33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Changes in Dynamical Characteristics of Epileptic EEG in Rats using Recurrence Quantification Analysis

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***Abstract*—In this paper, we used Recurrence Quantification Analysis (RQA) in order to study pre-epileptic characteristics in rat's EEG recordings. Four adult rats were used to collect epileptic EEG data in an experiment of animal model of epilepsy. Three RQA measures, recurrence rate, determinism, and entropy were calculated from EEG recordings from rats. A moving average filter was used to identify the decreasing trend in pre-epileptic dynamics which will be useful early detection of seizures.**

I. Introduction

Electroencephalogram (EEG) is temporal recording of brain electrical activity. EEG signals are primarily used to diagnose and monitor the most common and chronic neurological disorder epilepsy which is characterized by the occurrence of repeated and unprovoked seizures [1]. Seizures are due to abnormal excitation of large groups of neurons in various brain regions that temporarily alter one or more brain functions. Predicting seizure using quantitative analysis of noise corrupted and nonstationary EEG signals is not an easy venture [1]-[3]. Theory and practices from digital signal processing, chaos and fractals, nonlinear dynamical systems have been applied in analyzing electrical signals recorded from brain of epilepsy patients for anticipation of pre-ictal changes in EEG or prediction of epileptic seizures [1]-[5].

In a previous study, we proposed a fuzzy rule-based system for seizure prediction based on changes in correlation dimension of intracranial EEG [6]. However, we faced some drawbacks of using correlation dimension alone as characteristics feature. The reason is that yet it is not proved that nonlinear measures are better suited than linear measures (for example, coherence, synchronization and spectral measures) [1], [7] and it is unclear how correlation dimension behave prior to an impending seizure [8]. Moreover, bivariate and multi-variate measures are shown to perform better in literature [1]. Therefore, although we believe fuzzy logic could be extremely useful in designing early seizure detection or prediction system, the feature extraction methodology has to be sensitive enough to identify any earlier changes in brain dynamics. The drawbacks of the nonlinear dynamics based measures are their sensitivity to noise. Due to noise the phase space trajectory reconstruction and computation of characteristics measures may lead to wrong findings. Therefore, advanced and robust nonlinear data analysis method is required for the further advancement in this area.

Recurrence quantification analysis (RQA) is a method of nonlinear data analysis which has been developed by Webber et al. (1992) and Marwan et al. (2002) [9], [10]. One of the important advantages of this method is that it does not require the assumption of linearity, noiselessness, and stationarity of the EEG data [10]. However, since state space trajectory needs to be reconstructed to compute recurrence matrix, choice of embedding dimension and delay parameters plays an important role in RQA [10]-[12]. Phase space reconstruction is performed using Taken's time delay embedding theorem [11], [13]. Xioli Li et al. [14] introduced recurrence quantification analysis for characterizing rat's EEG in order to find the pre-ictal changes. It has been reported that RQA measures can be able to characterize the pre-ictal transition of brain dynamics [14]. We found this article very interesting and wanted to reproduce some of the results as well as finding suitable characteristics measures for our future works. The objective of the study was to identify if RQA measures can identify any pre-ictal changes or even earliest change prior to a seizure onset. In a previous study, we had utilized similar RQA measures (average recurrence rate, determinism and entropy) in order to design a fuzzy logic based prediction system [15]. However, the system merely worked as a detection method without much success of prediction. We still believe these RQA measures would be useful in designing an early detection method and lowering the detection delay could be possible.

In this study, we applied RQA measures in order to study the earliest changes in rat's EEG in an in vitro animal model of epilepsy. EEG signals were obtained from four adult rats. Three RQA measures: mean recurrence rate, mean determinism and mean entropy were computed from EEGs and a moving average filter was applied to identify the

Manuscript received April 12, 2011. This work was supported in part by the ND EPSCoR through National Science Foundation Grant #EPS-0814442.

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decreasing trends in the characteristics measures.

II. Materials and Methods

The EEG data used in this study were obtained from an experiment of animal model of epilepsy. The details of the data collection and signal processing are described in following sub-sections.

A. Experiments

In this study, four adult Sprague-Dawley rats (weighing 260-350 g.) were used to collect epilepsy EEG data. Animals were housed individually in polypropylene cages and maintained under a 12h light: 12 h dark cycle at 22±1 ºC. Food and water was provided ad libitum.

Rats were anesthetized, secured in a stereotaxic frame and operated upon to implant EEG electrodes as described previously [16]. Rats were allowed at least 7 days of recovery. Pilocarpine was used to induce status epilepticus. Scopolamine was injected 30 min prior to injecting pilocarpine to suppress peripheral cholinergic effects.

For EEG recording, rats were connected to flexible recording cables. EEG traces were conditioned using a software controlled preamplifier, Animal bio amp (Adinstruments Inc.) and acquired with the help of Power lab 4/30 (ADinstruments Inc.). Data were collected from single channel and recorded in a computer using Lab Chart software (ADinstruments Inc.) at a sampling rate of 200 Hz. The EEG recording prior to pilocarpine injection was considered as inter-ictal baseline. Seizure onset was identified by the first visual electrographic change in EEG. The time duration between the pilocarpine injection and first electrographic change was considered as the pre-ictal state.

The RQA measures were extracted from four rat's EEG data. The time lengths of EEG data files and pilocarpine injection time are given in following table 1.

TABLE I
STUDIES ON RAT EEG SIGNALS: TIME DETAILS OF EACH EXPERIMENT

Subject No.	Data Length (min)	Injection time (min)
1	40	11.93
2	50	9.98
3	35	11.63
4	80	12.31

B. Preprocessing & Segmentation

The raw EEG signal is first filtered using a 4th order digital Butterworth band pass filter with low pass cutoff at 40 Hz and high pass cutoff at 0.5 Hz to mitigate high frequency noise and low frequency artifacts. Data were normalized to zero mean and one standard deviation prior to applying recurrence quantification analysis. Then data were segmented using a moving window analysis technique. The length of the each segment of EEG was 5 seconds with 2.5 seconds overlapping between adjacent segments.

C. RQA Measures

Recurrence quantification analysis is an advanced method of nonlinear data analysis. Recurrence of states is a fundamental property of deterministic dynamical systems, nonlinear or chaotic systems [9], [10]. This recurrence property can be visualized in a phase space by using recurrence plots (RP) proposed by Eckmann et al. (1987) [17]. Recurrence matrix computation [10], [18] is given by

$$R(i,j) = \Theta(\varepsilon - ||\vec{x_i} - \vec{x_j}||) \quad (1)$$

where $\|.\|$ indicates the Euclidean norm, $\vec{x}$ is the reconstructed phase space vectors which has to be computed from EEG by time delay embedding in space for nonlinear analysis, ε is the predefined cut-off distance, and Θ is the Heaviside step function defined as:

$$\Theta(s) = \begin{cases} 1 \; if \; s \geq 0 \\ 0 \; if \; s < 0 \end{cases} \quad (2)$$

In this study, we applied RQA measures to rat EEG data and extracted three measures, recurrence rate, determinism, and entropy [10], [14]. The reason of choosing these three features is that they can reveal three important characteristics of the underlying dynamical systems. These are quantification of recurrence points, determinism and complexity of the system [10], [14], [18].

RQA is the quantitative analysis of RP. Recurrence rate is the quantification of the density of recurrence points in the phase space trajectory. Deterministic behavior produces longer diagonals and less single, isolated recurrence points in the recurrence plot [10], [14]. However, stochastic behavior produces non or short diagonals [10], [14]. Recurrence rate (RR) simply counts the black dots in the recurrence plot [10], [14]. Recurrence rate is computed as following and expressed in percentage [10]:

$$RR = \frac{1}{N^2} \sum_{i,j=1}^{N} R_{i,j} \quad (3)$$

Determinism is defined as the ratio of the recurrence points on the diagonal structure to all recurrence points [10] and is given by:

$$DET = \frac{\sum_{l=l_{min}}^{N} lP(l)}{\sum_{i,j}^{N} R_{i,j}} \quad (4)$$

where $P(l)$ is the frequency distribution of the lengths of the diagonal structures in the RP, l_{min} is the threshold which excludes the diagonal lines formed by the tangential motion of a phase space trajectory, and $R_{i,j}$ is the all recurrence points as described before.

Entropy represents the complexity of the deterministic structure in the dynamical system [10], [18]. The larger the entropy value, the more complex the deterministic structure [14]. The Shannon entropy of the probability $p(l)$ that a diagonal line has exactly length l [10], [18] is given by:

$$ENTR = -\sum_{l=l_{min}}^{N} p(l) \ln p(l) \quad (5)$$

where $(l) = {P(l)}/{\sum_{l=l_{min}}^{N} P(l)}$.

We used average of these three RQA measures as characteristics features where average was taken for each EEG segments [15]. In computing RQA measures, the embedding dimension m and delay τ are important parameters [10], [14], [17]-[18]. We had considered two different sets of these parameters. These are $m = 5$ and 15; $\tau = 11$ and 5 [14],[15]. The analysis was performed offline in MATALB® using CRP Toolbox which is available at http://www.recurrence-plot.tk/programmes.php.

III. Results And Discussions

The RQA measures revealed characteristics changes prior to and during the seizure onset. The changes were identified as deviation towards lower values from inter-ictal baseline. Decreased dynamics were observed for REC, DET during seizure onset. ENTR values showed slight decrease prior to seizure onset. Steady decrease in the feature values was dominant during status epilepticus (SE). The results look promising to be used in designing an early seizure detection system.

The analysis was performed for two set of parameters: 1) embedding dimension, $m = 15$, delay $\tau = 11$, size of the neighborhood or radius, $E = 1.5$ [14]; 2) embedding dimension $m = 5$, delay $\tau = 5$, size of the neighborhood or radius $E = 1.0$ (in units of the standard deviation σ of normalized EEG) [15].

The results are illustrated in from Fig. 1 to Fig. 3. Fig. 1 illustrates EEG and corresponding REC, DET, and ENTR for subject 1 with $m = 15$, $\tau = 11$, $E = 1.5$. Fig. 2 illustrates EEG and corresponding REC, DET, and ENTR for subject 1 with $m = 5$, $\tau = 5$, $E = 1.0$ (same as the standard deviation of normalized EEG).

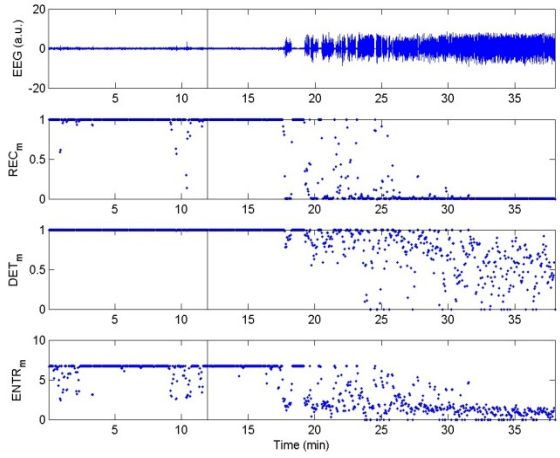

Fig. 1. Rat EEG data for rat 1 and three RQA measures (average): Recurrence Rate, Determinism, and Entropy for $m = 15$, $\tau = 11$, $E = 1.5$. Black vertical line marks the pilocarpine injection time. Seizure onset is identified by the first visual electrographic changes. At the onset of seizure decreased dynamics is found (Recurrence rate and Determinism). The entropy measure shows slight decrease in dynamics prior to the seizure onset.

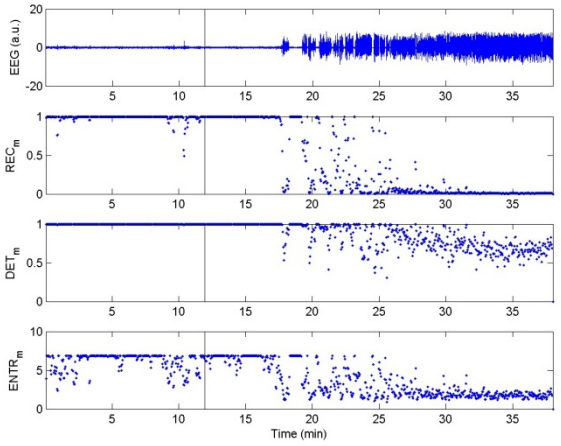

Fig. 2. Rat EEG data for rat 1 and three RQA measures (average): Recurrence Rate, Determinism, Entropy for $m = 5$, τ=5, $E = 1.0$. Black vertical line marks the pilocarpine injection time.

Dynamical characteristics of EEG signals for rat 2 are illustrated in Fig. 3. Although similar decrease in REC, DET, and ENTR values were observed during or prior to seizure, slightly different trend has been viewed. During the duration of five minutes after the injection from the injection time, dynamics decreased before coming back to interictal baseline within next five minutes. For other two rat's EEG (rat 3 and rat 4), similar changes were found.

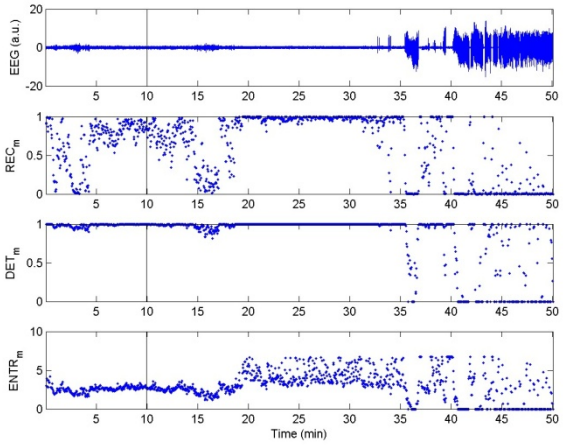

Fig. 3. Rat EEG data for rat 2 and three RQA measures (average): Recurrence Rate, Determinism, Entropy for $m = 15$, $\tau = 11$, $E = 1.5$. Black vertical line marks the pilocarpine injection time.

The characteristics measure time series provides another problem of pattern recognition which will be addressed in future analysis. The challenge remains in efficiently detecting the subtle changes by an automatic intelligent system. However, in this study, to identify the trend in the characteristics measures, we used a digital moving average filter with window size $w = 10$ points. Fig. 4. illustrates the trend identification for rat 1. From this figure, the gradual change towards lower values in dynamics is clearly visible.

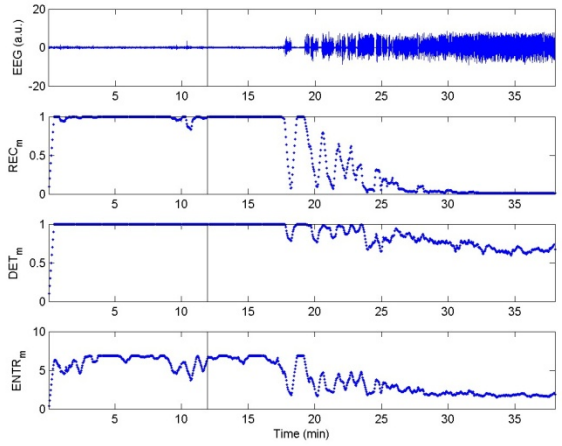

Fig. 4. Trend identification of RQA measures: mean REC, DET, and ENTR for rat 1 with $m = 5$, $\tau = 5$, $E = 1.0$. Window size of moving average filter is $w = 10$.

Although the RQA measures could identify the decrease in brain dynamics during a seizure onset, we could not find a smooth preictal transition in our experiment. The traditional and popular nonlinear measures such as correlation dimension or Lyapunov exponents require assumption of nonlinearity and nonstationarity as well as noiselessness [4], [5]. The advantage of RQA measures over the other methods is that it does not require the assumptions of nonlinearity or nonstationarity. However, noise could mislead the results, since this method also requires phase space reconstruction. We still believe these measures would be useful in designing an early seizure detection system. We used two empirical sets of parameters for embedding dimension and delay time. The optimal embedding dimension can be found using false nearest neighborhood method and optimal delay time can be found from mutual information [10]-[13].

IV. Conclusions and Future Works

We applied RQA measures in order to study the dynamical characteristics of EEG in animal epilepsy model. The idea was to identify if there is any pre-ictal transition trend or even earliest detection of seizure onset. To identify the trends in the characteristics measures time series profiles we used a moving window averaging filter.

In our future work, we will collect EEG data from more number of rats (10 rats). The data will include baseline recording, induced status epilepticus and spontaneous seizures which the rats experience when they are kept on observation after 2/3 days of injecting of pilocarpine. In future studies, we will apply RQA measures to these databases. We will also compute the optimal time delay and embedding dimension parameters which is computationally demanding in a hope that choice of optimal parameters might improve the low sensitivity of RQA measures in the present study. Moreover, we will present a statistical analysis on the data from rats in order reveal whether the subtle changes observed were due to random events or true preictal transition. Finally, we will design an early seizure onset detection system using fuzzy logic based approach based on the preliminary results presented in this paper.

Acknowledgment

The partial financial support from ND EPSCoR through National Science Foundation (NSF) Grant #EPS-0814442 is gratefully acknowledged.

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