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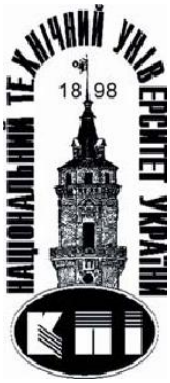

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Different permutation entropy patterns of electroencephalogram recorded during epileptiform activity

Behavior of permutation entropy for the orders from 3 to 7 was shown for the electroencephalogram (EEG) containing epileptiform activity. It was revealed that changing the order in the range from 3 to 7 has no significant effect on the results. Two different EEG groups containing epileptiform activity were distinguished, one with the tendency to a permutation entropy decrease in areas where epileptiform activity persists, another with increase of permutation entropy during epileptiform activity. Reference 17, figures 6.

Keywords: *permutation entropy, epilepsy, electroencephalogram, order, epileptiform activity.*

Introduction

More than 50 million people worldwide are affected by epilepsy which is one of the most common neurologic disorder. It is characterized by (repeated) seizures caused by excessive abnormal synchronous activity of neuronal groups in the brain. Clinical manifestations of epilepsy are unforeseen and abrupt motor phenomena, loss of consciousness, psychic and sensory symptoms etc., causing the low everyday life quality of sufferers. Despite the availability of variety of antiepileptic drugs, one third of patients have intractable seizures. For those positively reacting to treatment, therapy quality control must be conducted. Due to this fact, the need for automated techniques for epileptic seizures prediction and control is of great current interest. The most widespread way to analyze brain functioning in healthy and epileptic conditions is to apply various signal analysis techniques to the electroencephalogram (EEG) signal. This is the multichannel signal reflecting the time variations of brain biopotentials.

While many signal processing techniques are available for EEG analysis and classification, nonlinear approach to brain electrical activity analysis was paid many attention recently. A variety of techniques for nonlinear signal analysis have been developed, which allow better characterization of spatial and temporal dynamics of epileptic processes in the brain: effective correlation dimension, entropy related measures, Lyapunov exponents, similarity index, phase synchronization, nonlinear interdependency and other measures for generalized synchronization [8]. Entropy analysis of brain activity is widely used for analysis of brain electrical activity, since different types of entropy parameters can reflect unpredictability, chaoticity, complexity and nonlinearity of brain activity. One of the most commonly used entropy measure is Permutation Entropy (PE) [5], which reflects dynamics in time series of various complexity and over different time spans. PE gives quantitative characteristics of symbol patterns in EEG, and has two adjustable parameters to be set before calculation: PE order which controls the number of permutations and in this way influences the number of unique patterns which could be observable in the signal, and PE time lag corresponding to the duration of each pattern. Depending on the parameter's combination, one can get various values of PE [3, 12, 4].

It is generally assumed and experimentally proven on different datasets that complexity of EEG becomes less in ictal than in interictal period [2, 6, 9, 10, 11, 14, 16, 17]. Due to this fact it is possible to build classification system for distinguishing between seizure and normal activity and seizure prediction system as well. To do this, PE of EEG in different conditions should be studied for wide range of parameters (order and time lag) to get the optimal parameter set with respect to selectivity and specificity.

In paper [16] the study on genetic absence epilepsy rats was performed and PE was investigated as a tool for seizures prediction. It is shown that permutation entropy can track dynamical changes in EEG and can reflect transient dynamics prior to seizure in half of cases (169 out of 314) with the average anticipation time around 4.9 sec. In this study the EEG epoch

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duration was restricted by 1 sec, and PE of only one order and time lag combination (m=4, l=1) was used, which is insufficient.

In the work [17] authors presented preliminary results on detection of qualitative and quantitative dynamical changes in the clinically characterized brain wave data from epileptic patients. In the result they showed that the dynamics of the brain first becomes more regular right after the seizure, then its irregularity increases as it approaches the normal state, and concluded that PE has indicated all the seizures present in the analyzed data. They studied recordings from deep-brain electrodes from three patients and used PE order m=5 time window of 2048 samples (with 200 Hz sampling frequency) and time lag l=3 for their studies. Other orders and time lags have not been investigated in that paper.

Distinct vigilance states are also typically characterized by different degrees of regularity of EEG. Paper [6] was aimed to verify the reliability of permutation entropy in the detection of fluctuation of vigilance levels and in seizure prediction from scalp EEG. The goal was to test the capability of PE to distinguish between preictal and interictal states on the basis of scalp EEG. In the paper only three patients of different age and sex (17, 36 and 47 years old) were used, which is not sufficient for deriving any statistically proven results. Main result is the notion that all seizures occurred in association with the transition of vigilance states, and PE was able to discriminate between different vigilance states, independently of the occurrence of seizures. Hence, the good separability between pre- and interictal phases might depend exclusively on the coincidence of epileptic seizure onset with a transition from a state of low vigilance to a state of increased vigilance. Nevertheless this result is very important in enhancing the PE behavior in various brain states, in the paper only one PE order and time lag were used (m=4, l=1).

In paper [10] permutation entropy was used as a feature for automated epileptic seizure detection by Support Vector Machine (SVM) classifier. PE of order m=3 and m=4 was used as a feature for automated seizure detection, the best average discrimination of 93.55% is obtained for seizure activity versus activity obtained from awake healthy volunteers with eyes open. PE values for 1 sec. segments were used as a feature for linear and non-linear SVM, and time dependence of PE during seizure-free, pre-ictal and ictal periods was not considered, moreover, EEG from different subjects was used for discrimination.

Discrimination analysis between normal and epileptic EEG in the presence of additive Gaussiannoise was performed in [14]. As indicative parameters, PE and its mean and mean deviation were used for the same dataset as in abovementioned paper. The results indicated that the proposed measures can distinguish normal and epileptic EEG signals with an accuracy of more than 97% for clean EEG and more than 85% for highly noised EEG signals. In this study the time lag was changed from 1 sec to 30 sec, but for only one order (not specified).

In the paper [9], a spatio-temporal analysis of EEG synchronization based on trend of EEG Permutation Entropy in patients affected by absence seizure is proposed and the results are compared to the results obtained with a group of 40 healthy subjects. It was found that fronto-temporal areas appear constantly associated to PE levels that are higher compared to the rest of the brain, whereas the parietal/occipital areas appear associated to low-PE. While this is an important result, the study of PE order and time lag influence on synchronization characteristics was not conducted.

In the study reported in [11], auto mutual information which is derivative of PE is analyzed to evaluate EEG dynamics. In the result, authors showed that the permutation entropy was not effective in discriminating interictal phase from preictal phase. Again, only one PE parameter set was used, order m=5 and time lag l=1. Effect of order to identify patterns of epileptic activity has been considered previously [2]. But the research was conducted only for two EEG signals: EEG of a healthy person and signal contained only epileptic patterns.

The previous results don't give a complete picture of PE behavior during the periods of EEG transition from normal background activity to ictal activity for different orders. PE has not yet been studied systematically for wider range of orders for epileptic seizure onset. This can contribute to the improvement of prediction and detection of seizures. This paper aims to study PE dependence on the wider range of orders for EEG containing periods of normal activity, seizure onset and seizure oscillations.

This paper is organized as follows. In Section 1 the mathematical background of Permutation Entropy is presented, in Section 2 the experimental results on time-entropy analysis for EEG before, during and after seizure onset are given, and some discussion takes place. Last section concludes the research.

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1. Mathematical basis of Permutation Entropy

The PE is measure of disorder (randomness) of information contained in comparing the consecutive values of the signal, and it uses the relative frequencies of various patterns encountered in signal samples. Such approach benefits from the fact that PE does not depend on the signal values and uses only the symbol sequence.

Permutation entropy of integer order m ($m \geq 2$) of the signal $x[n]$, $n = 0...N-1$ is given [5] by:

$$PermEn_x(m,l) = -\sum_{j=1}^{m!} p(\pi_j) \log p(\pi_j).$$

This value is the measure of the amount of information contained in comparing m consecutive signal samples over some time interval. To calculate $PermEn_x(m,l)$, m successive samples of $x[n]$ with time lag l, $l \in N, l \geq 1$ should be selected starting from the first sample in the time window of interest:

$$v_l[i] = x[i], x[i+l], x[i+2l], x[i+3l], \ldots, x[i+(m-1)l],$$

where $i = 1...N-(m-1)l$, to obtain $N-(m-1)l$ embedded signal patterns $v_l[i]$.

Embedded pattern $v_l[i]$ thus consists of m different numbers, which represent one of $m!$ possible permutations. Therefore each pattern $v_l[i]$ can be considered as one of $m!$ permutation [14], and is denoted π_j, $j = 1...m!$ For signal $x[n]$ the relative frequency of permutation π_j is defined as:

$$p(\pi_j) = \frac{q(j)}{N-(m-1)l},$$

where $q(j)$ is the number of occurrence of permutation π_j.

It should be noted that method of calculating the PE [5] does not allow situation where the neighboring signal samples have the same value. But in real applications there is the problem of limited distribution capacity of electroencephalographs. Therefore sometimes there is the presence of the identical neighboring samples in the electroencephalograms. Example of solution of this problem is presented in the paper [15].

$PermEn_x(m,l)$ has values in the range $0 \leq PermEn_x(m,l) \leq \log m!$ $PermEn_x(m,l) = 0$ corresponds to the case when signal values are totally predictable, they are only ascending or descending. $PermEn_x(m,l) = \log m!$ corresponds to the case when signal contains all possible patterns with equal probability (the signal values are random numbers). To get rid of the PE dependence on the order, normalized PE is introduced with values lying between 0 and 1:

$$PermEn(m,l) = \frac{-\sum_{j=1}^{m!} p(\pi_j) \log p(\pi_j)}{\log m!}.$$

$PermEn(m,l)$ values depend on the order and lag:

- order m affects the number of patterns can be found in the signal. Order m equals to the number of samples to be taken from the signal to construct one pattern. Selecting large order leads to finding more patterns in the signal, i.e. more variations of successive samples' combinations;
- lag l is responsible for the time interval between signal samples with which they are elected in patterns (Fig. 1).

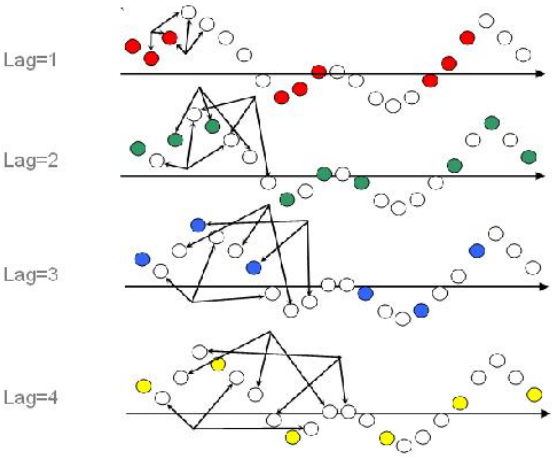

Fig. 1. Patterns in signal for different time lags [4]

Signal samples for patterns are picked consequently for the selected time window of analysis with time step equel to one sampling interval. There are only limited recommendations on selection of PE order and time lag. In the original paper of Bandt [5] usage of comparably low orders (3-5) is recommended due to the computation complexity. Order can be related to the variability of patterns which are to be found in the signal, thus this consideration can be used as well. In paper [4] it is recommended to draw a connection between time lag, sampling rate and time duration of pattern wherever it is meaningful, but there is no general recmmendations for selection of time lag for any

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particular case. Hence the selection of time lag and PE order should be done according to the aim of research.

In this work we restrict ourselves by orders of 3-7, and time lag was fixed at the minimal possible time interval between two samples. This was done for finding the possible order dependence of PE for the signals of interest, without possible presence of time lag dependence.

2. Experimental Results and Discussion

We used real EEG signals from public available Physiobank Database [7] "CHB-MIT Scalp EEG Database". This database was previously described and used in paper [13]. EEGs were collected at the Children's Hospital Boston, and this database consists of EEG recordings from pediatric subjects with intractable seizures. Subjects were monitored for up to several days following withdrawal of anti-seizure medication in order to characterize their seizures and assess their candidacy for surgical intervention [7].

For our research 12 EEG signals with epileptic seizures were selected. Recordings were collected from 8 subjects (3 males, ages 16-22; and 5 females, ages 13-19). All signals were sampled at 256 samples per second with 16-bit resolution. The International 10-20 system of EEG electrode positions and nomenclature was used for these recordings. All signals have 45 seconds length. Each seizure begins in a time instant near 30th second. Examples of EEG signals used for the analysis are given in Fig. 2.

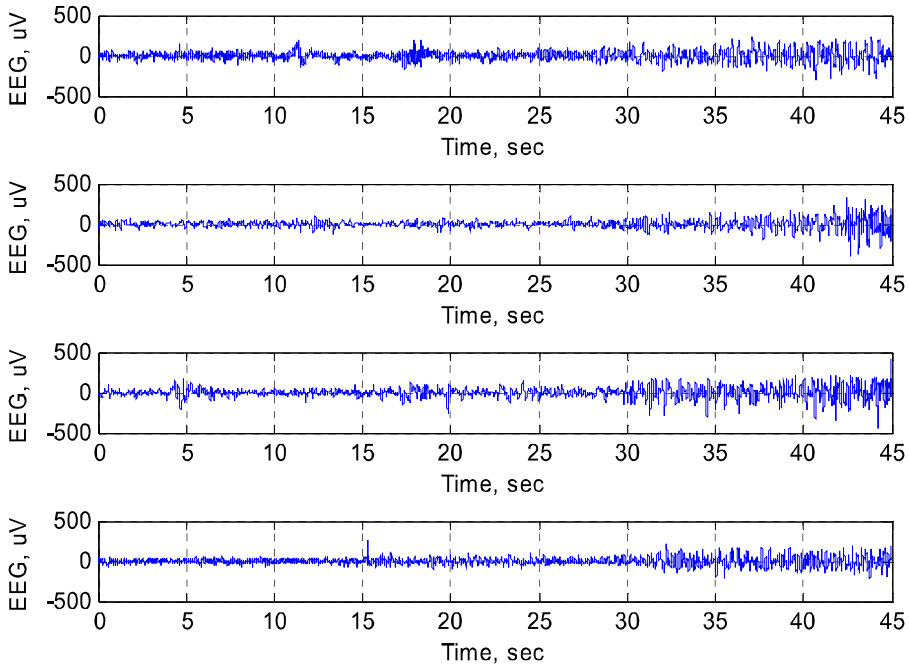

Fig. 2. Examples of EEG signals from the experimental dataset containing epileptic seizure activity starting approximately at 30th sec

The aim of the experimental part was to study PE behavior in wide range of orders, and to track the changes in PE while transition from interictal to ictal brain state. We selected the time window duration of 1 sec. and 90% overlapping of successive time windows, and then calculated $PermEn(m,l)$ for all signals with time lag equal to one sampling period. Obtained PE trends for each patients were synchronized to have the siezure start time at 30^{th} second, and then averaged to get the common trend.

During experiments different results were observed for different group of signals. In some signals (4 EEGs) PE decreased at the time of epileptic pattern onset and remains low, which is in agreement with the results reported elsewhere. This is generally considered as "regular" PE behavior in case of seizure. PE trend for this case is presented in Fig. 3, which is in agreement with the results of other studies.

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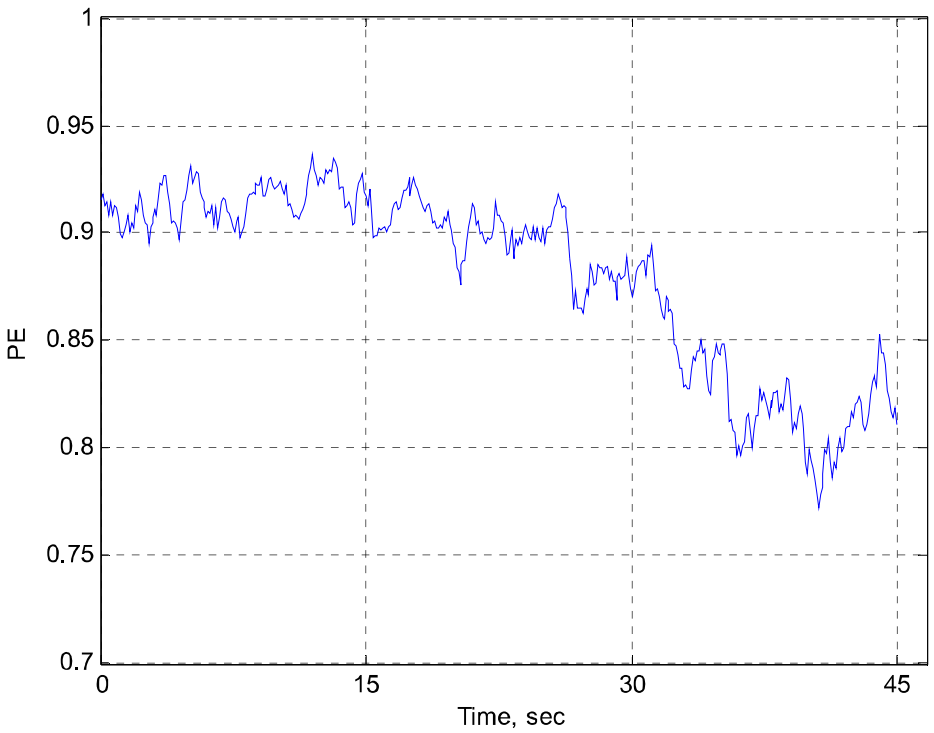

Fig. 3. Average PE trend with decay during and after seizure onset

But in the same time for significant group of signals (8 EEGs) the opposite situation was observed, when PE increase to the values larger than before seizure (Fig. 4) immediately after seizure onset. It can be noted, that before seizure PE has practically the same values (from 0.7 to 0.8) in both groups.

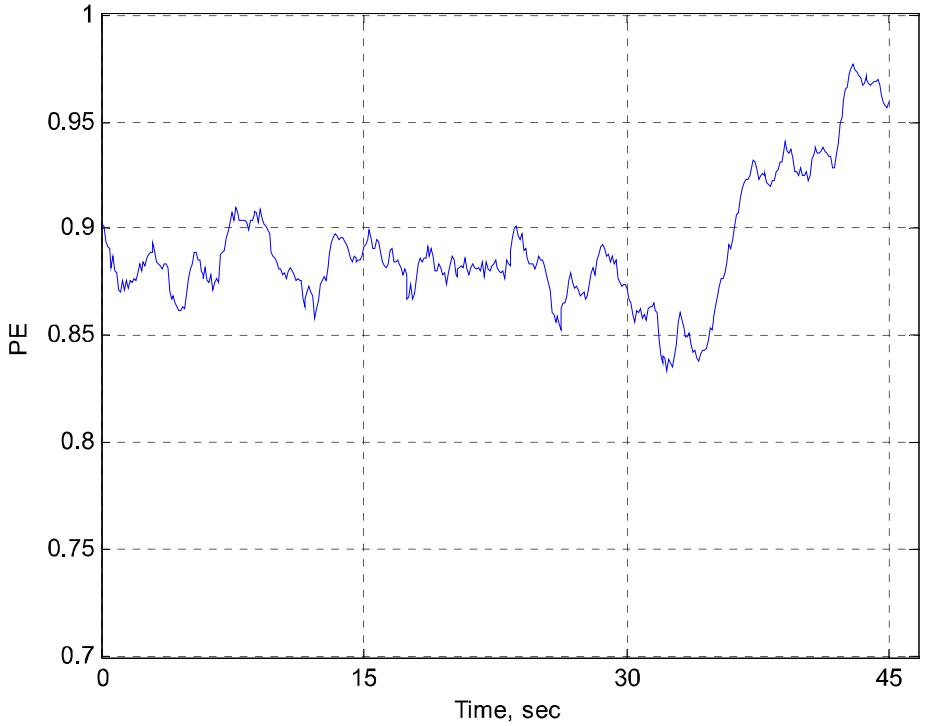

Fig. 4. Average PE trend with immediate increase after seizure onset

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Trends in Figs. 3-4 are obtained for order 3, and to study if this tendency persists for other orders, we calculated time-entropy dependence of PE for two groups of EEG signals with different behavior. In Fig. 5 the result for EEGs showing "regular" behavior is presented for orders from 3 to 7. In Fig. 6 the surface of PE dependence on the time and order is presented for the group of EEGs showing "abnormal" behavior, namely the increase of PE during and after seizure onset.

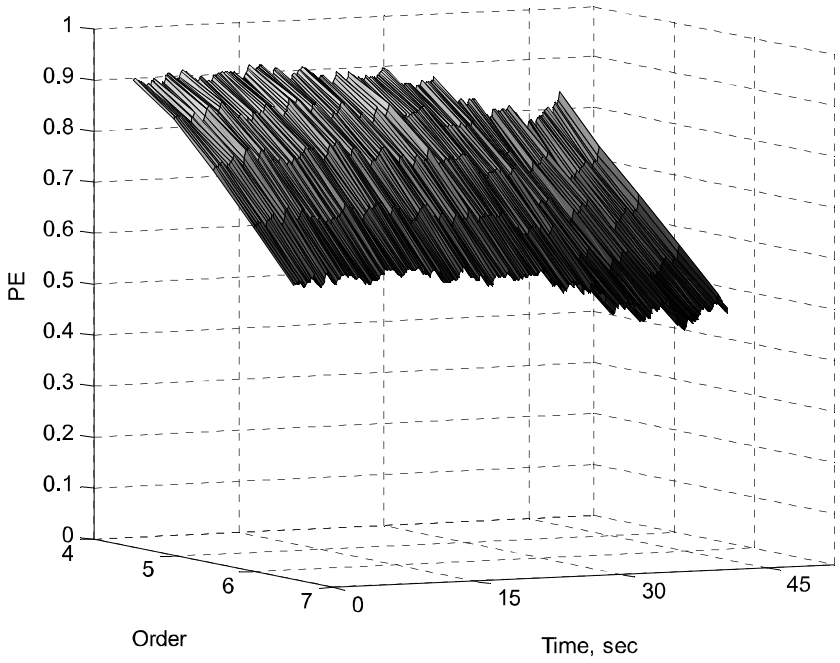

Fig. 5. Time-entropy dependence for EEG with PE decay for different orders

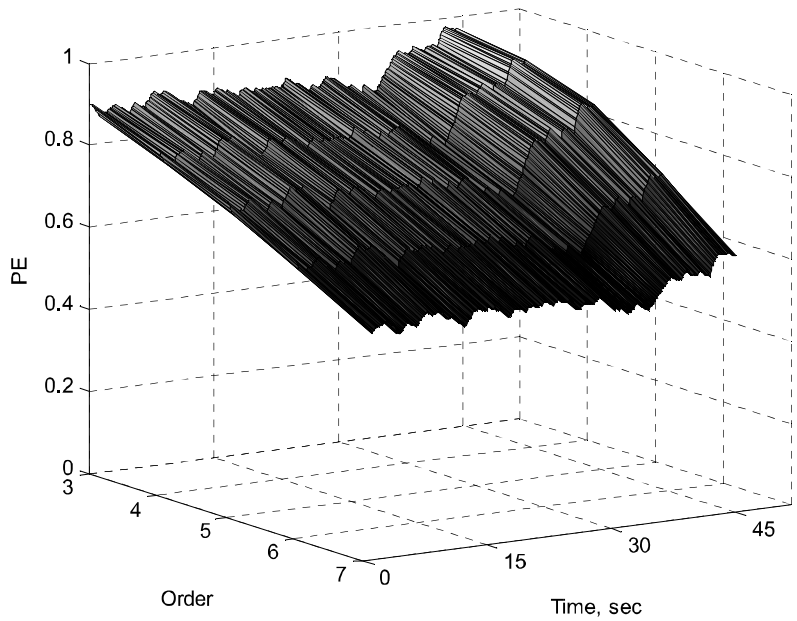

Fig. 6. Time-entropy dependence for EEG with PE immediate increase after seizure onset for different orders

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From Figs. 5 and 6 it can be seen that PE characteristics in each EEG groups have in general the same shape for all orders. The only difference is the decrease of offset of PE curve with order increase, which can be concluded from the obvious slant of PE surface towards higher orders. For smaller orders all PE values are larger, and PE decreases for signal parts before and during seizure for high orders.

Thus in our experiment with EEG containing seizure activity we have obtained the phenomenon of PE increase for significant group of EEGs. To the best of our knowledge it has not been previously reported in the literature. Although by now we can only present a few-case study, we have to emphasize that despite the fact that orders are different, there is obvious increase in PE values after seizure onset for at least some EEGs, which is not usual in general. Not going deeply into the nature of this phenomenon due to the lack of statistical evidence, at the moment we can only make speculations that the reason might be due to the different nature of seizures presented in EEGs from two groups. As reported in many papers, PE of a signal with epileptiform activity is less than PE of the EEG signal of a healthy person due to more regularity in brain functioning during seizure. It is often explained by shifting of the firing pattern of the thalamo-cortical neurons to an oscillatory, rhythmic, synchronized state of the EEG. Under these conditions, we are intended to observe the start of PE decline at that time. High PE values are connected to entirely random sequences. PE decrease during seizure activity in EEGs of this group might indicate noisy properties and is unpredictableness of brain activity. Thus it is very probable that one can distinguish two different patterns of ictal EEG with respect to PE behavior: with increased randomness (large PE) and with increased orderness (low PE). Such assumption is needed to be further investigated on larger datasets.

Conclusions

In this paper permutation entropy of EEG containing seizure activity was studied in wide range of orders, and the same behavior of EEG PE values for orders from 3 to 7 was shown during transition from pre-ictal to ictal stage. Two different types of EEG signals were distinguished, first with PE decrease during ictal stage and second with prominent increase of PE values during ictal stage. Obtained results suggest that increase of PE order for the purposes of epileptic activity detection might not be needed since the common tendency to PE change (whether increase of decrease) is presented for all orders.

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Різні патерни ентропії перестановок електроенцефалограми при епілептиформній активності

Показано поведінку часової залежності ентропії перестановок при зміні порядку з третього до сьомого для електроенцефалограм, що містять епілептиформну активність. Встановлено, що зміна порядку в межах від трьох до семи не має істотного впливу на одержувані результати. Було виділено дві різні групи сигналів, що містять епілептиформну активність, одна зі зниженням ентропії перестановок в області з епілептиформною активністю, а інша - із збільшенням ентропії перестановок при епілептиформній активності. Бібл. 17, рис. 6.

Ключові слова: *ентропія перестановок, епілепсія, електроенцефалограма, порядок, епілептиформна активність.*

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Различные паттерны энтропии перестановок электроэнцефалограммы при эпилептиформной активности

Показано поведение временной зависимости энтропии перестановок при изменении порядка с третьего до седьмого для электроэнцефалограмм (ЭЭГ), содержащих эпилептиформную активность. Установлено, что изменение порядка в пределах от трех до семи не имеет существенного влияния на получаемые результаты. Было выделено две различные группы сигналов,

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содержащих эпилептиформную активность, одна со снижением энтропии перестановок в области с эпилептиформной активностью, а другая – с увеличением энтропии перестановок при эпилептиформной активности. Библ. 17, рис. 6.

Ключевые слова: *энтропия перестановок, эпилепсия, электроэнцефалограмма, порядок, эпилептиформная активность.*

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