank Prof. T. Srinivas and Prof. D. Narayana Dutt for many useful discussions.

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