Metric Classification of Traumatic Brain Injury Epileptiform Activity from Electroencephalography Data

K Obukhov, I Kershner, I Komoltsev and Yu Obukhov

1Moscow Institute of Physics and Technology, Institutskiy per. 9, Dolgoprudny, Moscow Region, Russia, 141701
2Kotelnikov Institute of Radio-Engineering and Electronics of RAS, Mokhovaya 11-7, Moscow, Russia, 125009
3Institute of Higher Nervous Activity and Neurophysiology of RAS, Butlerova st. 5A, Moscow Russia, 117485
e-mail: ko.arsenalfc@gmail.com

Abstract. This paper considers the problem of epileptiform activity recognition in EEG. We conducted experiments on male rat before and after Traumatic Brain Injury (TBI). Experts in neurology performed a manual markup of signals as Epileptiform Discharges (ED) and Sleep Spindles (SS). We developed a proprietary Event Detection Algorithm based on time-frequency analysis of wavelet spectrograms. Feature space was based on Power Spectrum Density (PSD) and Frequency of signals, and each feature was assessed for importance of epileptic activity prediction. We used resulted predictors for training logistic regression model, which estimated features weights in probability of epilepsy function. Validation of proposed model was done by multiple train-test division. We shown that the accuracy of prediction is around 80%. Proposed Epilepsy Prediction Model, as well as Event Detection Algorithm, can be applied to identification of epileptiform activity in long term EEG records of rats before and after TBI and analysis of disease dynamics.

1. Introduction

It is known that post-traumatic epilepsy (PTE) requires timely treatment. In order to appoint an early treatment or prevention, it is important to know the factors of the disease. Such factors can be number of epileptiform discharges that appear in EEG, as well as changes in their time-frequency characteristics. A lot of papers on the search of epileptic discharges [1]–[6], sleep spindles (one of them [7]) and epileptiform discharges (for example [8]) were published. In all of these publications, authors know specific parameters of studied object. For instance, in [8] authors refer to the spikes as short fragments of spike-wave activities in the EEG signal, or epileptiform activity.

In current study, attention is paid to automatic distinction of sleep spindles (SS) and epileptiform discharges (ED). Experts manually marked epileptiform activity of different types, which complicates its comparison with the signal of a certain shape. The usage of methods that are focused on the study of signal form (as skewness and kurtosis [9], [10]) becomes difficult. However, experts pay attention not only to the signal form, but take into account the frequency of signal. This means that it is appropriate to use methods which analyse time-frequency characteristics of signal in order to detect suspicious activity. In this study, EEG in rats was examined before and after brain injury received after lateral fluid percussion (LFP). EEG feature extraction was done by wavelet transform of EEG signals.
Based on these features, Event Detection Algorithm (EDA) was built. Resulted features of detected events were used in Epilepsy Prediction Model (EPM), binary classification model – logistic regression.

With the application of proposed model, it is possible to calculate probability of epilepsy for a single event, previously detected by EDA. This probability can be further used for identification of epilepsy in other rats, including its dynamics over time.

2. Experiment Design
Experiment was conducted on adult male 24 months old wistar rat. Animal was kept in home cage with free access to food and water during the experiment. Rat was handled for one week prior to the operations. Electrode implantation was done four stainless steel screw electrodes that were placed bilaterally under somatosensory cortex (1 mm rostral, 3 mm lateral from bregma) and under visual cortex (7 caudal and 3 mm lateral from bregma); referential and ground electrode was located in occipital bone near midline. Electrodes were fixed with dental cement.

In 7 days after electrodes implantation, lateral fluid percussion brain injury model was used to reproduce TBI [11]. Brief, caniomyotomy (d = 3 mm) was drilled in the temporary bone (3 mm to caudal and 3 mm lateral from bregma). The injury with pressure of 3.4 atm was performed. Immediately after injury, rat was placed in home cage. Electroencephalography (EEG) was performed using a Bio Recorder (24-bit analog front-end for the measurement of Biopotentials) during 14 days: 7 days prior TBI and 7 days after TBI in acute post-traumatic period.

Three Experts in neurobiology performed a blind manual markup of the EEG records into SS and ED. The first expert examined the EEG records and selected suitable parts with ED with 2–3s backgrounds rhythm fragments before and after ED. A high-voltage rhythmic spikes (HVRS), or spike-wave-discharges (SWD) were selected. Recognition was based on next parameters: sudden or rapid onset with high amplitude spikes, rhythmicity of spikes (relatively stable interval between spikes), high voltage of spikes compared to background, asymmetry of ED (location of spikes in one direction from background signal); presence of small wave between spikes was additional, but not obligatory sign. The sleep spindles were extracted the same way. Recognition was based on next parameters: smooth onset and offset (spindle form), irregularity of spikes (including irregular interval between spikes and form of spikes), symmetry (location of spikes in both directions from background signal). 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 h record, and 127 parts were classified as discharges, while 106 were classified as sleep spindles. The third expert marked 123 EEG parts as discharges and 35 as sleep spindles. Seventy- five parts could not be accurately classified. The 96.5% matching ratio was achieved after comparison of the results. Actually, only full-match cases were selected as a train data for the further analysis.

3. Algorithms

3.1. Event Detection Algorithm
Notch filters and bandpass filters [12], [13] are used for signal preprocessing in order to suppress the interference of power supply, as well as to suppress the influence of frequencies that are not considered in the study. Since the sampling rate of signal is 250 Hz, it was proposed to use notch filters that suppress 50 Hz and 100 Hz power supply noise. There are many papers on selection of high-pass filter [1]–[6], [14] and a low-pass filter [15]–[18] for neurophysiological experiments. Given this information, it was decided to investigate the frequency range from 1.5 Hz to 40 Hz and use the eight-order digital Butterworth filter. The result of the preprocessing EEG signal is shown in Figure 1.

One needs to find a set of features of the suspicious activity in EEG. In time domain, it is difficult to find the characteristic features of such activity. However, there are different ways to acquire information about the signal [19]–[21]. For instance, transition to the time-frequency domain is often used for detecting signal features.
Figure 1. A fragment of rat EEG signal containing three epileptiform discharges. The signal before the filtration is shown on the left figure. The signal after the filtering is shown on the right figure.

The advantage of frequency-related characteristics is that they are more stable in the case of bad quality of EEG signal [22]. Thus, in the current study, the continuous Morlet wavelet transform was used [23]. Resulted wavelet-spectrogram consists of points with values of the power spectral density (PSD) located in the entire time-frequency domain (let denoted them as PSD(\(t_i, f_j\))), where \(f_j \in [1.5; 40]\) Hz and \(t_i\) is the entire period under consideration, in this example it is \([7060;7120]\) seconds, with a time step \(h_t = 0.004\) second and a frequency step \(h_f = 0.1\) Hz). In each time interval \(t_i\), the maximum value of the power spectral density (let denoted them as \(R_i\)) in the entire frequency range is calculated (equation 1).

\[
R_i = \max(PSD(t_i, f)), f \in [1.5;40]
\]  

(1)

These maxima \(R_i\) form the ridge \(R\) of the wavelet spectrogram. The ridge reflects the changes of the leading frequency over the time (Fig.2).

Figure 2. A ridge on a wavelet spectrogram (3D view and top view).

It is clear that the ridge contains points related to the background activity, since there are regions with low PSD, which are difficult to attribute to suspicious activity. Firstly, we removed points with sufficiently small values of PSD. It is necessary to understand which values of PSD can be considered as small. For this purpose, we will construct the histogram of the PSD values in the ridge of wavelet transform (Fig.3).

Figure 3. A PSD Histogram of the points of the ridge.

It is known that both background and suspicious activity are observed in the signal. Suspicious activity can be of different kinds (sleep spindles, epileptiform discharges, etc.), thus later we will call the fragments of the signal with suspicious activity as events. Both events and background may contain points with small values of PSD.
One can see in the histogram (Fig.3) that most of ridge points are in the region of low PSD values. Some of these points do not refer to background activity. Therefore, we will not consider single points, but groups of nearest points in the ridge. We are looking for the number of events (Fig.4) as the function of threshold value $T(h_k) \in [\min(R); \max(R)]$ (for example $k \in [1; 100]$). For each value of the threshold $T(h_k)$, the points of the ridge that are above this threshold ($R_i > T(h_k)$) are searched. If such points are next to each other, they are combined into one event. The maximum of this function is considered at the threshold value $T(h_{\text{max}})$. The main reason for choosing such threshold is to identify all events that can be attributed to suspicious activity, regard-less of its type.

One of the characteristics of events is duration. Events were truncated by the threshold, which means that the actual duration of events is not calculated. To find actual or approximate duration we expand events until values of the power spectral density at the end and the beginning of the event not reach the nearest local minima of the ridge. For example, event is extended to the right. Let $R_i$ be the right point of the event on the ridge. The event extends to the right while $R_i > R_{i+1}$.

Then we selected events using rules given by experts. Between each event there is a delay. In practice, a delay of less than 0.15 of a second is almost invisible for the eye. Therefore, events with a delay of less than or equal to 0.15 of a second are combined into one. Now the number of events decreased and their duration increased. But there are still events with a short duration. In the project, which is conducted by our team, events with duration of less than 0.5 seconds are not considered. The reason is that usually sleep spindles and epileptiform discharges, which at the moment are of great interest for neurophysiologists, last more than a half second. This correction added to the algorithm (Fig.5). This is the last stage of the EDA.

Thus, the idea of the EDA is to transit to the time-frequency domain using the wavelets transform, and then the wavelet spectrogram ridges are calculated. The ridge points related to the suspicious activity are combined into events, at the end these events are selected in accordance with additional rules. As a result of the operation of the EDA, events related to suspicious activity with the minimum possible duration were found.

3.2. Epilepsy Prediction Model

Proposed event detection approach was applied to previously marked EEG records. As a result, the dataset of 365 observations was created, where 198 of observations were labeled as ED and 167 as SS.
We would refer to binary variable as target, which indicates class of event according to markup: 1 in case of epileptiform activity (ED) and 0 in case of normal (SS) observation. Each detected event represents PSD and Frequency over time, while duration of event can be different among events. Table 1 shows proposed features and their description. As discussed with the experts, these features can potentially indicate presence of epileptiform activity. Based on these feature space, further analysis was done.

Obviously, it is proposed to use only important features in classification model. Thus, feature importance analysis was done by plotting Receiver Operating Characteristics (ROC) curve and measuring Area Under Curve (AUC). ROC curve shows dependency between True Positive Rate and False Positive Rate for each possible threshold where first indicates the share of True Positive cases among all positively classified and second refers to share of False Positive cases among all negatively classified. AUC is simply area under resulted ROC curve and shows predictive power (or correlation) of certain feature or attribute: if AUC is 0.5, then feature has no influence on target, and if AUC is 1, then feature ideally predicts target variable. From Table 1, one can also see resulted AUC for each proposed feature.

Features like $P_{\text{min}}$, $\frac{\text{std(f)}}{\text{mean(f)}}$, $t(P_{\text{max}})$ are the most important, while $f_{\text{max}}$, $f_{\text{min}}$ and $\Delta f$ have no correlation with epileptiform activity. Finally, only important features were used to train a classifier, so that AUC of particular feature is more than 0.6.

It is proposed to train a linear classifier due to (i) low number of observations and (ii) uncertainty in target variable, which is based on human diagnosis. Usage of non-linear models would most likely lead to overfitting. That is why Logistic Regression model was used. This model was successfully used in different applications, for example in a problem of improving the accuracy of identifying human activity in buildings based on an ecological feature space [25]. Logistic Regression model is a binary classification model, which estimates features weights (or coefficients) as in probability formulas (2), (3) [26]:

\[
f(z) = \frac{1}{1+\exp(-z)} \quad (2)
\]

\[
P\{y=1|x\} = f(z) = a_1x_1 + \ldots + a_nx_n \quad (3)
\]

In formula above, $f(z)$ is the probability of positive outcome (is our case, epileptiform activity of event), and $x_i$ refers to feature $i$ value. The estimation of weights is done by maximizing likelihood function using gradient descent algorithm.

| Feature  | Description                  | AUC  |
|----------|------------------------------|------|
| $f_{\text{min}}$ | Minimal Frequency of event | 0.52 |
| $f_{\text{max}}$ | Maximal Frequency of event | 0.51 |
| $\Delta f$ | $f_{\text{max}} - f_{\text{min}}$ | 0.51 |
| $P_{\text{min}}$ | Minimal PSD of event | 0.72 |
| $P_{\text{max}}$ | Maximal PSD of event | 0.53 |
| $\Delta P$ | $P_{\text{max}} - P_{\text{min}}$ | 0.5 |
| mean(f) | Average Frequency of event | 0.61 |
| std(f) | Frequency Standard Deviation of event | 0.64 |
| $\frac{\text{std(f)}}{\text{mean(f)}}$ | Standard Deviation to Mean ratio of Frequency | 0.67 |
| $t(P_{\text{max}})$ | Relative Time of maximal PSD | 0.65 |

4. Results

In order to validate the model, it was proposed to perform multiple train/test split method. Dataset was randomly divided into train and test parts in 70/30 proportion. Coefficients evaluation was performed on a train subset, and prediction was made on test subset. As a result, AUC was measured on a validated data. This training and testing procedure was done 1000 times in order to reach statistically stable results. After 1000 models were created, AUC for each model was estimated on a test subset. As
a result, distribution of AUC was analyzed. Table 2 shows AUC statistics: minimal and maximal values of distribution, mean and median, as well as 1st and 3rd Quartiles of distribution. It can be seen that median AUC is nearly 80%. Average coefficients of predictors are provided in a Table 3. In this table, Intercept is addition to \( z \) in formula (3), which is not multiplied on any feature value. Figure 6 shows distribution of AUC after simulations and Figure 7 shows model ROC curve.

![Histogram of AUC over simulations.](image1)

**Figure 6.** Histogram of AUC over simulations.

![Sample model ROC curve, where Sensitivity is True Positive Rate, Specificity is False Positive Rate.](image2)

**Figure 7.** Sample model ROC curve, where Sensitivity is True Positive Rate, Specificity is False Positive Rate.

| Min.   | 1st Quartile | Median | Mean    | 3rd Quartile | Max.   |
|--------|--------------|--------|---------|--------------|--------|
| AUC    | 0.643        | 0.769  | 0.796   | 0.795        | 0.822  |

**Table 2.** Summary of models AUC values.

| Intercept | Pmin      | mean(f) | std(f) | mean(f) /         | t(Pmax)  |
|-----------|-----------|---------|--------|-------------------|----------|
| -1.8203   | -3.682e-05| 0.5165  | -1.5043| 1.9391            | 0.6578   |

**Table 3.** Average feature coefficients in logistic regression models.

From Figure 6 and Table 2 one can see that models’ AUC lies in range 0.769 – 0.822, while there are some outliers with AUC less than 0.65 and more than 0.85. The cause of these outliers can be relatively small number of events in train set. Thus, on average, accuracy of 80% can be expected from proposed models.

5. Application

Proposed methods and algorithms can be used for epileptiform activity recognition in long durable EEG records, where human analysis is not possible. For instance, model can evaluate probability of
ED for Events, which were automatically detected in daily EEG data of rats before and after TBI. Such experiment was conducted on two rats: one of them had TBI, and the other one did not (false surgery case). EDA was applied for these long records, and features of EPM were extracted from Events. Finally, probability of ED was calculated on every Event before and after TBI for one rat and before and after false surgery for the other rat.

Figure 8 shows distribution of ED probability for false surgery rat, while Figure 9 represents distribution for TBI rat. It can be seen that distribution shifts significantly for TBI rat after injury — the percentage of high epileptic Events raises from 1.2% to more than 2.5%. On the contrary, for false surgery rat distribution does not change a lot — the same 1.5% of Events belong to high risk of ED probabilities range. This results ensures that method can effectively separate epileptiform activity and detect its dynamics after TBI.

Figure 8. Share of Events Distribution of ED probability before and after false surgery in Channel 3.
Additional analysis was done by partitioning distributions over channels. From Figure 10, one can see distribution of ED probability in Channel 1 and Channel 3. Most of the epileptiform activity cases are located and Channel 3 (and Channel 4, symmetrically). This result corresponds to common understanding of epilepsy in rats.

6. Conclusions
This paper describes methods of recognition of epileptic signals in brain activity. EEG records of laboratory rat with PTE were measured before and after TBI. Experts in neurobiology performed a markup of signals into ED and SS in order to make a dataset for training the model. A new method that allows finding suspicious activity in EEG signals was developed – Event Detection Algorithm. In the paper, an algorithm that allows finding events of interest is described.
The main advantage of the method is in that it is adaptive. The idea of the method is in that the analysis of the ridge of the wavelet spectrogram is applied. This allows to obtain both the characteristics of the detected fragments of the signal and to find unusual fragments that can be considered as suspicious electrical activity. In addition to detecting events, their time-frequency characteristics were calculated. This enables to classify events represented in the signal (such as sleep spindles and epileptiform discharges [24]). On detected events, PSD and Frequency features were calculated from EEG. On a resulting dataset, logistic regression model was built with binary target variable of epilepsy. Although, only important factors were considered in a model. Models were validated on different subsets of data and performance was measured in AUC. Proposed algorithm of ED and SS recognition shows good performance results with average of 80% accuracy of prediction. Further, this approach can be applied to identification of epileptic activities in a long term EEG records. For instance, long EEG records can be automatically processed, and parts with high risk of epilepsy could be identified with proposed model. This paper shows results of proposed method application to recognition of epileptiform activity in TBI rat and false surgery rat. The analysis shows, that distribution of ED events significantly changes after injury to the area of high-probability, while distribution does not change for false surgery rat. Moreover, majority of ED cases were found in Channel 3 and Channel 4, which corresponds to common understanding of epileptiform activity development.

7. References

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