Detection of epileptic seizures by means of morphological changes in the ECG

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Abstract

Epilepsy strongly affects the autonomic nervous system. Control mechanisms such as the one regulating the heart rate can be deeply affected during epileptic seizures. This effect of epilepsy can be measured in the ECG signal. In this paper, ECG segments of 35 children suffering from refractory epilepsy are studied. The goal is to determine whether pre-ictal, ictal or post-ictal tachycardia is present in partial and generalized seizures. A new set of features extracted from the ECG is proposed. These features are derived by means of principal component analysis (PCA) of a matrix formed by consecutive QRS-complexes, and they measure the heterogeneity of the QRS along the ECG. This new set of features together with the RR interval series is used to detect seizure onsets. Three approaches are implemented, namely thresholding, k-means and kernel spectral clustering (KSC). The best positive predictive value (PPV) was 85.7% for partial seizures, and 57.3% for generalized seizures.

1. Introduction

Epileptic seizures seriously affect the control mechanisms of the autonomic nervous system [1]. For example, changes in heart rate can occur during and even a few seconds before and after the EEG onset of the seizures [2–6]. These changes can be caused by involvement of the central autonomic centres during the seizures, or by motor activity and/or stress responses to the seizures.

Different studies have shown that not only the heart rate, but also the morphology of the ECG changes during the seizure. In [5] it was shown that the QT interval was shortened during the early post-ictal phase in patients suffering from refractory temporal lobe epilepsy. Additionally, ECG abnormalities such as T wave inversion and ST elevation/depression, have been observed in the pre-ictal period of partial and generalized seizures [4]. These studies have focussed on the presence of ictal tachycardia in adults with refractory epilepsy. In [6] the focus was however, on childhood epilepsy and it was reported that changes in heart rate can be observed in temporal-lobe and frontal-lobe seizures. Generalized seizures represent a bigger challenge due to deep motor involvement and/or a lack of significant changes in heart rate.

Due to heart rate changes during the pre-ictal, ictal and post-ictal phases it is possible to think about the development of user friendly warning systems that can improve the quality of life of patients suffering from epileptic seizures. It is clear that the ECG has an inherent advantage over EEG in the sense that it is easier to measure in a long-term setting, and changes can be observed before the EEG onset. Different methodologies to detect seizure onsets from the ECG have been proposed [2, 3], where the heart rate signal is modelled using curve fitting.

This paper proposes to extract some features describing the morphology of the ECG signal by means of principal component analysis (PCA). These new features are strongly affected by the occurrence of a seizure which allows to identify when the morphology of the ECG, in particular of the QRS-complex, is affected.

2. Data

The dataset used in this study consists of single-lead ECG recordings from children suffering from refractory epilepsy. These children were admitted to the epilepsy clinic of UZ Leuven in Belgium, and were monitored using 24-hour video-EEG. Surface ECG and EEG signals, amongst others were measured in parallel. In total, 35 patients were monitored and 80 seizures were identified. The onset of the seizures was annotated based on EEG and video, by two different EEG specialists. Of the 80 seizures, 40 were of focal nature and 40 were generalized. Half of the focal seizures (20) originated from the frontal lobe and the other half from the temporal lobe. The generalized seizures were tonic, tonic-clonic, or myoclonic.

The ECG signals were measured with a sampling frequency of 250Hz, and 80 segments of 5 minutes were ex-

tracted starting 3 minutes before the onset of the seizures in the EEG. These 80 ECG segments make up the dataset used in this study.

3. Methodology

The methodology implemented in this paper consists of three different phases. Firstly, the ECG signals were preprocessed and the R-peaks were identified. Secondly, different signals and features were extracted from the ECG. Lastly, supervised and unsupervised learning techniques were implemented in order to detect the onset of the seizures.

3.1. Preprocessing and R-peak detection

Initially, the power line interference in the ECG was reduced using a notch filter at 50Hz. Next, the R-peaks were detected using the Pan-Tompkins algorithm. Then, automatic correction for ectopic and missing beats was done by means of the search back procedure presented in [7]. Finally, visual verification of the position of the R-peaks was performed.

3.2. Signals and features

Once the R-peaks were detected, 6 signals were computed from the ECG. The first one corresponds to the RR interval time series, which is computed from the time differences between consecutive R-peaks. The other 5 signals were obtained after implementing the procedure described below, and outlined in Figure 1. This procedure was inspired by the derivation of the respiratory signal from the ECG presented in [8].

a) A window of 40ms (m samples) before and after each R-peak is selected in order to capture the QRS-complexes.
b) Five ($n = 5$) consecutive QRS complexes are assembled into one *QRS*-matrix $X \in \mathbb{R}^{n \times m}$, and aligned with respect to the R-peaks.
c) Principal component analysis (PCA) is performed on X, and the first five highest eigenvalues are selected as the new set of parameters.
d) Shift one heart beat and repeat the algorithm until the end of the ECG segment.

After this procedure, the evolution of the first five highest eigenvalues is obtained with a resolution of 5 heart beats. These 5 signals, together with the RR interval time series, are unevenly sampled, hence, each one is resampled to 2Hz using cubic spline interpolation. Then, they are normalized, and segmented into epochs of 5 seconds, and the mean value is computed for each epoch. This results in a new vector $\mathbf{f}_{ij} = [\bar{RR}_j; \bar{\lambda}_{1j}; \bar{\lambda}_{2j}; \bar{\lambda}_{3j}; \bar{\lambda}_{4j}; \bar{\lambda}_{5j}]$, with $i = 1, \ldots, 80$ and $j = 1, \ldots, 60$, that characterizes each epoch of 5 seconds. In other words, each ECG segment of 5 minutes is characterized by 60 vectors of length 6.

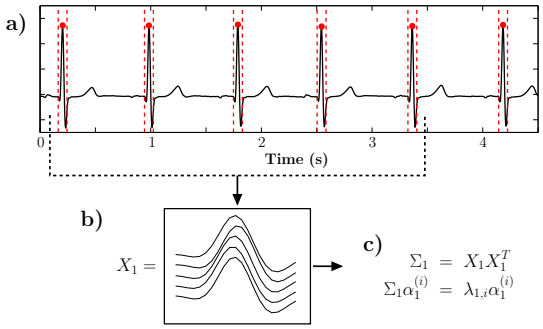

Figure 1. Procedure to construct the *QRS*-matrix, and derive the first five highest eigenvalues $\lambda_{1,i}$ of the matrix X_1, where $i = 1, \ldots, 5$. The window of 5 heart beats is shifted throughout the whole ECG segment and the evolution of the eigenvalues $\lambda_{j,i}$, where $j = 1, \ldots, n$ and n the total number of heart beats in the segment minus one, is obtained.

3.3. Seizure detection

The main goal is to detect the moment when the heart rate and the morphology of the ECG change, using the feature vectors computed in the previous step. To do this, three different algorithms were implemented, namely, a simple threshold, k-means, and kernel spectral clustering (KSC) [9]. The thresholds were defined for each feature separately, as the 25th and 75th percentiles of the first 2 minutes, which were considered to be free of seizures. An epoch of 5s was considered as seizure when the eigenvalues were larger than the 75th percentile, or when the mean RR was lower than the 25th percentile. For k-means and KSC the number of clusters was set to 2, and then characterized as seizure or normal.

The training set for the three different approaches consisted of 40 segments, 20 of focal and 20 of generalized nature, selected at random.

4. Results and discussion

After preprocessing the ECG segments and detecting the R-peaks, 11 segments were identified as containing artefacts around 180s. Of these 11 segments, 9 correspond to the generalized group. This can be related to motor involvement during the seizure. Manual correction of these segments was performed, but for most of the cases it was not possible to assess the location of the R-peaks. For this reason, it is important to keep in mind that EMG artefacts must be removed from the ECG before any seizure analysis. This was not done in this study but should be consid-

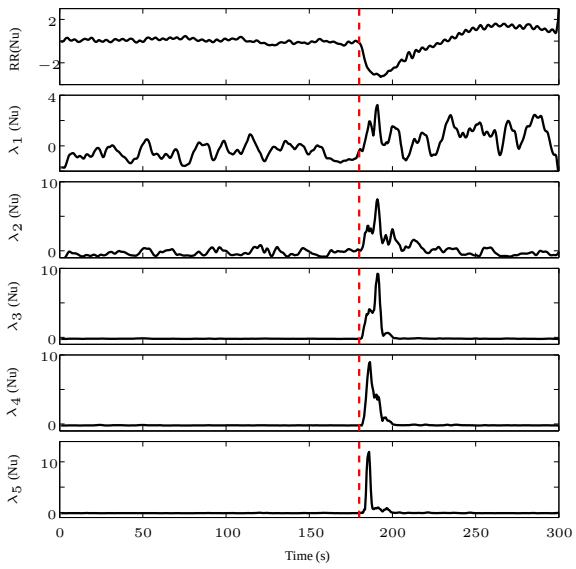

Figure 2. Signals derived from the ECG after R-peak detection. The first one corresponds to the RR interval time series, and the other 5 indicate the evolution of the eigenvalues throughout the ECG segment. The dashed lines indicate the EEG onset of the seizure at 180s.

ered in future studies.

Once the position of the R-peaks was manually corrected, the eigenvalue signals and the RR interval time series were computed for each ECG segment separately. Figure 2 shows an example of these 6 signals for a given segment. Note that the onset of the seizure, around 180s is clearly visible in the RR series and in the different eigenvalues. However, changes around the onset of the seizure (dashed line) are more visible in RR and λ_{3-5}. The reason for this is that the first components (λ_1, λ_2) are more affected by the respiratory modulation, as discussed in [8], and the other components become more relevant when the morphology of the QRS complex becomes more heterogeneous. In other words, the complexity of the QRS cannot be described only by the first two components.

The extracted signals were then segmented into epochs of 5 seconds, and each epoch j was characterized by the vector $\mathbf{f}_{ij}$, with $i = 1, \ldots, 80$. These epochs were first classified as being *normal* or containing a *seizure* by means of the threshold defined as the 75th percentile of the first 2 minutes in all training segments. The training set included seizures of all types. Figure 3 shows this threshold for λ_5, together with the 25th, 50th, and 75th percentiles of all epochs. A distinction is made between different types of seizures, where it is clear that the partial seizures are easier to detect by means of a simple threshold.

In addition to the classifier, k-means and KSC were trained with the same set used in the threshold definition,

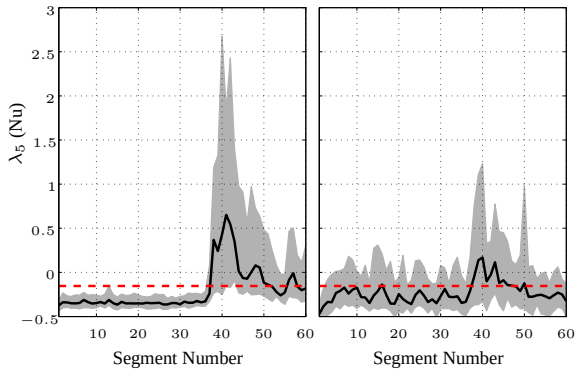

Figure 3. Threshold for λ_5. Nu stands for normalized units. The shaded area indicates the 75th and 25th percentile per segment of 5 seconds. The median values are indicated by the solid line, and the dashed line corresponds to the threshold used for classification. A distinction between partial (left) and generalized (right) seizures is done. Note that in partial seizures, most of the segments around 200s (segment 40) lie above the threshold.

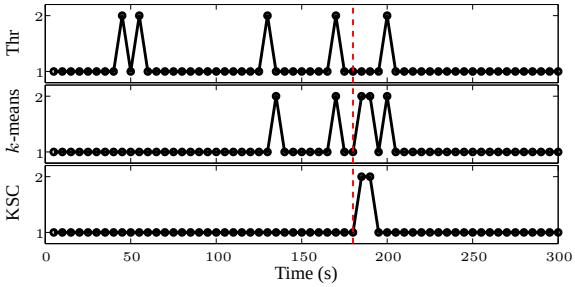

Figure 4. Labels for each segment of 5 seconds after classification using threshold (top), clustering using k-means (middle), and KSC (bottom). The dashed line indicates the EEG onset. Note that cluster number 2 can be associated to seizure onsets.

and the number of clusters was set to 2. Each cluster was then manually characterized as containing seizure onsets or normal segments. Figure 4 indicates an example of cluster identifiers for each approach. It is observed that cluster 2 may contain onsets of seizures.

As mentioned before, not all the eigenvalue signals indicate a clear change around the seizures. Therefore, the three different seizure detection approaches were implemented on different sets of features, and the best results were obtained with the following parameters: $\hat{\mathbf{f}} = [\bar{RR}; \bar{\lambda}_3; \bar{\lambda}_4; \bar{\lambda}_5]$. Table 1 indicates the results for each approach and each type of seizures. From the table it is clear that kernel spectral clustering (KSC) detects 85% of the partial seizures, and only 57% of the generalized ones. If all the segments corresponding to generalized seizures that contain EMG artefacts are removed (24 out of 40), the PPV

increases to 87%. It is important to remember that the generalized seizures used in this study involve motor activity, which implies the presence of EMG artefacts on the ECG. These artefacts reduce the reliability of the R-peak detection, and seizure detection algorithms. For this reason, the ECG should be cleaned from EMG artefacts, and different features derived from signals like EMG and/or accelerometers should be used to complement this study.

Taking the results of KSC, for both types of seizures, about 75% of the changes in the ECG were lagging the onset in the EEG, while the rest was leading or simultaneous. The detection window for partial seizures was 7.4 ± 14.3 seconds, and for generalized 9.6 ± 20.5 seconds.

These results are in accordance with previous studies [2] where the PPV for partial seizures was larger than 80%. It is important to remember that the methodologies used in [2, 6] study the full ECG segment in order to find the best curve fitting, and the exact seizure onset. However, the methodology proposed in this paper uses a window of 5 seconds, hence, the detection of the seizure will be done with at least 5s delay.

Table 1. Seizure detection results.

Seizures	Approach	TP	FP	PPV
Partial	Thr	37	11	77%
	k-means	36	15	70.5%
	KSC	**36**	**6**	**85.7%**
Generalized	Thr	32	32	50%
	k-means	38	42	47.5%
	KSC	35	26	57.3%

5. Conclusion

The methodology proposed in this paper can be used to improve monitoring systems for detection of epileptic seizures. It can complement other approaches such as those based on accelerometers and EMG. Furthermore, it has an added value in the fact that it can be used online, because the features are easily computable, and only 5 second windows are needed for the analysis. An important consideration is that the ECG needs to be cleaned from EMG artefacts in order to be able to detect seizures with motor involvement, as it is the case for the generalized seizures used in this work and some partial seizures involving the frontal lobe.

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