Disponible en ligne sur
SciVerse ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com

IRBM

IRBM xxx (2012) xxx–xxx

Original article

Application of a dissimilarity index of EEG and its sub-bands on prediction of induced epileptic seizures from rat's EEG signals

L'application d'un indice de dissimilarité de l'EEG et de ses sous-groupes sur la prévision des crises d'épilepsie chez les rats induites par des signaux EEG

M. Niknazar [a,*], S.R. Mousavi [a], M.B. Shamsollahi [a], B. Vosoughi Vahdat [a], M. Sayyah [b], S. Motaghi [b], A. Dehghani [b], S.M. Noorbakhsh [b]

[a] *Biomedical Signal and Image Processing Laboratory (BiSIPL), School of Electrical Engineering, Sharif University of Technology, PO Box 11365–9363, Tehran, Iran*

[b] *Physiology and Pharmacology Department, Pasteur Institute of Iran, Tehran, Iran*

Received 6 November 2011; received in revised form 17 July 2012; accepted 20 September 2012

Abstract

Objective. – Epileptic seizures are defined as manifest of excessive and hyper-synchronous activity of neurons in the cerebral cortex that cause frequent malfunction of the human central nervous system. Therefore, finding precursors and predictors of epileptic seizure is of utmost clinical relevance to reduce the epileptic seizure induced nervous system malfunction consequences. Researchers for this purpose may even guide us to a deep understanding of the seizure generating mechanisms. The goal of this paper is to predict epileptic seizures in epileptic rats.

Methods. – Seizures were induced in rats using pentylenetetrazole (PTZ) model. EEG signals in interictal, preictal, ictal and postictal periods were then recorded and analyzed to predict epileptic seizures. Epileptic seizures were predicted by calculating an index in consecutive windows of EEG signal and comparing the index with a threshold. In this work, a newly proposed dissimilarity index called Bhattacharyya Based Dissimilarity Index (BBDI), dynamical similarity index and fuzzy similarity index were investigated.

Results. – BBDI, dynamical similarity index and fuzzy similarity index were examined on case and control groups and compared to each other. The results show that BBDI outperforms dynamical and fuzzy similarity indices. In order to improve the results, EEG sub-bands were also analyzed. The best result achieved when the proposed dissimilarity index was applied on Delta sub-band that predicts epileptic seizures in all rats with a mean of 299.5 s.

Conclusion. – The dissimilarity of neural network activity between reference window and present window of EEG signal has a significant increase prior to an epileptic seizure and the proposed dissimilarity index (BBDI) can reveal this variation to predict epileptic seizures. In addition, analyzing EEG sub-bands results in more accurate information about constituent neuronal activities underlying the EEG since certain changes in EEG signal may be amplified when each sub-band is analyzed separately.

Significance. – This paper presents application of a dissimilarity index (BBDI) on EEG signals and its sub-bands to predict PTZ-induced epileptic seizures in rats. Based on the results of this work, BBDI will predict epileptic seizures more accurately and more reliably compared to current indices that increases epileptic patient comfort and improves patient outcomes.

1. Introduction

Epilepsy is the second most common neurological disorder after stroke [1]. Epileptic seizures reflect the clinical signs of an excessive and hyper-synchronous activity of neurons, which may cause electrical disturbances in brain and make changes in sensation, awareness and behavior [1]. About 1% of the people in the world suffer from epileptic seizures. Epileptic seizures can be

* Corresponding author.
E-mail addresses: niknazar@alum.sharif.edu (M. Niknazar), moosavir@alum.sharif.edu (S.R. Mousavi), mbshams@sharif.edu (M.B. Shamsollahi), vahdat@sharif.edu (B. Vosoughi Vahdat), sayyahm2@pasteur.ac.ir (M. Sayyah), motaghis@vetmed.ut.ac.ir (S. Motaghi), yasad490@yahoo.com (A. Dehghani), smn2133@columbia.edu (S.M. Noorbakhsh).

1959-0318/$ – see front matter © 2012 Elsevier Masson SAS. All rights reserved.
http://dx.doi.org/10.1016/j.irbm.2012.09.002

controlled by antiepileptic drugs in two thirds of patients while another 8% may benefit from epilepsy surgery. Unfortunately, the remaining 25% of epilepsy patients cannot be treated with any available therapy [2]. Epileptic seizure prediction could help epilepsy patients to have a normal life.

Since epilepsy is a condition related to the electrical activity of the brain, it can be assessed by analyzing electroencephalogram (EEG) signals. Epilepsy is characterized by occurrence of recurrent seizures in EEG signal [3]. Conventional seizure detection methods such as visual inspection of the EEG by a trained neurologist are challenging because of the presence of myogenic artifacts. These methods are also unable to detect the characteristic changes that precede seizure onsets. Hence, prediction of seizures with these methods is challenging. Spectral analysis, which is another primary approach, is based on earlier observations that the EEG spectrum contains some characteristic waveforms that fall primarily within four frequency bands. Such methods have proved to be beneficial for various EEG characterizations. However, Fast Fourier Transform (FFT) suffers from having large noise sensitivity.

Newer spectral approaches based on parametric methods for power spectrum estimation such as autoregressive (AR) [4,5] reduce the spectral loss problems and give better frequency resolution. Since the EEG signals are non-stationary, the parametric methods are not suitable for frequency decomposition of these signals. More recently, algorithms that are more sophisticated have been used, yielding increasingly accurate results. For example, in [6] wavelet packet transform has been used for seizure detection and in [7] it has been confirmed that the complex Gaussian wavelet transform can be used to analyze of phase synchronization of EEG signal for seizure prediction. In Fact, there is very little confirmed knowledge of the exact mechanism responsible for the seizure [8]. Over the years, many researchers have attempted to assess long-term EEG recordings to recognize epileptic form transients [9,10]. Some relative weaknesses in this literature are the lack of extensive testing on baseline data free from seizures, the lack of technically rigorous validation and quantification of algorithm performance in many studies.

Studies in seizure prediction vary in their theoretical approaches, validation of results, and amount of data analyzed. EEG-based seizure detection and prediction methods are mostly based on two approaches: firstly, examination of the waveforms in the seizure-free EEG to find markers or changes in neuronal activity such as spikes which may be precursors to seizures; secondly, analysis of the nonlinear spatiotemporal evolution of the EEG signals to find a governing rule as the system moves from a seizure-free to seizure state [11]. Recurrence quantification analysis [12] and similarity index methods [13] are among the second approach. Some other nonlinear analyses of epileptic EEGs such as the one proposed in [14] can also be categorized as the second approach.

Dynamical similarity index [15] and its modification, fuzzy similarity index [16], have been widely employed for seizure detection and prediction. In a recent study [17] dynamical similarity index was also combined with mean phase coherence to improve the results of seizure prediction. However, both dynamical and fuzzy similarity indices suffer intrinsic problems. As it will be further explained in the next sections, the concept of dynamical similarity index is strict or binary according to the Heaviside function, and both indices need to determine a radius scale, which can be problematic.

In this study, we aim to examine the performance of a dissimilarity index proposed by the authors [18], on epileptic seizure prediction in rats. This dissimilarity index does not have abovementioned problems. Moreover, results of recent investigations [8] indicate that in some cases, EEG sub-bands: delta, theta, alpha, beta, and gamma may yield more accurate information about constituent neuronal activities underlying the EEG and consequently, certain changes in the EEGs that are not evident in the original full-spectrum EEG may be amplified when each sub-band is analyzed separately. Therefore, we wonder if the results can be improved using these sub-bands.

Various animal studies are currently conducted to test epileptic seizure detection and prediction methods. The most popular and widely used animal models are the maximal electroshock seizure test and the subcutaneous (s.c.) pentylenetetrazole (PTZ) test. Development of various new antiepileptic drugs is mostly based on these two seizure models [19]. The s.c. PTZ test is used to find drugs effective against generalized seizures of the petit mal (absence) type [19]. People with absence epilepsy have repeated seizures that cause momentary lapses of consciousness. These sudden and abrupt seizures most commonly occur in childhood or adolescence and may have significant impact on the educational development of sufferers [20].

The goal of this study is to predict epileptic seizures in rats with clonic seizures induced by s.c. injection of PTZ. The EEG signals in interictal, preictal, ictal and postictal periods were recorded and analyzed. The rest of this paper is structured as follows: the utilized data set is introduced in Section 2. The third section discusses the materials of our work. Our proposed method is explained in detail Section 4. In this section, results of our method tested on the dataset are discussed. Finally, in Section 5, a conclusion is reported.

2. Dataset

Data used in this study were collected at Pasteur Institute of Iran. In this work, Male Wistar rats were used to study PTZ-induced epileptic seizures. Twenty-one male Wistar rats weighing 200–250 g were housed in a controlled environment (6 a.m./6 p.m. light/dark cycle; $22 \pm 3\,^{\circ}C$) with free access to food and water. Two screw electrodes were inserted into the skull over the frontal and occipital cortex under ketamine (60 mg/kg, i.p.) -xylazine (10 mg/kg, i.p.) anesthesia. The epidural electrodes were fixed on the skull using dental acrylic and an extra screw. The animals were allowed 3 days to recover and handled gently to get familiar with the recording procedure. These rats were divided to case (six rats) and control (15 rats) groups. EEG signals were then recorded in the control group for approximately 60 minutes. For the test group, EEG signals were recorded a few minutes before administration of a convulsive dose of pentylenetetrazole (60 mg/kg, i.p.). Then, PTZ was injected s.c. to freely moving rats through a polyethylene tube and electrical activity was recorded for 60 minutes. All

Please cite this article in press as: Niknazar M, et al. Application of a dissimilarity index of EEG and its sub-bands on prediction of induced epileptic seizures from rat's EEG signals. IRBM (2012), http://dx.doi.org/10.1016/j.irbm.2012.09.002

Table 1
Time recording of each experiment.

Rat No.	Injection time	Seizure onset	Seizure end
1	21:34	29:02	30:35
2	10:33	15:09	16:24
3	6:05	9:18	9:36
4	7:16	20:05	20:36
5	5:55	21:25	22:39
6	5:11	9:59	11:01

Time format is minute:second. Starting time is always 00:00.

measurements and injections took place between 10:00 a.m. and 3:00 p.m. EEG signals were recorded using an amplifier with band-pass filter setting of 0.1–1000 Hz. The sampling rate was 10 kHz, and the analog-to-digital conversion is performed with a 12-bit resolution. The start time, injection time, seizure onset time and seizure end time were also written down.

Seizure onset was determined by an experienced experimental scientist by observation of animal behavior including head nodding and general clonus in whole body [21]. The start time, injection time, seizure onset time and seizure end time of experiment is reported in Table 1. The interval between the seizure onset time and injection time is considered as the maximum prediction duration or extended preictal phase. The EEG dataset has been downsampled to 1 kHz, and preprocessed by a 50 Hz notch filter and a low pass 60 Hz filter.

3. Materials and methods

3.1. Phase space and trajectory matrix

Based on the recent studies, EEG signals are multivariate time series caused by highly nonlinear, dynamic and multidimensional systems [22]. One of the approaches for analyzing epileptic EEG signals is to analyze the nonlinear spatiotemporal evolution of the EEG signals to find a governing rule as the system moves from a seizure-free to seizure state [11]. Dynamic systems can be described by a set of states and transition rules, which specify how the system may proceed from one state to another. Each state is the state of all independent variables involve in operation of a system that is defined as a vector. Vectors of different states make a vector space called phase space. Dynamics of a system can be studied by assessing this phase space [23]. In experimental situations, not all relevant variables constructing phase space are known or can be measured. We often have a discrete-time measurement of only one observable quantity. This yields scalar discrete-time series $s_k = s(k\Delta t)$. In such cases, the phase space has to be reconstructed. A single record of a dynamic system is the outcome of all interacting variables of the system and thus, in principle, contains information about the dynamics of all significant variables [24]. Hence, phase space can be reconstructed from single record of the system. A frequently used method for the reconstruction is the time delay method proposed by Takens [25] in which phase space is reconstructed by its trajectories

$$x_j = \left(s_j, s_{j+\tau}, \ldots, s_{j+(m-1)\tau}\right) \quad (1)$$

where $j = 1, 2, \ldots, N-(m-1)\tau$, in which N is the total number of data points in the present window, m is embedding dimension and τ is time delay.

For finite and noisy datasets like EEG recordings, m and τ should be carefully determined. The most common method for choosing a proper time delay is based on calculation of the first local minimum of the mutual information (MI) function [26], since the first minimum of the $MI(\tau)$ portrays the time delay where the signals $(s_T, s_{T+1}, \ldots, s_{L-\tau})$ and $(s_{T+\tau}, s_{T+\tau+1}, \ldots, s_L)$ have the minimal overlapping information. After the selection of the optimum lag, minimum embedding dimension is determined based on Cao's method [27].

3.2. Dynamical similarity index

One of the most common nonlinear methods that analyzes the nonlinear spatiotemporal evolution of the EEG signals to find the transition from a seizure-free to seizure state is called dynamical similarity index method [15] formulized based on nonlinear time series basics proposed by Baulac and Varela [28]. The method consists of reconstruction of EEG dynamics and measurement of similarity between reference state S_{ref} and present state S_t. Reference windows should be recorded during an interval quite distant in time from any seizure. For each window, trajectory matrix is constructed using the vectors of phase space

$$A_{ij} = s_{j+(i-1)\tau} \quad (2)$$

where $1 \le i \le m$ and $1 \le j \le N-(m-1)\tau$. Trajectory or augmented matrix is a complete record of patterns occurs within a window. To reduce noise, the trajectory matrices $A(S_t)$ of the sliding window and $A(S_{ref})$ of the reference window are projected on the principal axes of the reference window resulting from singular value decomposition (SVD) of the reference window, yielding $X(S_t)$ and $X(S_{ref})$, respectively [16]. In order to have more reliable reference window, it is better to select it from a long interval of interictal period. However, this increases computational cost of the algorithm. To achieve a significant reduction in the volume of data without loss of potentially valuable dynamical information, a random selection $Y(S_{ref})$ of $X(S_{ref})$ is done [16]. In this study, the size of $Y(S_{ref})$ equals the size of $X(S_t)$. The second step is to compare $Y(S_{ref})$ with $X(S_t)$ using cross-correlation integral:

$$C_{XY}(r) = \frac{1}{N_{ref} N_t} \sum_{m=1}^{N_{ref}-(m-1)\tau} \sum_{n=1}^{N_t-(m-1)\tau} \times \Theta\left(r - \left\|Y_m\left(S_{ref}\right) - X_n\left(S_t\right)\right\|\right) \quad (3)$$

Here, $||\cdot||$ denotes the Euclidian norm and Θ is the Heaviside step function. N_{ref}, N_t, m and n are the number of points in the phase space of reference window, the number of points in the phase space of sliding window, index for columns of $Y(S_{ref})$ and index for columns of $X(S_t)$, respectively. The distance r is usually defined as the 30% quintile of the cumulative neighborhood distribution of the reference window [29]. In order to further improving the discriminatory power between two dynamics,

Please cite this article in press as: Niknazar M, et al. Application of a dissimilarity index of EEG and its sub-bands on prediction of induced epileptic seizures from rat's EEG signals. IRBM (2012), http://dx.doi.org/10.1016/j.irbm.2012.09.002

cross-correlation integral is normalized by autocorrelation integrals $C_{XX}(r)$ and $C_{YY}(r)$ yielding the dynamical similarity index γ_{XY}:

$$\gamma_{XY} = {}^{C_{XY}}/_{\sqrt{C_{XX}C_{YY}}} \tag{4}$$

Dynamical similarity index provides a sensitive measure of closeness between two dynamics. If the reference and present window share the same underlying dynamics, the value of γ_{XY} is around 1, on the contrary, it goes down to 0.

3.3. Fuzzy similarity index

Fuzzy similarity index was extracted from dynamical similarity index by Ouyang et al. [16] with some modifications. The concept of dynamical similarity index is strict or binary according to the Heaviside function. As a result, all data points just outside the hyper-sphere are discarded and all data points inside the hyper-sphere are treated equally. In the fuzzy similarity index, a Gaussian function is employed to replace the Heaviside function in the dynamical similarity; consequently, the strict boundary in the dynamical similarity becomes smooth. The Gaussian function represents a fuzzy similarity between each data point and adjacent points. After replacing Heaviside function with Gaussian function, correlation integral becomes:

$$C^F_{XY}(r) = \frac{1}{N_{ref}N_t}\sum_{i=1}^{N_{ref}}\sum_{j=1}^{N_t}\exp\left(-\left\|Y_i\left(S_{ref}\right) - X_j\left(S_t\right)\right\|^2/r^2\right) \tag{5}$$

Fuzzy similarity index is then defined as:

$$\gamma^F_{XY} = {}^{C^F_{XY}}/_{\sqrt{C^F_{XX}C^F_{YY}}} \tag{6}$$

Similar to Dynamical similarity index, if the reference and present window share the same underlying dynamics, the value of fuzzy similarity index is around 1, otherwise it goes down to 0.

3.4. Bhattacharyya Based Dissimilarity Index (BBDI)

In [18], a new dissimilarity index inspired by dynamical and fuzzy similarity indices was proposed and is called Bhattacharyya Based Dissimilarity Index (BBDI) in this paper. As mentioned above, the concept of dynamical similarity index is strict or binary according to the Heaviside function. Fuzzy similarity index has been proposed to overcome this problem using Gaussian function instead of Heaviside function. However, for fuzzy similarity index again we need to determine a radius scale based on the cumulative neighborhood distribution of reference set that is challenging. In order to overcome both above-mentioned problems, BBDI was proposed. Calculating BBDI is also computationally faster than calculation of former indices. Bhattacharyya distance is employed to measure dynamical dissimilarity between dynamics of reference state and current state. BBDI can illustrate the temporal distribution of changes in epileptic EEG signals. In this method, Bhattacharyya distance between $X(S_t)$ and $Y(S_{ref})$ is defined as:

$$D_B\left(X\left(S_t\right), Y\left(S_{ref}\right)\right) = \frac{1}{8}\left(m_{X(S_t)} - m_{Y(S_{ref})}\right)^T P^{-1}\left(m_{X(S_t)} - m_{Y(S_{ref})}\right) + \frac{1}{2}\ln\left(\frac{\det(P)}{\sqrt{\det\left(P_{X(S_t)}\right)\det\left(P_{Y(S_{ref})}\right)}}\right) \tag{7}$$

where $m_{X(S_t)}$ and $m_{Y(S_{ref})}$ are mean values of columns of matrices $X(S_t)$ and $Y(S_{ref})$, and $P_{X(S_t)}$ and $P_{Y(S_{ref})}$ are covariance matrices of these matrices, and $P = \frac{P_{X(S_t)}+P_{Y(S_{ref})}}{2}$. If the reference and present windows share the same underlying dynamics, BBDI has low values; on the contrary, it increases.

3.5. Detection of a preictal phase

EEG recording of a seizure activity can be characterized by four stages:

- ictal stage that starts at seizure onset and finishes at seizure end;
- postictal stage which is the period following seizure end and represents a return to normal background activity;
- interictal stage which is the period between postictal stage of one seizure and the moments before next seizure onset;
- preictal stage that is moments before seizure onset.

The goal of seizure prediction is to detect transition from interictal stage to preictal stage. Since there is not certain definition for preictal stage onset, we try to calculate an index in consecutive windows and comparing this index with a threshold. Crossing of index and threshold is considered as an alarm for possibility of seizure onset in following moments. In the literature of prediction of induced epileptic seizures in rats, definition of preictal stage is different from its definition in humans. For induced epileptic seizures in rats, time interval between injection and seizure onset is considered as extended preictal. Therefore, an alarm must be issued in the extended preictal stage to be considered as a correct alarm. The goal of this study is to design an automated method to detect preictal phase. For this purpose, the first step is to calculate the mean value μ and standard deviation (S.D.) σ of each index during interictal phase. The second step is to obtain a baseline for preictal phase detection. As for any given baseline, a local rise can be characterized by its height k and duration d. The height of the rise k can be obtained in units of the S.D. of the baseline epoch, then the threshold value can be set to $(\mu + k\sigma)$, whereas its duration d can be quantified by the time during which the value of a profile rises over this threshold [30]. During practical implementation of this detection method, a backward moving-average filter was first applied to smooth the profiles of each index to avoid abrupt variations. Then the time smoothed index reseeds over the threshold value $(\mu + k\sigma)$ and remained over it within duration d is considered as detection point. The parameters k and d govern the mean height of a rise over a certain time and the threshold for preictal phase detection.

Please cite this article in press as: Niknazar M, et al. Application of a dissimilarity index of EEG and its sub-bands on prediction of induced epileptic seizures from rat's EEG signals. IRBM (2012), http://dx.doi.org/10.1016/j.irbm.2012.09.002

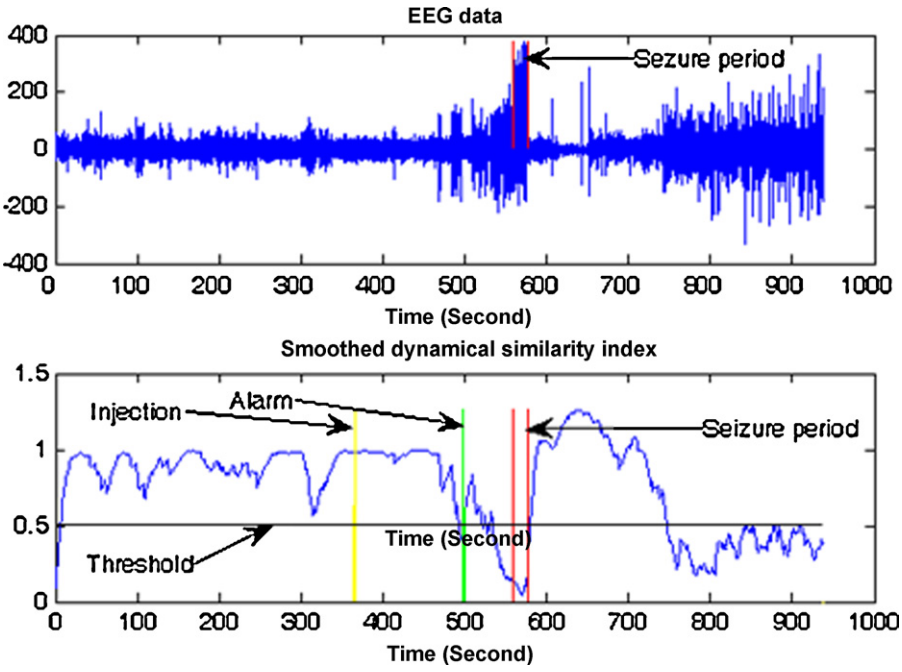

Fig. 1. Top: long-term EEG recording of rat 3 in the test group. Bottom: smoothed dynamical similarity index versus time, which gradually decrease until seizure onset. Solid black line represents the baseline for preictal phase detection parameters $k = -2.3$ and $d = 5$. Administration of pentylenetetrazole was done at 06:05 and epileptic seizure occurred at 09:18. Detection point of preictal phase is at 08:17. The anticipation time is 61 s.

The parameters k and d can be optimized for the whole dataset. The performance of detection [30], Q, is defined as:

$$Q = \sqrt{\frac{Se^2 + Sp^2}{2}} \tag{8}$$

where Se is sensitivity, defined as fraction of correct detections to all seizures; Sp is specificity rate, defined as one minus the average number of false positive detections per hour of interictal EEG in test and the control groups (for more than one false positive per hour, Sp is set to zero).

4. Results

In this section, the results of implementation of the three indices are presented. EEG data of six rats in the test group and 15 rats in the control group were analyzed. Length of each sliding window was 1 s (1000 points), length of reference window was 100 seconds (100,000 points) and threshold value was set to $(\mu + k\sigma)$. Optimum performance for the seizure prediction algorithms based on dynamical similarity index and fuzzy similarity index values were $k = -2.3$ and $d = 5$ for dynamical similarity index and $k = -2.6$ and $d = 5$ for fuzzy similarity index. Both dynamical similarity and fuzzy similarity indices could predict four seizures out of six seizures correctly and had no false alarm in the control group. For both indices, sensitivity and specificity were 67% and 90%. Therefore, value of 79% for Q was obtained for both indices. Fig. 1 shows a correct prediction using dynamical similarity index, and Fig. 2 shows smoothed dynamical similarity index versus time for a rat in the control group. It is observed that dynamical similarity index fluctuations appear at high level over the long-term EEG recording.

Fig. 3 shows a correct prediction using fuzzy similarity index, and Fig. 4 shows smoothed fuzzy similarity index versus time for a rat in the control group.

Dynamical similarity index and fuzzy similarity index had similar results on this dataset. In this dataset mean of duration of extended preictal period was 484 s and mean of anticipation time for dynamical similarity index and fuzzy similarity index in their correct predictions were 324.5 s and 325.5 s, respectively. Table 2 shows anticipation times in terms of second for all rats.

The last index, studied in this work was BBDI. Optimum performance for seizure prediction based on BBDI was obtained with parameters $k = 2.5$ and $d = 5$. Fig. 5 shows a correct prediction using BBDI, and Fig. 6 shows smoothed BBDI versus time for a rat in the control group.

BBDI could predict all six seizures correctly and had no false alarm in the control group. Sensitivity, specificity and Q are all 100% for this index. Fig. 7 summarizes the anticipation time from all six rats in the test group, which shows that BBDI can efficiently predict epileptic seizures. The green and yellow

Table 2
The anticipation times in second for dynamical similarity index and fuzzy similarity index for all rats. Both indices failed to predict seizure for rats 2 and 4.

Rat No.	Dynamical similarity index	Fuzzy similarity index
1	390	391
2	–	–
3	61	63
4	–	–
5	701	702
6	146	146

Please cite this article in press as: Niknazar M, et al. Application of a dissimilarity index of EEG and its sub-bands on prediction of induced epileptic seizures from rat's EEG signals. IRBM (2012), http://dx.doi.org/10.1016/j.irbm.2012.09.002

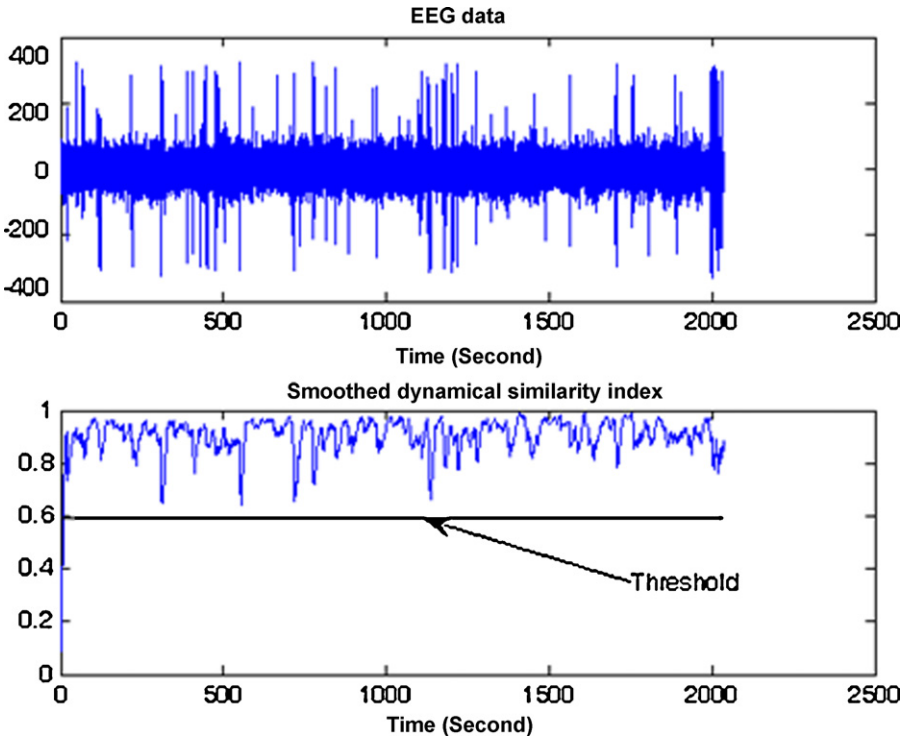

Fig. 2. Top: long-term EEG recording of a rat in the control group. Bottom: smoothed dynamical similarity index fluctuations appear at high level. Solid black line represents the baseline for preictal phase detection with parameters $k = -2.3$ and $d = 5$.

bars in Fig. 7 represent the extended preictal duration and the anticipation time, respectively. Mean times of the extended preictal duration and the anticipation time are 484 s and 293.5 s, respectively. A paired Student t-test was also conducted for the extended preictal duration and the anticipation time. The paired Student t-test showed that there is a significant difference between the mean extended preictal duration and the mean anticipation time ($P < 0.02$).

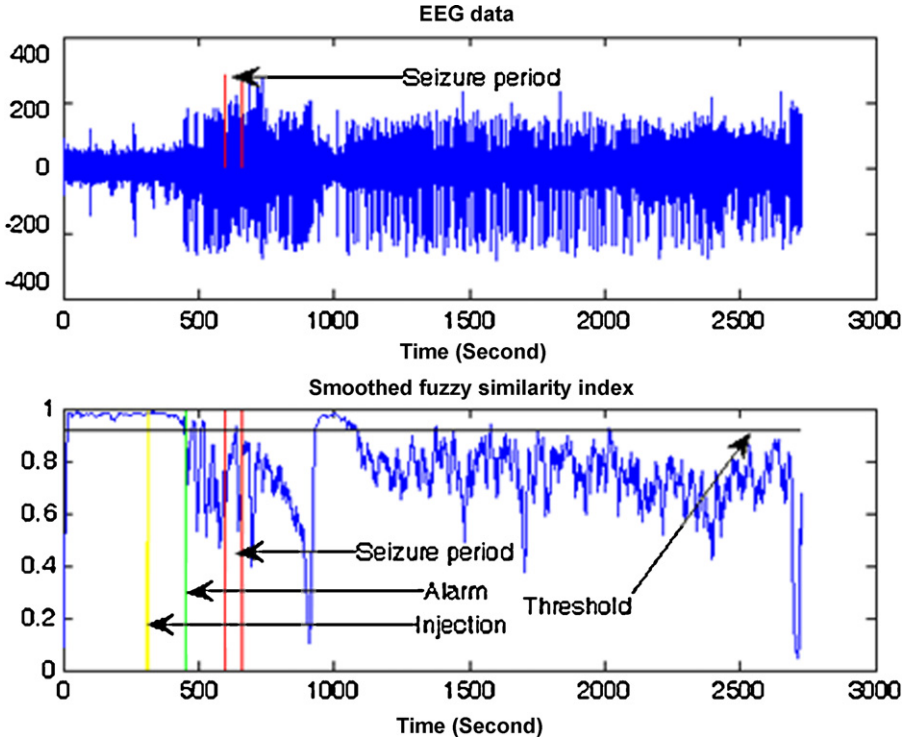

Fig. 3. Top: long-term EEG recording of rat 6 in the test group. Bottom: smoothed fuzzy similarity index versus time, which gradually decrease until seizure onset. Solid black line represents the baseline for preictal phase detection parameters $k = -2.6$ and $d = 5$. Administration of pentylenetetrazole was done at 05:11 and epileptic seizure occurred at 09:59. Detection point of preictal phase is at 07:23. The anticipation time is 146 s.

Please cite this article in press as: Niknazar M, et al. Application of a dissimilarity index of EEG and its sub-bands on prediction of induced epileptic seizures from rat's EEG signals. IRBM (2012), http://dx.doi.org/10.1016/j.irbm.2012.09.002

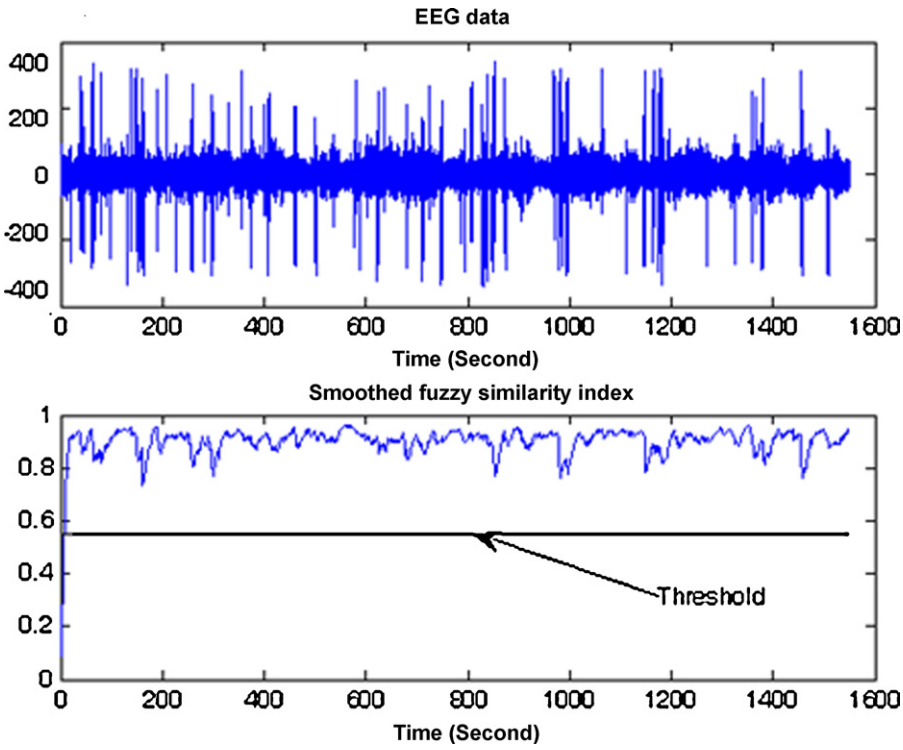

Fig. 4. Top: long-term EEG recording of a rat in the control group. Bottom: smoothed fuzzy similarity index fluctuations appear at high level. Solid black line represents the baseline for preictal phase detection with parameters $k = -2.6$ and $d = 5$.

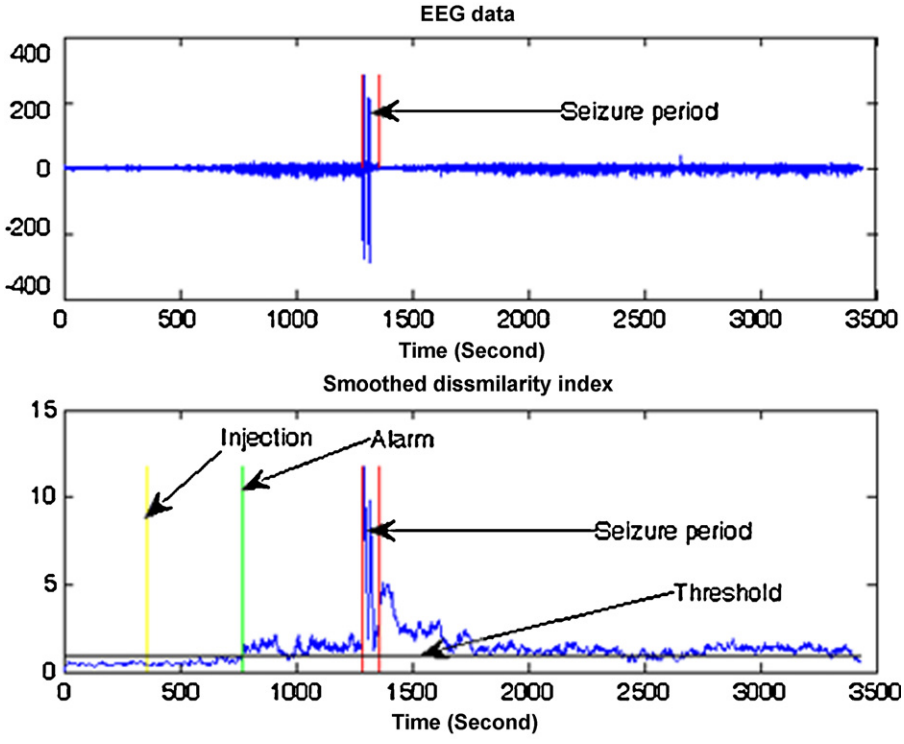

Fig. 5. Top: long-term EEG recordings of rat 5 in the test group. Bottom: smoothed BBDI values versus time, which gradually increase up to seizure onset. Solid black line represents the baseline for preictal phase detection with parameters $k = 2.5$ and $d = 5$. Administration of pentylenetetrazole was done at 05:55 and epileptic seizure occurred at 21:25. Detection point of preictal phase is at 12:51. The anticipation time is 514 s.

Please cite this article in press as: Niknazar M, et al. Application of a dissimilarity index of EEG and its sub-bands on prediction of induced epileptic seizures from rat's EEG signals. IRBM (2012), http://dx.doi.org/10.1016/j.irbm.2012.09.002

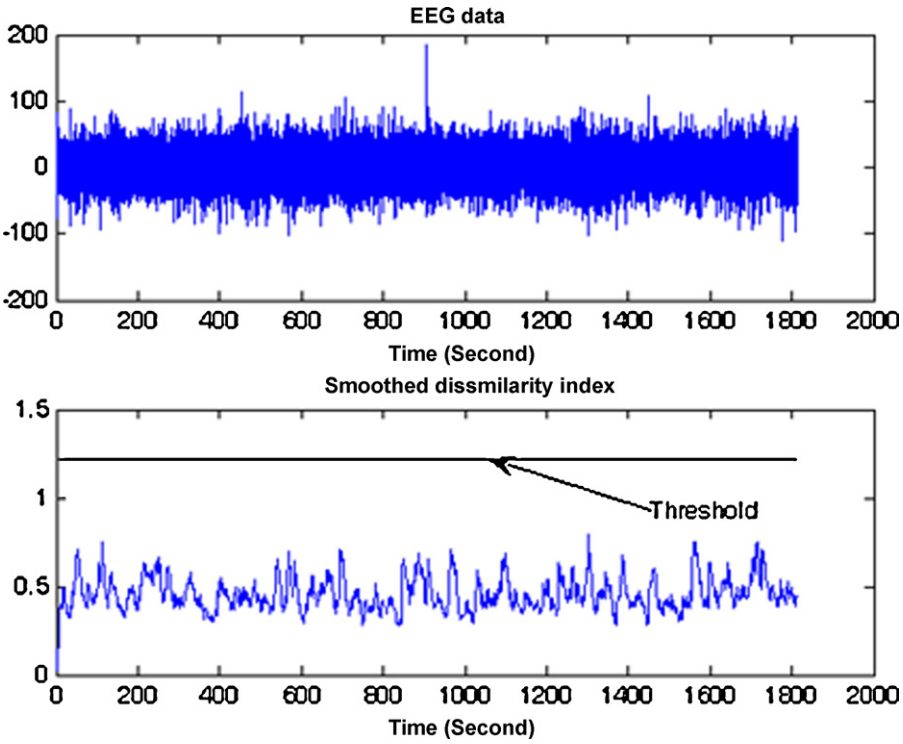

Fig. 6. Top: long-term EEG recording of a rat in the control group. Bottom: smoothed BBDI fluctuations appear at high level. Solid black line represents the baseline for preictal phase detection with parameters $k = 2.5$ and $d = 5$.

Results show that BBDI is more reliable for PTZ-induced epileptic seizure prediction. EEG sub-bands were also analyzed to check if results would be improved. In order to extract individual EEG sub-bands, a wavelet filter was employed. Wavelet transform has the advantages of time-frequency localization, multi-rate filtering, and scale-space analysis [8]. Wavelet transform uses a variable window size over the length of the signal, which allows the wavelet to be stretched or compressed depending on the frequency of the signal. This results in excellent feature extraction from non-stationary signals such as EEG signals. In this study, discrete wavelet transform (DWT) based on dyadic (powers of 2) scales and positions was used which is computationally efficient. EEG signal was decomposed into progressively finer details by means of multi-resolution analysis using DWT. After the first level of decomposition, two sequences representing the high (details) and low (approximations) resolution components of the signal were obtained. The low-resolution components were further decomposed into low and high-resolution components applying a second level decomposition and so on. Continuing up to four levels of decomposition yielded five separate EEG sub-bands. The five EEG sub-bands: delta, theta, alpha, beta, and gamma span the 0–60 Hz frequency range. To correlate the wavelet decomposition with frequency ranges of physiological sub-bands, the wavelet filter used in this application requires frequency content limited to 0–60 Hz band. Due to above-mentioned reasons, the EEG was band-limited to 0–60 Hz range using a low-pass finite impulse response (FIR) filter. EEG signals were then subjected to a four level decomposition using fourth-order Daubechies wavelet transform. After the first level of decomposition, EEG signal, s (0–60 Hz), was decomposed into its higher resolution component, d1 (30–60 Hz) and lower resolution component, a1 (0–30 Hz). In the second level of decomposition, the a1 component was further decomposed into higher resolution components, d2 (15–30 Hz) and lower resolution components, a2 (0–15 Hz). Following this process, after four levels of decomposition, the components retained were a4 (0–4 Hz), d4 (4–8 Hz), d3 (8–15 Hz), d2 (15–30 Hz), and d1 (30–60 Hz). Reconstructions of these five components using the inverse wavelet transform approximately correspond to the five physiological EEG sub-bands delta, theta, alpha, beta, and gamma [8].

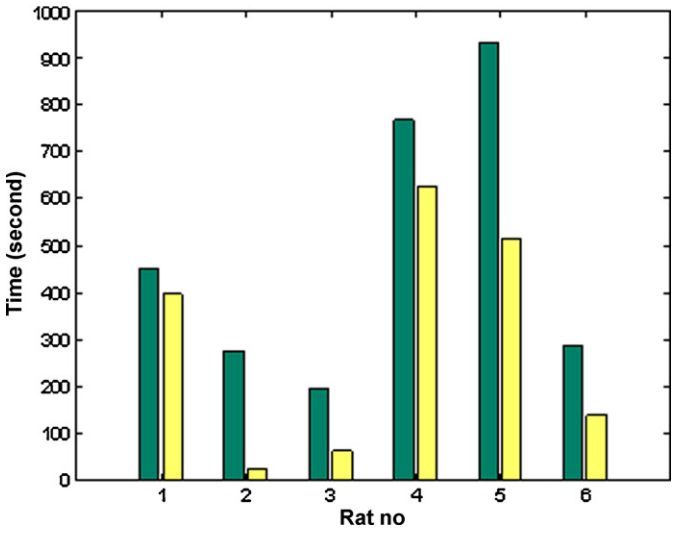

Fig. 7. The extended preictal duration and the anticipation time for all rats in the test group. The extended preictal duration and the anticipation are represented with green and yellow bars, respectively. Their mean times are 484 s and 293.5 s.

Please cite this article in press as: Niknazar M, et al. Application of a dissimilarity index of EEG and its sub-bands on prediction of induced epileptic seizures from rat's EEG signals. IRBM (2012), http://dx.doi.org/10.1016/j.irbm.2012.09.002

Table 3
The anticipation times of original EEG and its sub-bands using BBDI for all rats.

Rat No.	Original EEG	Delta sub-band	Theta sub-band	Alpha sub-band	Beta sub-band	Gamma sub-band
1	395	395	395	395	395	395
2	26	42	28	30	32	36
3	63	63	–	–	–	3
4	652	616	616	616	616	616
5	514	535	402	429	503	510
6	138	146	104	103	138	138

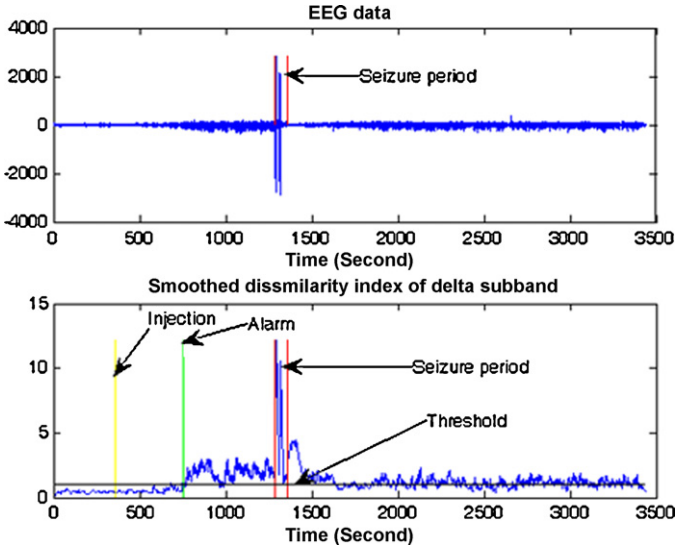

Fig. 8. Top: long-term EEG recording of rat 5 in the test group. Bottom: smoothed BBDI values of delta sub-band versus time that gradually increase until seizure onset. Solid black line represents the baseline for preictal phase detection with parameters $k = 2.5$ and $d = 5$. Administration of the pentylenetetrazole was done at 05:55 and epileptic seizure occurred at 21:25. Detection point of preictal phase is at 12:30. The anticipation time is 535 s.

For delta, theta, alpha, beta and gamma sub-bands, BBDI was computed to predict PTZ-induced epileptic seizures. Table 3 presents the anticipation time for original EEG signals and their sub-bands for all rats in the test group.

For all sub-bands, best results were achieved with parameters $k = 2.5$ and $d = 5$. Table 3 shows that only delta and gamma sub-bands led to sensitivity, specificity and Q equal to 100. Mean anticipation time for gamma sub-band is 283 s which is less than the anticipation time using original EEG but mean anticipation time for delta sub-band is 299.5 s which is a few seconds more than the anticipation time of original EEG signal. Fig. 8 shows prediction result for the rat of Fig. 5 using delta sub-band. It can be seen that the anticipation time for this rat is increased by 21 s, which means that using EEG sub-bands may lead to prediction improvement.

5. Conclusion

So far, several methods have been proposed to analyze EEG data for predicting epileptic seizures. For the first time, BBDI of EEG signal and its sub-bands were calculated that yielded better results than dynamical and fuzzy similarity indices. In our case, BBDI of delta sub-band yielded the best anticipation time for epileptic seizures prediction. This animal study showed that BBDI value can reveal the hidden dynamics of EEG data. It was found that the dissimilarity of neural network activity between reference window and present window has a significant increase prior to an epileptic seizure. Based on such increase in dissimilarity, the preictal phase can be successfully detected using the automated detection algorithm proposed in this work. Another important point confirmed by the results of this animal study is that EEG sub-bands delta, theta, alpha, beta, and gamma help to get more accurate information about constituent neuronal activities underlying EEG signal and consequently, certain changes in EEG signal that are not evident in the original full-spectrum EEG may be amplified when each sub-band is analyzed separately. As a result, using these sub-bands leads to superior diagnostic results. As a future work, new dissimilarity indices will be defined and tested on human EEG signals and their sub-bands to track changes of neural network activity over time with more details.

Acknowledgement

The authors would like to thank Mr Tyley Kaster from Schulich School of Medicine and Dentistry, University of Western Ontario for his assistance in editing the paper.

References

[1] Firpi H, Goodman ED, Echuaz J. Epileptic seizure detection using genetically programmed artificial features. IEEE Transactions on Biomedical Engineering 2007;54(2):212–24.
[2] Lehnertz K, Mormann F, Kreuz T, Andrzejak RG, Rieke C, David P, et al. Seizure prediction by nonlinear EEG analysis. IEEE Engineering in Medicine and Biology Magazine 2003;22:57–63.
[3] Srinivasan V, Eswaran C, Siraam N. Approximate entropy-based epileptic EEG detection using artificial neural networks. IEEE Transactions on Information Technology in Biomedicine 2007;11(3):288–95.
[4] Mousavi SR, Niknazar M, Vosoughi Vahdat B. Epileptic seizure detection using AR model on EEG signals. Biomedical Engineering Conference, CIBEC 2008. Cairo International, Egypt 2008; p. 1–4.
[5] Faust O, Acharya RU, Allen AR, Lin CM. Analysis of EEG signals during epileptic and alcoholic states using AR modeling techniques. ITBM-RBM 2008;29:44–52.
[6] Zandi AS, Javidan M, Dumont GA, Tafreshi R. Automated real-time epileptic seizure detection in scalp EEG recordings using an algorithm based on wavelet packet transform. IEEE Transactions on Biomedical Engineering 2010;57(7):1639–51.
[7] Wang L, Wang C, Fu F, Yu X, Guo H, Xu C, et al. Temporal lobe seizure prediction based on a complex Gaussian wavelet. Clinical Neurophysiology 2011;122(4):656–63.

Please cite this article in press as: Niknazar M, et al. Application of a dissimilarity index of EEG and its sub-bands on prediction of induced epileptic seizures from rat's EEG signals. IRBM (2012), http://dx.doi.org/10.1016/j.irbm.2012.09.002

[8] Adeli H, Ghosh-Dastidar S, Dadmehr N. A wavelet-chaos methodology for analysis of EEGs and EEG subbands to detect seizure and epilepsy. IEEE Transactions on Biomedical Engineering 2007;54(2): 205–11.
[9] Esteller R. Detection of seizure onset in epileptic patients from intracranial EEG signals. Atlanta GA: Ph.D. dissertation. Dept. Electrical Eng. Georgia Inst. Tech; 1999.
[10] Gotman J. Automatic recognition of epileptic seizures in the EEG. Electroencephalography and Clinical Neurophysiology 1982;54(5): 530–40.
[11] Iasemidis LD, Olson LD, Sackellares JC, Savit RS. Time dependencies in the occurrences of epileptic seizures: a nonlinear approach. Epilepsy Research 1994;17:81–94.
[12] Li X, Ouyang G, Yao X, Guan X. Dynamical characteristics of pre-epileptic seizures in rats with recurrence quantification analysis. Phys Lett A 2004;333:164–71.
[13] Ouyang G, Dang C, Richards DA, Li X. Ordinal pattern based similarity analysis for EEG recordings. Clinical Neurophysiology 2010;121:694–703.
[14] Kunhimangalam R, Joseph P, Sujith O. Nonlinear analysis of EEG signals: surrogate data analysis. ITBM-RBM 2008;29:239–44.
[15] Le Van Quyen M, Mattinerie L, Navarro V, Boon P, D'Have M, Adam C. Anticipation of epileptic seizures from standard EEG recordings. Lancer 2001;357:183–8.
[16] Ouyang G, Li X, Guan X. Use of fuzzy similarity index for epileptic seizure prediction. The 5th World Congress on Intelligent Control and Automation. Hang Zhou, China. 2004 June; 14–18:5351–5.
[17] Feldwisch-Drentrup H, Schelter B, Jachan M, Nawrath J, Timmer J, Schulze-Bonhage A. Joining the benefits: combining epileptic seizure prediction methods. Epilepsia 2010;51:1598–606.
[18] Niknazar M, Mousavi SR, Vosoughi Vahdat B, Shamsollahi MB, Sayyah M. A new dissimilarity index on EEG signals for epileptic seizure detection. 4th International Symposium on Communications, Control and Signal Processing (ISCCSP 2010) 2010; p. 1–5.
[19] Loscher W, Schmidt D. Which animal models should be used in the search for new antiepileptic drugs. A proposal based on experimental and clinical considerations. Epilepsy Research 1988;2:145–81.
[20] Ouyang G, Li X, Dang C, Richards D. Using recurrence plot for determinism analysis of EEG recordings in genetic absence epilepsy rats. Elsevier Clin Neurobiol 2008;119:1747–55.
[21] Danober L, Deransart C, Depaulis A, Vergne M, Marescaux C. Pathophysiological mechanisms of genetic absence epilepsy in the rat. Progress in Neurobiology 1998;55:27–57.
[22] Thomasson N, Hoeppner T, Webber C, Zbilut J. Recurrence quantification in epileptic EEGs. Phys Lett A 2001;279:94–101.
[23] Paivinen N, Lammi S, Pitkanen A, Nissinen J, Penttonen M, Gronfors T. Epileptic seizure detection: a nonlinear viewpoint. Computer Methods and Programs in Biomedicine 2005;79(2):151–9.
[24] Elsner JB, Tsonis AA. Singular spectrum analysis: a new tool in time series analysis. New York: Plenum; 1996.
[25] Marwan N, Wessel N, Meyerfeldt U, Kurths J. Recurrence plots for the analysis of complex systems. Phys Rep 2007;438:237–329.
[26] Fraser AM, Swinney H. Independent coordinates for strange attractors. Phys Rev 1986;A33:1134–40.
[27] Cao L. Practical method for determining the minimum embedding dimension of a scalar time series. Physica D 1997;110(1-2):43–50.
[28] Kantz H, Schreiber T. Nonlinear time series analysis. Cambridge: Cambridge University Press; 1997.
[29] Quyen M, Adam C, Martinerie J, Baulac M, Clemenceau S, Varela F. Spatio temporal characterization of non-linear changes in intracranial activities prior to human temporal lobe seizures. European Journal of Neuroscience 2000;12:2124–34.
[30] Shannon CE. A mathematical theory of communication. Bell Syst Tech J 1948;27:379–423.

Please cite this article in press as: Niknazar M, et al. Application of a dissimilarity index of EEG and its sub-bands on prediction of induced epileptic seizures from rat's EEG signals. IRBM (2012), http://dx.doi.org/10.1016/j.irbm.2012.09.002