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Heart Beat-to-Beat Intervals Classification for Epileptic Seizure Prediction

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***Abstract* — This work is devoted to the prediction of epileptic seizures using heart rate variability (HRV) characteristics. Several HRV features were extracted (statistical, spectral, histogram, polynomial approximation coefficients) for various durations of sliding time windows and various lengths of preictal intervals. The data from 14 subjects with generalized epileptic seizures was used. Support Vector Machine was exploited as a classifier. Leave-One-Group-Out validation, yielded the following values of classifier performance: AUC = 0.7622, sensitivity = 0.7252, specificity = 0.7252. These results indicate the possibility of seizure prediction using HRV characteristics. Our findings regarding positioning and sizing of used time windows, namely the imitations in finding optimal parameters between different subjects, could be used for further advancement of methods for epileptic seizure prediction using the heart rate variability characteristics.**

Keywords— epilepsy; epileptic seizure; seizure prediction; heart rate variability

I. INTRODUCTION

Heart rate variability (HRV), i.e. the variations of beat-to beat intervals, is caused by many sophisticated and nonlinear processes in the human body. Epilepsy is believed to have cardiovascular implications, which is the cause of increased interest in connecting the heart rate with the epileptic activity. Of particular interest is the applicability of heart rate characteristics to the prediction of the epileptic seizures. This is the unforeseen disruption of normal body functioning, accompanied by the loss of consciousness, tremor, vocalization, muscle rigidness etc., which causes problems to those suffering from epilepsy. Prediction of the seizures can be of great help to improve the patient's lives.

Many researchers have been working on heart rate characteristics in epilepsy in general and in prediction of epileptic seizures in particular (see the review papers [1-2]). In [3] HRV features were used to predict seizures with sensitivity 91%. In [4] linear features in the time and frequency domain of HRV signal were employed resulting in 88.3% sensitivity and 86.2% specificity. Some other detection algorithms are promising for seizure prediction. In [5] all seizures in 16 of 17 patients were detected, some of them 60 sec. prior to seizures' onset. In some other published works joint analysis of EEG and ECG was done for seizure forecasting [6, 7, 8, 9, 10]. In almost all of them, the HRV features were calculated using complicated and often nonlinear equations, which is potentially harnessing the usability of such feature extraction techniques in real time. Moreover, many works on seizure prediction use a "patient-specific" approach, where the prediction system has to be trained for each patient individually before seizure prediction. This requires large amounts of historical recordings with labelled seizure episodes, which might not always be available. In this regard, there is the need to develop non-patient specific solutions, which will work for groups of patients (with similar diagnosis, epileptic focus localization, etc.).

One important aspect concerning seizure prediction is the period of time the prediction can be done before seizure. An early prediction will enable warning patients. However, the task of prediction can be assumed to be more complex the longer the time period is.

In this work, we seek to find optimal parameters to extract predefined statistical and spectral features for seizure prediction for a non-patient specific approach. Basic cardiotachogram preprocessing operations are used, followed by the Support Vector Machine classifier with a grid search to extract most suited parameters. The results of seizure prediction are obtained for a group of patients with generalized seizures.

II. MATERIALS AND METHODS

The dataset of electroencephalogram (EEG) and electrocardiogram (ECG) recordings was collected in the TMO "Psychiatry" clinic (Kyiv, Ukraine). Data was used. In total, 18 recordings were obtained from 14 patients with generalized epileptic seizures (6 males and 8 females, aged between 1 and 15 years). Recording examples are given in Figures 1-2.

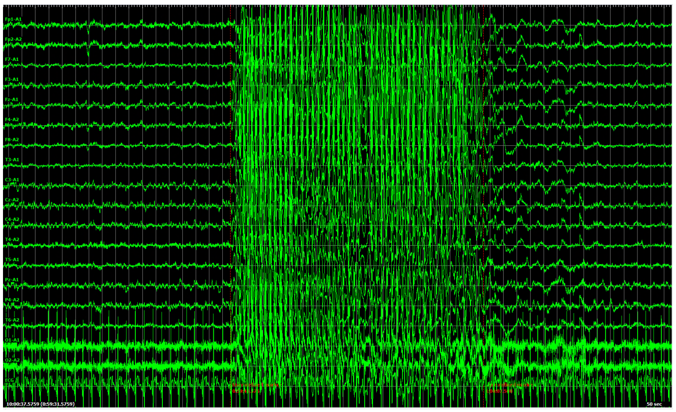

Fig. 1. Example of the record with one epileptic seizure

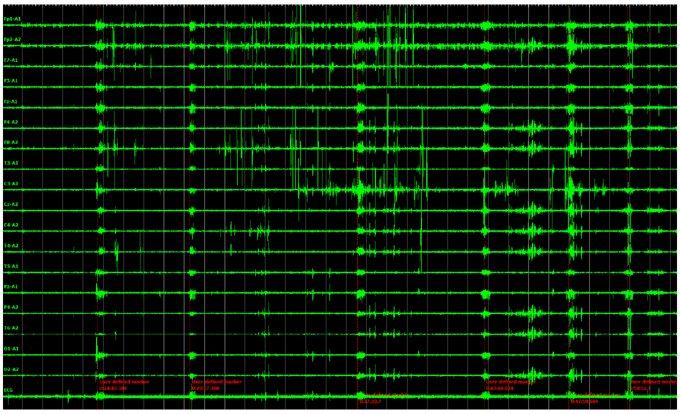

Fig. 2. Example of the whole record with several marked seizures (vertical red lines)

In the present study, patients were sleeping while EEG and ECG was recorded, along with the video monitoring. For ECG, standard lead II was recorded, while EEG was recorded using International 10/20 system. Sampling rate for both signals was 250 Hz. For some patients, other signals were collected (sound, respiration, chin myogram, electrooculogram form left and right eye etc.), but these were not used in this study. Seizure episodes were identified using the video records by the qualified neurologist: seizure start and stop were labeled as the beginning and disappearing of the visible seizure activity.

III. ECG PREPROCESSING AND CLASSIFICATION

A. Extraction of RR time series

RR intervals were extracted from ECG using a custom technique based on a modified Pan-Tompkins method [11]. The preprocessing of EEG and ECG, QRS complex detection and RR intervals extraction and preprocessing was done in Matlab. Feature extraction, classification and validation was performed in Python 3.5.

B. RR time series filtration

In order to account for incorrect detections and arrhythmic heart beats the time series of RR intervals was filtered. We applied a method similar to the one proposed in [12]. In short, all RR intervals were removed that differed more than 25% from the interpolated mean of immediately preceding and following RR. After each step of removal the remaining RR intervals were checked again resulting in an iterative procedure until no further intervals had to be removed.

C. HRV features

Preprocessed RR time series was windowed with 50% overlapping, and for every time window 112 HRV features were calculated:

- Statistical (mean, median, standard deviation etc.),
- Spectral (power spectral density in typical HRV frequency ranges),
- Histogram characteristics (using 5 and 7 bins),
- 1st degree polynomial approximation coefficients,
- Characteristics of low-pass and high-pass filtered interpolated RR time series with cut-off frequency 0.25 Hz.

D. Classification and validation scheme

As classifier, the Support Vector Machine with radial basis function kernel was used. Balanced class weights were used to take into account the difference in the number of objects from two classes. After balancing, the weights are adjusted automatically inversely proportional to class frequencies in the input data. As a classification effectiveness characteristics, the standard measures were used, namely Area Under Curve (AUC), specificity and sensitivity.

To validate the classification results, the Leave-One-Group-Out scheme was adopted. In this approach, seizures from one patient are considered as one group of data. In each classification run, the data from all patients except one are combined and used as training set. The data from the remaining patient are used as a test set. This procedure is repeated, until the classifier is tested on every patient; then the performance characteristics are averaged with the weights according to the number of seizures. Therefore, a non-patient specific approach is used in this work [13].

Classification into two classes is used in this work: interictal and preictal state. Interictal is the period of time "between seizures" while there is no seizure foreseeable. Every warning about an forthcoming seizure is considered as false positive. Preictal is the state "before seizure", and if classifier identifies it, that means the seizure is going to occur after this period. The objects to be classified are the HRV features calculated from sliding time windows. The preictal period duration is considered as a parameter of classification, since it can be adjusted to get the maximal prediction efficiency for the given set of features. The longer the preictal period is, the earlier the seizure can be predicted.

Two parameters of feature extraction from RR time series are considered: T_w – is the duration of time window in which the features are calculated, and T_{pi} – is the duration of preictal period in the recording. To identify the optimal parameters, a grid search is used, where T_w was in the range between 60 and

600 s, and T_{pi} was selected from the range between 600 and 3600 s.

IV. EXPERIMENTAL RESULTS

In Figures 1-3 the classification performance characteristics are presented (weighted AUC, selectivity and specificity, respectively). They are depicted as functions of two parameters of grid search: the duration of the time window in which the features were calculated, and the length of the preictal period.

As can be seen the surfaces in Figs. 1-3 are quite homogeneous, and prominent extrema are absent. Nevertheless, it is possible to find the optimal combination of feature extraction parameters, yielding the highest performance. The following combinations of T_{pi} and T_w resulting in highest AUC, sensitivity and specificity are obtained:

- AUC = 0.7622 (optimal T_w = 550 s,

  optimal T_{pi} = 1200 s),
- Sensitivity = 0.7252 (optimal T_w = 470 s,

  optimal T_{pi} = 1550 s),
- Specificity = 0.7252 (optimal T_w = 470 s,

  optimal T_{pi} = 1550 s).

One can note that the values of the optimal duration of time windows are quite close, and differ only by approximately one minute. The optimal preictal length is 1550 s for sensitivity and specificity, and 6 minutes less (1200 s) for AUC.

V. DISCUSSION

In the present work, we searched for optimal parameters for epileptic seizure prediction using heart rate variability. A grid search on the preictal length and duration of used time windows to calculate the parameters of HRV is done. In the result, all three obtained measures of classifier performance (AUC, sensitivity and specificity) are higher than 0.72 for a quite similar time window, which might be considered as satisfactory result for non-patient specific prediction using heart rate. On the other hand, preictal interval length differs substantially while yielding the highest values (20 minutes for AUC and 26 minutes for sensitivity and specificity). This indicates the need for additional tuning, to find the unique set of parameters for classification leading to the maximization of AUC, sensitivity and specificity.

Furtheron, the surfaces in Figures 3-5 are not smooth which could indicate a limited generalized applicability of HRV features in their current form. One could expect a smooth surface if the used features and found parameters are of general importance, so further research on feature extraction, selection and reduction should be done. For a real application a more stable behavior, i.e. a feature set that is more stable, would be of interest.

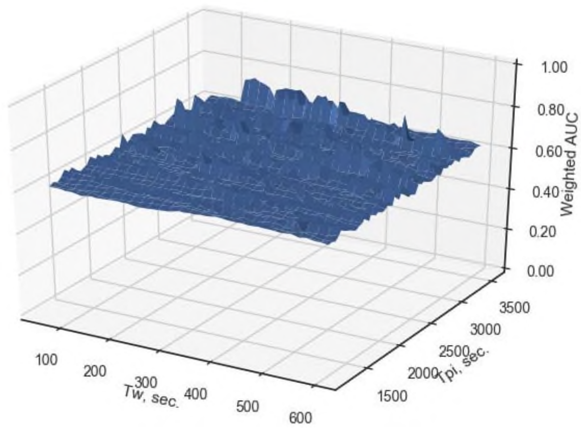

Fig. 3. Weighted AUC as a function of preictal length and time window duration

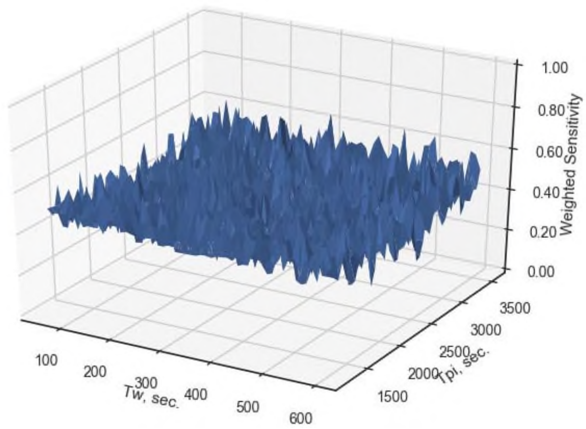

Fig. 4. Weighted sensitivity as a function of preictal length and time window duration

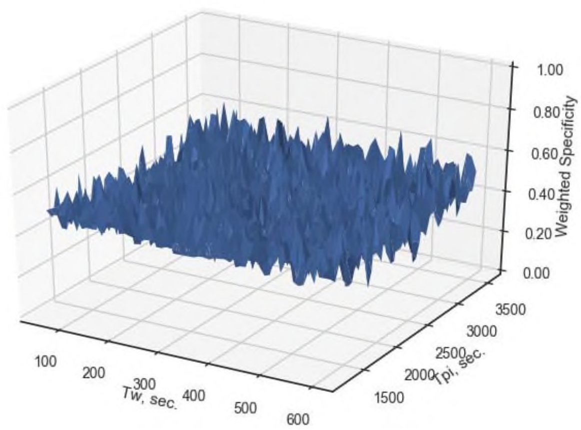

Fig. 5. Weighted specificity as a function of preictal length and time window duration

At the early stage of the work, the filtration of raw RR time series was not performed, and the results were approximately 0.1-0.2 lower than those presented in this paper. This might indicate that much attention should be paid to the preprocessing of RR intervals, to remove inaccurate detections, and non-valid intervals. It is possible that more sophisticated preprocessing algorithm can result in higher performance.

The important thing to consider in future works is the need to classify the beat-to-beat intervals in real-time in wearable or implanted device, therefore ECG processing, R-peak detection, RR time series preprocessing and the feature extraction algorithms should be as lightweight as possible. To this respect, the feature selection might be one of the tasks to solve to optimize the performance. Another need in optimization emerges because three classifier performance measures should be maximized simultaneously (AUC, sensitivity and specificity), and they are not clearly connected to each other. So multi-objective optimization can be used to solve this task.

VI. CONCLUSIONS

With the optimal set of feature extraction parametersit is possible to predict epileptic seizure using heart rate variability characteristics. In this work, a grid search for the required duration of time window for HRV parameters calculation and for the length of preictal interval was performed. The generalized epileptic seizures prediction using the non-patient specific approach is described by the following measures: AUC = 0.7622, sensitivity = 0.7252, specificity = 0.7252.

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