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A MIDDLE- TIME RECOGNITION OF EPILEPTIC SEIZURES FROM GEOMETRICAL PATTERNS OF EEG DATA

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An approach for middle- time recognition of epileptic seizures from EEG data is proposed. The method considers sharp changes in the recorded data using geometrical patterns of the signal in phase-space. The approach was developed using experimental clinical EEG data recorded from ten patients and reliably predicted epileptic seizures in the ten-minute interval before the seizure onsets. An estimation of sensitivity and specificity of the proposed method is also provided.

1. INTRODUCTION

Epilepsy is one of the most common diseases and is observed in about 1% of the population [1–3]. The prediction of epileptic seizure is important from many points of view, e.g. the pharmaceutical design, localization of the epileptogenic zone, recognition of neurological intracranial signals.

Recent information technologies provide new tools for such purposes. There are many different methods for prediction of epileptic seizures hat are based on spectral analysis, frequency plane, methods of dynamical systems and chaos theory, correlation analysis and others [4–6]. However, the existing methods provide only short time predictions before seizures (seconds in linear analysis and about 2–7 minutes in nonlinear methods). One of the most promising approaches in this field [6] is based on phase space reconstruction using an extension of methods developed by F. Takens and P. Grassberger (see for description refs [7, 8]).

This article introduces a new algorithm based on the analysis of geometrical structure of signals in phase space. This approach is in the mainstream of our earlier recognition of HPLC data [9, 10]. and extracellular neuronal spikes in the brain by phase space and correlation measure methods [11] and the complexity measure of functions. The proposed approach makes possible to predict an appearance of seizures in ten-minute interval before the onset of epileptic seizures.

2. EXPERIMENTAL DATABASE

The investigation was made on the background of clinical data with patients EEG recorded at the Department of Neurology at the University of Bern. The EEG data were recorded with the Biomedical Monitoring Systems Inc (Nicolet-BMSI,

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Madison, Wisconsin, USA). The Extended International 10–20 System (32 channels) was used and the data were sampled at 200 Hz frequency. The data were stored on a CD using HARMONY format. These raw data were translated into ASCII text format using utilities developed by Dr. V.V. Volkovich and the authors.

The data collected from ten patients were analyzed [12]. The analysis of records was made at several different states: before seizure onset, during the seizures, after the seizure and at a reference stage, at least one hour before or after the seizures. There were about 80 records available for our analysis. The data from all patients were analysed using the proposed method. However, the patients had different sex, different localization of the epilepsy (left or right hemisphere) and the epileptic diseases also had a different origin (mesial temporal sclerosis or tumor). In addition, the provided data were of different duration ranging from 1 to 23 minutes of pre-ictal recordings. Therefore, in this particular study that is aimed to introduce and to show a feasibility of a new approach, only data from two patients (patient A and B) with the most similar characteristics that have particularly long (12–19 minutes) records in the pre-ictal states were analysed. After some preliminary visual inspection of data we selected electrode FP1 for all results reported in this study. The results recorded from other electrodes were similar but they are not considered in this article.

Some typical records of initial EEG are shown on Fig. 1.

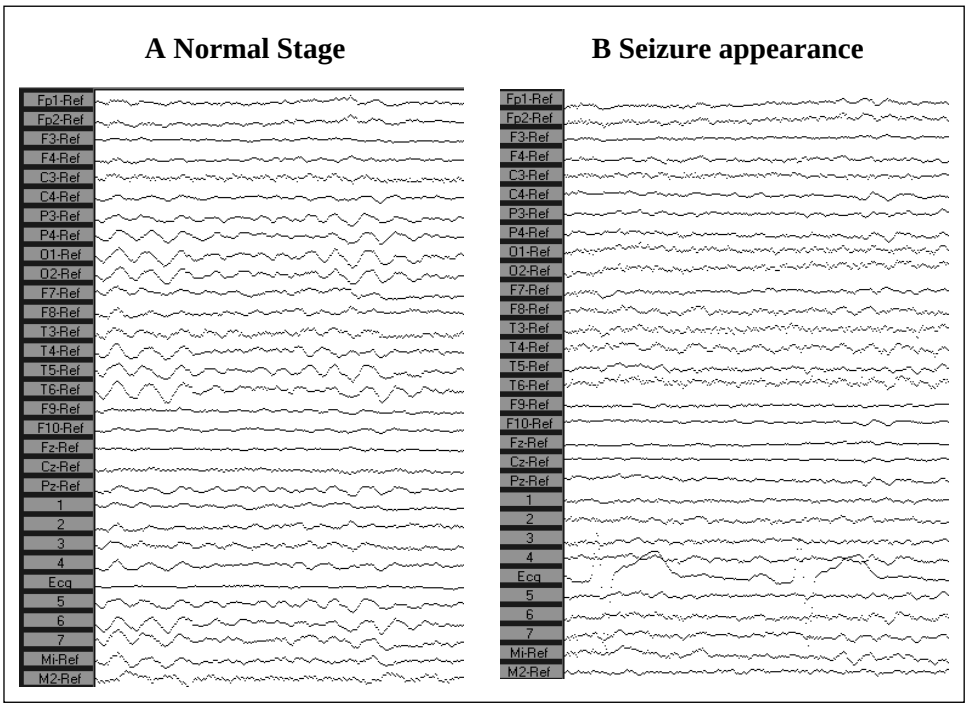


Fig. 1. EEG signals recorded for a patient A in normal (panel A) and in the pre-ictal (panel B) states several minutes before the seizures. The amplitudes of different electrode signals are shown as a function of time. The labels of electrodes correspond to the Extended International 10–20 System. Full recording time is 4 seconds for each panel. Sampling frequency rate is 200 Hz

The left panel A shows an example of recording in the normal state. The right panel contains data in pre-ictal state several minutes before the seizure and it is characterized by an appearance of high-frequency components. We performed an analysis of data in order to determine if the same effect can be observed and quantified to reliably detect epileptic seizures and to monitor state of the patient in automatic way.

3. METHODOLOGY

The main goal of this investigation was to detect which changes in the EEG signals could be used to predict epileptic seizures. Our basis hypothesis was to investigate the changes in the high-frequency components of the epileptic signal before the seizure onset. Following the previous analysis that indicated a success of analysis of signals in phase space [5, 6] we developed an original approach described in Appendix A. While most of the previous methods were based on the reconstruction of parameters of attractors (i.e., estimation of correlation dimensions, embedding space, Lyapunov exponents, etc.) our approach directly considers changes of the geometrical patterns of EEG signals in phase space. The signal parameters were calculated by finite difference numerical methods (first differences for the first derivative, etc.). Examples of the signals in the normal and the pre- ictal states are shown in the Fig. 2 and 3.

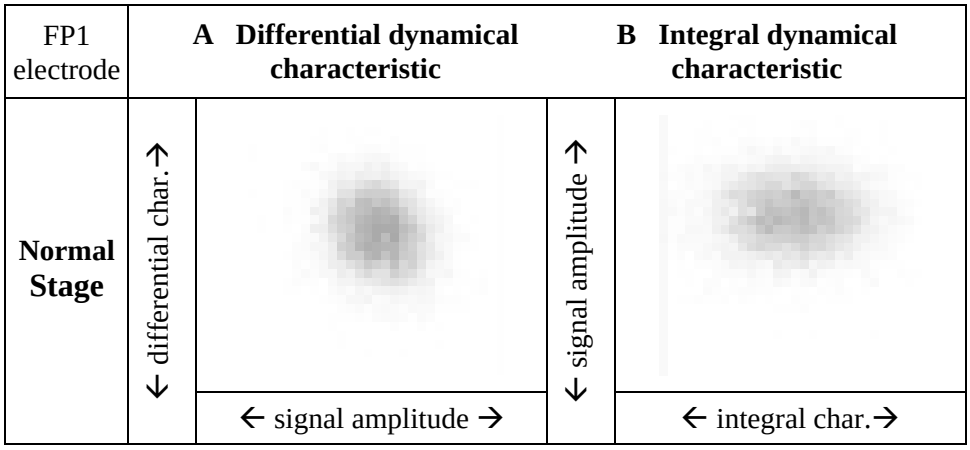


Fig. 2. The signals from Fig. 1 (panel A) in phase space. The coordinates of points in the left picture correspond to the values of the first derivative of signal (y-axis) and signal amplitude (x-axis). The coordinates of points in the right picture correspond to the values of the integral approximation of the signal (x-axis) and the signal amplitude (y-axis)

The patterns shown on both Figures were calculated using 5 sec (1000 points per pattern) for channel FP1 as indicated in Appendix A.2. The geometrical differences of signals on Figure 2 and 3 are evident. Therefore there was a need to develop a method that could formalize the observed difference and can be used for automatic monitoring of the patient state.

We developed a special numeric deviation index (DIC) that provided an adaptive comparison of phase-space patterns in normal and the analyzed state by considering the differences of individual patient parameters from the seizure-free state (Appendix A.3).

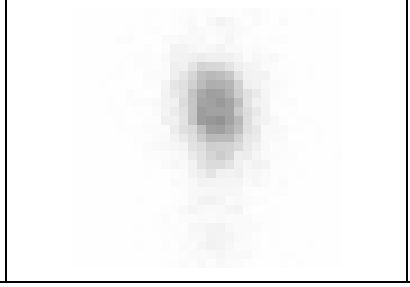
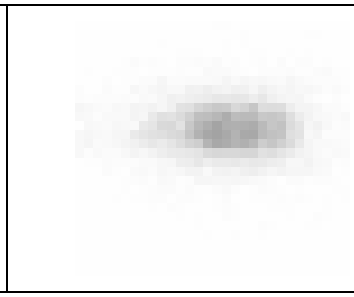
FP1 electrode	**A Differential dynamical characteristic**	**B Integral dynamical characteristic**
17 minutes before seizure		

Fig. 3. The distribution of points in phase-space of the same patient from Figure 1 & 2 in the pre-ictal state 17 minutes before the seizure. The difference between normal and the analyzed state can be easily observed

4. CALCULATED RESULTS

The introduced index was calculated for all analyzed patients. Examination of data indicated that the proposed index could be reliably used to detect the approaching of seizures. An example of such analysis is illustrated on Fig. 4 and in Table.

Table

Alarm level(index)		**Prediction status**	**Time before the seizure onset**
FP1 – CONTROL	**FP1 – PRESZ**		
0,125055285	0,587137577		635
0,249336978	0,513365047		630
0,256995382	0,94740823		625
0,203734454	0,327842294		620
0,461058119	0,439615508		615
0,263394124	1,265349021		610
0,230498485	1,118525366		605
0,157853545	1,133283503		600
0,135868341	8,143915624	Seizure	595
0,057482662	9,559343495	Seizure	590
0,168661222	11,84986324	Seizure	585
0,062955558	11,54262492	Seizure	580
0,261158555	12,33985246	Seizure	575
0,127643911	11,15360036	Seizure	570
0,090919277	13,14521231	Seizure	565
0,13670642	13,06123044	Seizure	560
0,226164765	14,83807468	Seizure	555
0,209961843	13,79559341	Seizure	550
0,108803929	14,25365139	Seizure	545
0,842898843	14,67213868	Seizure	540
0,099201891	14,03969703	Seizure	535

The Table 1 show numeric values of the DIC calculated for the patient B. As in the previous example a reliable detection of seizure was performed in ten-minute time interval.

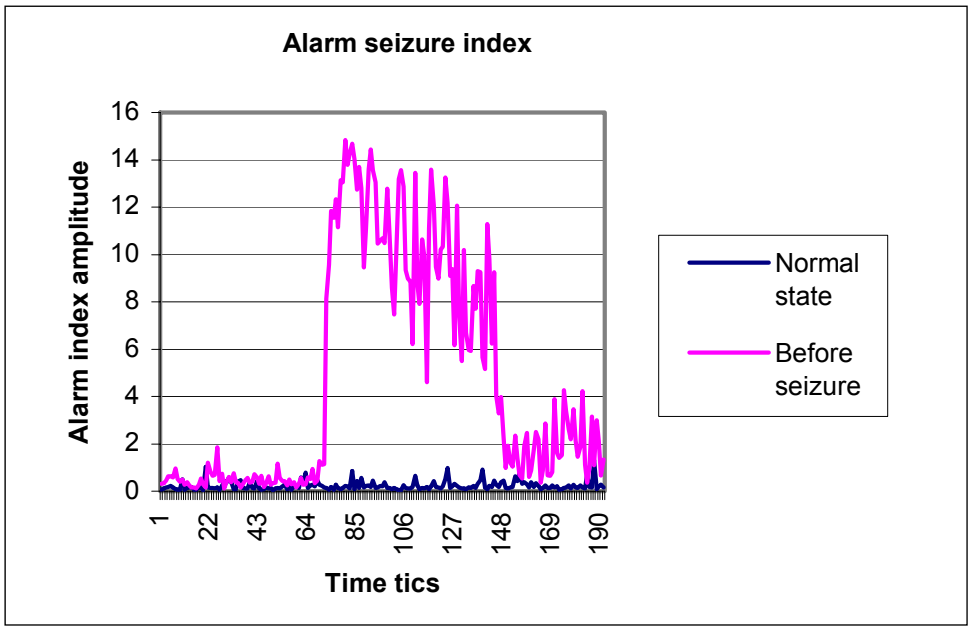


Fig. 4. Dynamics of deviation index (DIC) before the seizure calculated using data recorded with FP1 electrode for patient A. The seizure corresponds to time tic 190 (one tic is equal to 5 sec). The DIC detects approaching of the seizure starting with 74th tic, i.e. about 9 minutes before the seizure

The second row indicates DIC values calculated at different times (indicated in the last row) before the start of the seizure. The first row shows the values of the same index calculated for an arbitrary period of the same length in the normal state of the patient. There is a sharp increase (about 10 times in the magnitude) in the value of the DIC index about 600 sec before the onset of the seizures.

Similar results were calculated for other analyzed patients and they will be described in details in a separate study considering individual features of each patient (Makarenko et al, in prep.). Thus the proposed approach represents a promising method to detect epileptic seizures in the ten-minute interval before the onset of seizures.

Some remarks should be posed about sensitivity and specificity of the developed index. Some simple estimation of the sensitivity of the proposed approach could be performed using the Shewhart control chart method [13]. This method predicts an alarm signal whenever the average value of the observed parameter (in our case of DIC, that is calculated each $\Delta t = 5\,\text{sec}$) measured over time $t = N^* \Delta t$ exceeds some threshold level μ_k

$$\bar{y}(K) \geq \mu_h = \mu + h\frac{\sigma}{\sqrt{N}},$$

$$\bar{y}(K) = \frac{1}{N} \sum_{i=1,\ldots,N} DIX_i .$$

In this formula μ and σ^2 corresponds to the mean and variance of the DIC recorded in the normal state. The number N and parameter h represents adjustable parameters that should be specified by the user. The larger values of parameter N will provide more reliable detection of epileptic seizures and will decrease number of false alarms. However, at the same time the larger values of this parameter will require longer times to produce an «alarm signal» of the system for the prediction of the onset of epileptic seizure, i.e., will decrease its sensitivity. For example, let us fix the value of parameter N to be 12, i.e., the detection of the alarm signal is done by considering a continuous record of 60 sec duration. The increase of parameter h decreases the sensitivity of the method, while the decrease of this coefficient increases probability of false positive errors (false alarm signals). If we assume that the signal in the normal state is generated according to the Gauss distribution, than the number of false alarm in the Shewhart control chart method is given by Gauss cumulative distribution function $1-\phi(h)$. For example, for h=3 one can expect to have only 1 error in 12 hours of recording. Our analysis has indicated, that for such value $h=3$ the method correctly predicted all seizures for all analyzed patients. At the same time, there were no false alarms for the data recorded in the normal state of the patients. However, the last result can be biased since only very short records (ca. 20 minutes) in the normal states of the patients were available for our analysis. Thus, further analysis of data is required to better evaluate the performance of the proposed method. It is possible that an assumption about the Gauss distribution of DIC index in the normal state of patients is not correct. In this case, more complex methods of data analysis, such as neural networks [14] or Group Methods of Data Handling [15, 16] can be also used.

5. DISCUSSION

The results described in this paper indicate high predictive power of the proposed approach. The time of seizure prediction (about 10 minutes from the seizure onset) is sufficient in many cases for medical purposes, such as preparing of drugs and treatment of patient by medical staff. These results are in good agreement with another methodology based on the time- series analysis and phase space reconstruction [6]. Indeed, both methods take into account geometrical features of the signals in phase space. The method proposed in the current article has similar sensitivity and it makes possible to detect the epileptic seizures 10 minutes before the seizures (ca 7 minutes in ref. [6]). A proper comparison of both approaches requires that both methods will be be applied to the same datasets.

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APPENDIX A. ALGORITHM FOR DEVIATION INDEX CALCULATION (DIC).

The algorithm counts some measures of deviating of analyzed patient states from its normal (without seizure) states. The algorithm consists from three stages: pre-processing of signals, pattern building and evaluation DIC.

A.1. Preprocessing of signals in normal and current states of patient

Firstly the signals are normalized to new variables with zero mean value on the selected time interval Δt:

$$\tilde{x}_i = x_i + \alpha ,$$

$$\tilde{c}_i = c_i + \beta ,$$

where $\alpha = \frac{-\sum x_i}{N}$, $\beta = \frac{-\sum c_i}{N}$, $N = \Delta t * 200$, c_i is the signal in the normal state, x_i is the signal in the analyzed state and $\tilde{c}_i$, $\tilde{x}_i$ are the normalized signals.

Secondly we normalize the amplitudes of the signals on each time interval to have the same average mean squared deviation:

$$\breve{x}_i = \gamma * \tilde{x}_i , \ \gamma = \sqrt{\frac{N}{\sum x_i^2}} ,$$

$$\breve{c}_i = \eta * \tilde{c}_i , \ \eta = \sqrt{\frac{N}{\sum c_i^2}} .$$

A.2. Construction of the geometrical pattern in phase space.

The two-dimensional pattern is constructed. The first axis corresponds to $\frac{dx}{dt}$ (i.e., differential characteristic that is estimated as $(x_i - x_{i+1})/\Delta t$) and another corresponds to the sum of two nearest points $x_i + x_{i+1}$, (i.e., the integral characteristic). The total region is divided on the rectangle sub-regions and the numbers of points in each sub-region is calculated. The calculated counts are normalized on the analyzed number of considered time intervals.

A.3. DIC calculation

Firstly we calculate an average pattern for the normal state of the patient. In order to calculate this pattern, available data from the normal state are subdivided on *n* time records each of which has duration *t* (see above). The pattern of interest is the average value of all n patterns. In addition to mean values, the standard deviations are calculated for each point in the phase space. The weight of each point in the phase space is calculated as

$$w_{i,j} = \frac{1}{\sqrt{\text{height} * \text{width}} + \sqrt{\text{dispersion}_{i,j}}} .$$

The DIC is calculated as a difference between patterns in normal and in the analyzed states as «»

$$DIC = \sum (\text{AveragePattern}_{i,j} - \text{CurrentPattern}_{i,j})^2 \cdot w_{i,j}^2$$

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