An Approach for EEG of Post Traumatic Sleep Spindles and Epilepsy Seizures Detection and Classification in Rats

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ABSTRACT

The electroencephalographic (EEG) features of post traumatic epilepsy (PTE) are analyzed in the paper. The proposed method allows detection and classification of sleep spindles and epilepsy seizures. The experiments were conducted on a laboratory rats before and after traumatic brain inquiry (TBI). In the introduction, the details of the experiment along with the information about manual markup are provided. In the first part, the new method of Sleep Spindles (SS) and Epilepsy Seizures (ES) detection is described. The method is based on the analysis of the wavelet spectrogram extrema. Moreover, the described procedure of background extraction and ridge segmentation helps to classify signals as epilepsy seizures and sleep spindles. In the second part, the information about the clustering is given. K-means clustering of seizures and spindles was performed based on signals power and frequency. The results of the clustering, along with the research of TBI effect on the EEG, are provided in the third part. It was shown that PTE may be considered as the cause of the frequency variance among clusters of sleep spindles and epilepsy seizures.

Keywords: post traumatic epilepsy, electroencephalography, sleep spindles and epilepsy seizures recognition, high voltage rhythmic spikes of EEG, wavelet spectrograms, k-means clustering.

1. INTRODUCTION

The association of epilepsy and head injury has been recognized since antiquity. At present, though epidemiological estimates regarding the prevalence of post-traumatic epilepsy (PTE) vary, it has been suggested that as many as 20% of acquired epilepsy cases are due to traumatic brain injury (TBI), with a 30 year cumulative incidence of up to 16% in the case of severe injuries. Some authors have reported that the likelihood of developing epilepsy after TBI is as high as 30–50%, and that PTE is among the most common forms of acquired epilepsies. Overall, TBI patients are almost 30 times more likely to develop epilepsy than the general population, and the probability for PTE to be pharmacologically resistant is high in both focal as well as generalized cases of the disease [1,2].

The research of PTE development may lead to the identification of the most important factors, which should be affected on the early stages [3]. As the post-traumatic seizures or Epilepsy Seizures (ES) are one of the strongest features of PTE risk, then it is suggested that these seizures are ideal target for disease prevention [4]. That is why the research of mechanism of ES activity after TBI has practical importance.

Among different phenomena visible on EEG: Sleep Spindles (SS), bursts of oscillatory brain activity occurring during stage 2 sleep, and high voltage rhythmic spikes (HVRS) can be revealed in control animals. SS refer to the group of rhythmic signals, which show gradual increase and then decrease of the amplitude. While SS are doubtless attributed to sleep, the genesis and significance of HVRS in the normal brain remains less clear. Though HVRS are mostly attributed to epileptic activity, there are reports showing that HVRS in rat brain may be not necessarily of epileptic origin [5,6]. As a rule, experts subjectively differentiate SS and HVRS in the normal brain.

There are no validated EEG biomarkers for the process of epileptogenesis in humans. However, the knowledge about the process of epileptogenesis and its underlying mechanisms provide a hope that we will be able to prevent the development of epilepsy after TBI [2].

2. MATERIALS AND METHODS

For the analysis of PTE brain activity, the experiments were conducted on male rats aged 24 months. In order to avoid effects of the estrous cycle only male rats were used in experiments. For the TBI simulation it was proposed to use a wide-known method called water hummer. However, the data of brain activity was also recorded before TBI. The brain activity data was taken via 4 electrodes in frontal and parietal lobes. The surgery of electrodes implantation was done in 7 days before TBI. For this 7 day period the data of background EEG was collected and video monitoring of rats' behavior was performed. The TBI was modeled by water hummer with pressure of 3-4 atm. Then the EEG data was collected for the next 7 days. It was proposed to select only three 24 hours durable parts of the whole EEG record: before TBI, in 1 day after TBI and in 6 days after TBI.

The recognition of SS and ES in the background EEG data in the early posttraumatic period poses a significant problem. It is known that one of the ES features is the incremental of signal amplitude, but it also can be found in SS. Three expert volunteers, experienced neurophysiologists of PhD or MS grade, performed a blind manual markup of the EEG records into sleep spindles and epilepsy seizures. The first expert examined the EEG records and selected suitable parts with epilepsy activity and 2-3 second before and after the seizure. The SS were extracted the same way. The second and the third experts performed a blind markup (without knowing the results of the each other) of the EEG parts, which were randomly shuffled.

As a result, the second expert extracted 233 EEG parts from 24 hour record, and 127 parts were classified as ES, while 106

were classified as SS. The third expert marked 123 EEG parts as ES and 35 as SS. 75 parts could not be accurately classified. The accuracy of 96.5% was achieved after comparison of the results of markup among experts. Actually, only full-match cases were selected as a train data for the further analysis.

3. METHODOLOGY

After the EEG records were marked up into SS and ES, it was proposed to create an automatic recognition algorithm based on the training data. To remove signal trend, the discrete eight-order Butterworth filter with 2-124 Hz bandwidth was used for the processing of 24 hour EEG data, as its amplitude-frequency characteristic is smooth in the passband, and high order provides a steeper decline of frequency and amplitude on suppression frequency bands. On the Fig.1 below is the example of filtered EEG record after TBI. The chart on the left presents the EEG data of a record marked as an ES, while chart on the right refers to the SS according to the markup.

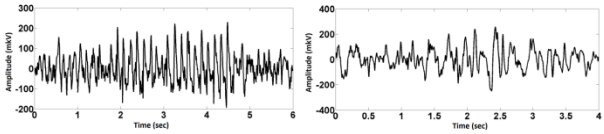

Fig 1. The example of after TBI EEG records using Butterworth filter: left chart refers to ES, right chart refers to SS.

The detection method of ES and SS is based on the analysis of wavelet spectrogram. The power spectrum density (PSD) of a time-frequency signal S_x is calculated according to function (1):

$$S_x = |W(\tau, f)|^2 \quad (1)$$

The continuous wavelet transform is defined by formula (2):

$$W(\tau, f) = \frac{1}{\sqrt{f}} \int x(t)\psi^*\left(\frac{t-\tau}{f}\right)dt \quad (2)$$

In the formula (2) x(t) refers to the source signal, and Ψ(η) refers to the Morlet mother function [7]:

$$\psi(\eta) = \frac{1}{\sqrt{\pi F_b}} e^{2i\pi Fc\eta} e^{-\frac{\eta^2}{F_b}} \quad (3)$$

It was proposed to use the equation above with Fc = Fb = 1.
The examples for the wavelet spectrograms and their ridges for the signals on Fig.1 are presented on the Fig.2 below.

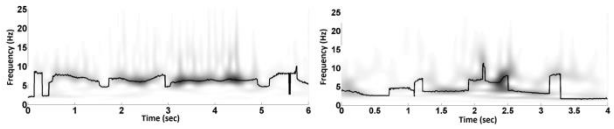

Fig. 2. Wavelet spectrograms and their ridges for the ES (left) and SS (right). The grey shadow reflects PSD value.

Actually, the wavelet spectrogram consists of the background as well as the ridges. Moreover, both ES and SS have high PSD in comparison to the background. That is why it is important to filter the background from the spectrogram. In order to do that, it was proposed to analyze the ridges PSD histograms (provided in Fig. 3).

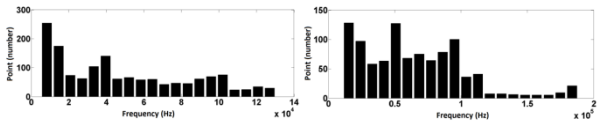

Fig 3. PSD histogram of wavelet spectrogram ridges for ES (left) and SS (right).

It can be seen that both ES and SS records have a high quantity of low-PSD values and low quantity of high-PSD values. The high-PSD values refer to the ridges, while low-PSD values refer to the background parts of the EEG record. The histogram shows steep decrease in a particular PSD values, and these values are selected as adaptive thresholds for the detection of ES and SS respectively. The charts on the Fig. 4 show the results of the proposed filtering.

The special segmentation algorithm is then applied to the ridges. The algorithm was designed so that the ridges, which are located close together, form a segment in case their frequencies do not differ more than on 1 Hz. The number of data points would then decrease, and the ridge curve would be smoother. The results of the segmentation algorithm are provided on the Fig. 5.

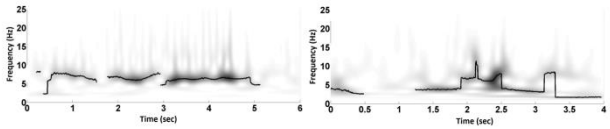

Fig. 4. Wavelet-spectrograms with their ridges of ES (left) an SS (right). The gray shadow reflects PSD value.

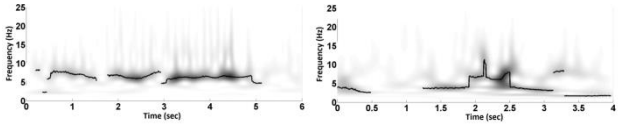

Fig. 5. Wavelet-spectrograms with their ridges of ES (left) an SS (right) after ridge segmentation. The gray shadow reflects PSD value.

The charts on the Fig. 6 show the 3D example signals of ES and SS in the space of time-frequency-PSD after all the transformations described above. The signals are placed together in the same initial time point. It can be seen than SS and ES differ by shape, power and frequency.

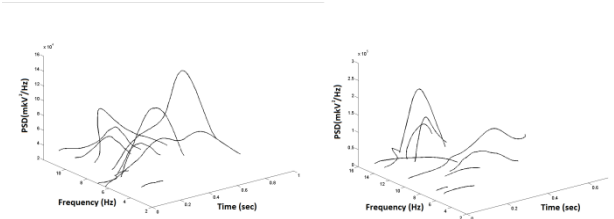

Fig. 6. 3D chart of wavelet-spectrogram ridges for ES (left) and SS (right) examples after background filtering and ridge segmentation.

Proposed detection method may be applied to all of the EEG records, which were manually marked up by the experts. This detection algorithm of ES and SS is based on the connectivity

of local extrema of EEG wavelet spectrograms. Moreover, the procedure of background extraction and ridge segmentation may help to further classify signals as ES and SS.

In order to automatically classify an EEG record as a SS or ES, the dataset of detected signals was created. For each of the 4 channels the time-dependent information of signals power and frequency was given. After the preparation, all of the records were cut into short signals with around 60 time points. The target class of the signal – ES or SS was provided according to the markup.

The analysis of the wavelet spectrograms showed that ES and SS signals have different shapes. That is why it is important to extract the common shape of ES and SS signals from the dataset. It was proposed to use a clustering method in the space of power or frequency. This N-dimensional space should be created so that each signal is present as a one point, regardless of the signals duration. Obviously, the signals should be scaled to the equal length firstly. All of the signals are linearly transformed into 40 time points signals given equation (4):

$$Index_{scaled} = [40 * \frac{Index}{Length}] \quad (4)$$

In the formula above, Index refers to a time point, Length refers to the signal duration, and Index_scaled is the value of scaled time point. The records with less than 40 time points can be considered as outliers, thus they are not used in the analysis. The number of these outliers is less than 5% of total number of signals. Then, all of the signals are mapped into 40-dimensinal space, where each dimension corresponds to the value of power (or frequency) in a particular scaled time point. In this space, each signal is transformed into one point.

It was proposed to use k-means clustering algorithm in this 40-dimensional space separately for the signals marked as seizures and spindles. This is a basic algorithm of clustering, thus it can be applicable to this task. K-means clustering aims to partition observations into predefined number of clusters so as to minimize the within-cluster sum of squares (the sum of distance functions of each point in the cluster to the center). The centers of the clusters are called centroids. The algorithm divides the observations into pre-defined number of clusters. Moreover, the centroids can reflect the most common observation among the cluster. To extract the shape of the centroids, the reverse mapping from 40-dimensional space into time-dependent space needs to be done. The reverse transformation is done by matching each dimension of the space into a correspondent time point.

The method described above may be used to extract the common shapes of ES and SS signals in each of the 4 EEG channels. It was proposed to use two clusters due to the small quantity of signals. For the quantitative assessment of the signals assigned to a particular cluster, it was proposed to use the metric sm of relative standard deviation sd(F) of signal frequency to mean(F). Each signal has its own value of this metric, which can be calculated according to formula below:

$$sm = \frac{sd(F)}{mean(F)} \quad (5)$$

4. RESULTS

It is important to analyze the distribution of sm before TBI. In the table below, the mean sm and standard deviation of sm are given for each group of ES and SS for all of the 4 channels.

Table 1. Mean and standard deviation of sm for groups of signals measured before TBI. Number of signals for each group is given in brackets.

Type	Channel_1	Channel_2	Channel_3	Channel_4
ES	23±12% (42)	19±10% (41)	17±8% (50)	18±8% (54)
SS	20±11% (47)	22±10% (45)	22±10% (47)	21±11% (51)

It can be seen, than the sm distributions of signals marked as ES and SS overlap in each of the 4 channels. It means that there is no significant difference in EEG before TBI. However, the distributions change for signals measured after TBI. Table 2 provides figures of sm for signals measured in 1 day after TBI.

Table 2. Mean and standard deviation of sm for groups of signals measured 1 day after TBI. Number of signals for each group is given in brackets.

Type	Channel_1	Channel_2	Channel_3	Channel_4
ES	27±20% (21)	20±8% (15)	13±6% (19)	16±10% (23)
SS	26±10% (10)	23±10% (12)	22±10% (14)	26±12% (15)

On the contrary, the sm distributions shift after TBI for ES and SS. For example, in the 3rd and 4th channels, sm values differ significantly. However, the distributions still overlap due to high variance. It is necessary to analyze the sm distributions in of ES and SS after the clustering has been performed.

The clustering was performed on the time-dependent PSD of signals with 2 clusters. Clustering was done in each group of ES and SS for each of the 4 channels respectively. The Fig.7 shows the results of the clustering of signals before TBI. The centroids of clusters for each group are shown on the chart. Circles represent seizure-based clusters, and triangles refer to spindle-based clusters. One can see that there is no significant difference in the centroids before TBI.

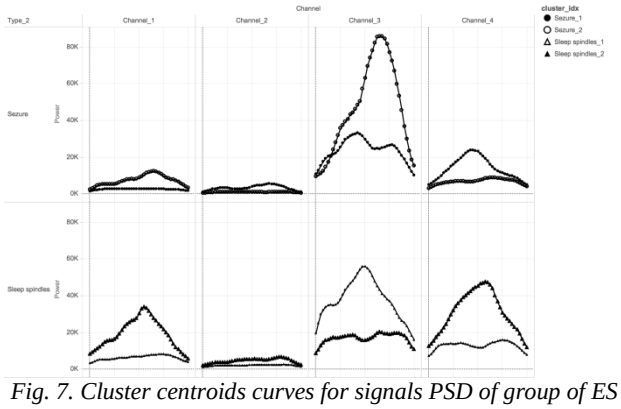

Fig. 7. Cluster centroids curves for signals PSD of group of ES and SS for 4 channels. Signals are measured before TBI.

In the Table 3 below, the distributions of sm among clusters are present. Clustering does not help to extract groups with different sm before TBI.

Table 3. Mean and standard deviation of sm for groups of signals after clustering measured before TBI. Number of signals for each group is given in brackets.

Type	Cluster	Channel_ 1	Channel_ 2	Channel_ 3	Channel_ 4
ES	1	24±12% (36)	30±16% (4)	18±8% (41)	18±6% (20)
ES	2	17±8% (6)	18±9% (37)	14±6% (9)	18±8% (34)
SS	1	14±5% (8)	24±13% (14)	22±9% (29)	18±10% (9)
SS	2	21±12% (39)	21±9% (31)	22±10% (18)	21±11% (42)

Later the clustering was performed on the signals measured after TBI. The clustering results are provided on the Fig. 8. The significant difference between ES and SS can be found in 3rd and 4th channels – there the PSD of SS signals is higher than the power of ES signals.

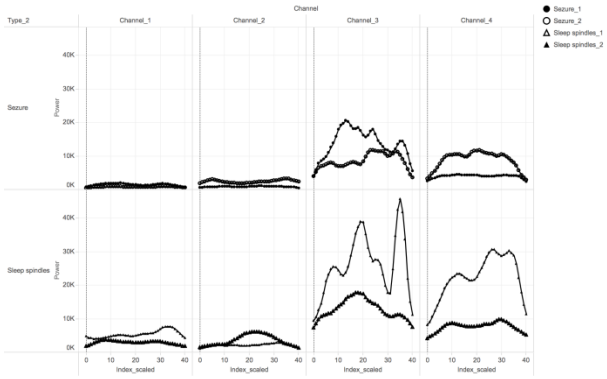

Fig. 8. Cluster centroids curves for signals PSD of group of ES and SS for 4 channels. Signals are measured in 1 day after TBI.

The sm distributions for signals measured after TBI are provided in the Table 4.

Table 4. Mean and standard deviation of sm for groups of signals after clustering measured in 1 day after TBI. Number of signals for each group is given in brackets.

Type	Cluster	Channel_ 1	Channel_ 2	Channel_ 3	Channel_ 4
ES	1	22±11% (7)	20±8% (13)	13±5% (8)	19±11% (15)
ES	2	30±24% (14)	19±14% (2)	13±7% (11)	10±3% (8)
SS	1	23±11% (6)	17±5% (4)	20±11% (12)	25±11% (10)
SS	2	32±5% (4)	26±12% (8)	29±0% (2)	29±14% (5)

From Table 4 one can see that the pairs of distributions do not overlap in the 3rd and 4th channels. For example, the sm distribution in cluster Sleep spindles_1 does not overlap with the sm distribution in cluster Seizure_2. Vice versa, the sm distribution in cluster Sleep spindles_2 does not overlap with the sm distribution in cluster Sezure_1. Summarizing, in the calculated clusters sm values of the SS are higher than sm values of the seizures. It means that SS signals have significantly higher variance of frequency, than ES signals.

In order to verify that point, the clusters of frequency were built. The Fig. 9 provides details regarding centroid curves of frequency.

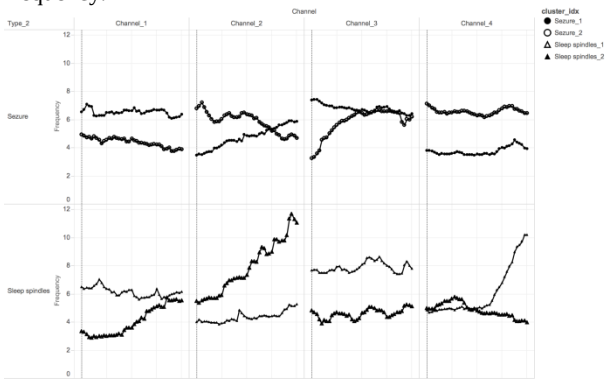

Fig. 9. Cluster centroids curves for signals frequency of group of ES and SS for 4 channels. Signals are measured in 1 day after TBI.

The figure above proves that centroids of SS show higher variance in frequency, especially in the 3rd and 4th channels. This feature appeared after TBI, and this leads to the hypothesis, that in fact TBI is the cause of sm difference among power clusters.

5. CONCLUSIONS

The new method of EEG signals like SS and ES seizures detection and classification is proposed in the paper. The measurements were taken on a laboratory rats before and after TBI. The HVRS appearing after experimental head trauma were recognized by experts and, by eye, appeared similar to those revealed before trauma. However, the proposed approach revealed the appearance of a new type of HVRS after head trauma which the experts could not differentiate visually.

The proposed method detects ES and SS in the EEG record. This detection algorithm is based on the connectivity of local extrema of EEG wavelet spectrograms. Moreover, the procedure of background extraction and ridge segmentation helps to classify signals as ES and SS. The clustering method was proposed for the identification of common signal of ES and SS. The k-means clustering was done in N-dimensional space, where each dimension refers to a PSD (or frequency) of signal in a particular time point. It was shown that signals from various clusters have different frequency deviations. The relative metrics of frequency standard deviation to mean was

proposed for tracking. After clustering of signals measured in 1 day after TBI, it was shown that centroids of SS show higher variance in frequency than centroids of ES, especially in 3rd and 4th channels. PTE may be considered as the cause of this variance. The data suggest that the genesis and physiological significance of class 1 and 2 discharges are different. This is a working hypothesis for further development of approaches for detecting and classifying ES as well as for elaborating automated discrimination between them and SS.

The problem of automatic recognition and classification of SS and ES in EEG is very relevant, and the inability to discriminate between these brain electric activities still prevents the development of proper analysis and interpretation of post-traumatic EEG in clinics and experiments.

The research was supported by the Russian Science Foundation, project #16-11-10258.

6. REFERENCES

[1] R. D'Ambrosio, E. Perucca, "Epilepsy after head injury", **Current Opinion in Neurology**, 2004 Dec; 17(6) pp: 731–735.

[2] M. Dichter, "Posttraumatic epilepsy: the challenge of translating discoveries in the laboratory to pathways to a cure", **Epilepsia**, 2009;50 Suppl 2:41-5.

[3] P. Ferguson, G. Smith, B. Wannamaker, D. Thurman, E. Pickelsimer, A. Selassie, "A population-based study of risk of epilepsy after hospitalization for traumatic brain injury", **Epilepsia**, 2010 May;51(5):891

[4] N. Temkin, "Risk factors for posttraumatic seizures in adults", **Epilepsia**, 2003;44 Supp. 10 pp.:18-20

[5] K. Semba, B. Komisaruk, "Neural substrates of two different rhythmical vibrissal movements in the rat", **Neuroscience**. 1984 Jul;12(3) pp.:761-74;

[6] F. Shaw, "Is spontaneous high-voltage rhythmic spike discharge in Long Evans rats an absence-like seizure activity?", **Journal of Neurophysiology**, 2004 Jan;91(1): pp. 63-77.

[7] P. Goupilland, A. Grossman, J. Morlet, "Cycle-octave and related transforms in seismic signal analysis", **Geoexploration**, 1984-1985. Vol. 23, pp. 85-102.