Detection of epileptic seizures from single lead ECG by means of phase rectified signal averaging*

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***Abstract*— Epileptic seizures have a clear effect on the regulatory mechanisms of the autonomic nervous system, especially on the cardiac and respiratory controls. Changes in heart rate and respiration are well known to occur around the onset of the seizure. This paper studies the ECG signals recorded from patients suffering from epilepsy, whose ages ranged from 3 to 48 years. Both focal and generalized seizures are considered. Changes in cardiorespiratory control and coupling, are assessed using phase rectified signal averaging (PRSA), and a positive predictive value (PPV) of 86.21% was obtained for focal seizures, and of 84.3% for generalized seizures.**

I. INTRODUCTION

Epilepsy is known to deeply affect the cardiac function and the control mechanisms of the autonomic nervous system [1], [2]. Different algorithms have been proposed to detect epileptic seizures using single-lead ECG [3], [4]. Most of the algorithms exploit the fact that the heart rate variability (HRV) is significantly reduced during seizures, and the heart rate (HR) might increase even before the EEG onset is observed. These changes in HR are considered to be a pre-ictal (immediately before the seizure onset) autonomic symptom in epilepsy. However, these changes are not only due to the involvement of the central autonomic centers during seizures, but they can also be caused by motor activity or by a stress response to the seizure [2]. A different effect of epilepsy was observed in [1], where it was reported that epileptic seizures can be accompanied by apnea episodes, especially when the onset is localized in one of the temporal lobes.

Keeping in mind these previously reported autonomic effects, it is expected that changes in cardiorespiratory coupling also occur around the seizure onset. In order to determine whether this is the case, and if a complete decoupling can be detected at the seizure onset, this paper proposes a detection algorithm based on phase rectified signal averaging (PRSA). PRSA was originally proposed in [5], as a method to detect quasi-periodicities in non-stationary data. Later, in [6], PRSA was used in the context of autonomic assessment and cardiovascular risk. An extension to a bivariate version (BPRSA) was proposed in [7], and it was implemented to analyze the interactions between respiration and heart rate.

In this study, both the PRSA and BPRSA version are implemented on the RR-interval time series (*RRI*) and the ECG derived respiratory signal (*EDR*). The coupling between these two signals is assessed using BPRSA, and the quasi-periodicities in the heart rate are quantified using PRSA on the *RRI* series. Different types of seizures are considered, namely, focal seizures with onset in the frontal lobe or in one of the temporal lobes, and generalized seizures. In addition, both childhood and adult epilepsy are considered. The biggest challenge is to detect generalized seizures, especially those with deep motor involvement, and with no obvious effect in HR.

II. METHODS

A. Data

In this study, two datasets of single-lead ECG recordings, extracted from continuous video-EEG monitoring of patients suffering from epileptic seizures, are used. The first dataset was collected in the epilepsy clinic of UZ Leuven, Belgium, and it contains 80 seizures recorded from 35 children suffering from refractory epilepsy. The mean age of the patients was 9.2 years (range 3-16 years). The onset of the seizures was annotated by two different EEG specialists, based on video and EEG. Two types of seizures were recorded: 40 with focal onset and 40 with generalized onset. Twenty of the focal seizures were originated from the frontal lobe and the other 20 were originated from the temporal lobes. Additionally, 11 of the generalized seizures were myoclonic. Once the seizures were identified, a 5 min ECG segment was extracted, starting 3 minutes before the EEG onset of the seizure. The sampling frequency was 250Hz.

The second dataset used in this study is the *Post-Ictal Heart Rate Oscillations in Partial Epilepsy*[8], which contains 10 partial seizures and is publicly available in the Physionet *databank* [9]. This set consists of 7 ECG recordings, extracted from video-EEG monitoring of 5 women whose age ranged from 31 to 48 years, and who were suffering from epilepsy. All the seizures contained in this dataset were of focal nature with or without secondary generalization. The ECG signals were sampled at 200 Hz, and their duration

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ranged from 1h30m up to 3h45m. This dataset is used in order to test the algorithm on long term ECG recordings.

From each ECG signal/segment, the RR-interval time series (*RRI*) and the ECG derived respiration (*EDR*) are computed. The Rpeaks are detected by means of the Pan-Tompkins algorithm, and all missing beats are corrected using a search back procedure as in [4]. The EDR signal is computed using kernel principal component analysis (kPCA) [10].

B. Phase rectified signal averaging

Phase rectified signal averaging (PRSA) [5] is able to detect quasi-periodicities in non-stationary signals like the *RRI*, in the presence of noise and artefacts. This is done after reducing a given time series $\mathbf{x} = \{x_i\}_{i=1}^{N}$ to a shorter sequence $\mathbf{x}' = \{x'_j\}_{j=-L}^{L}$, with $x, x' \in \mathbb{R}$, and $L < N$. The shorter sequence $\mathbf{x}'$ of length K is computed following the three steps represented in Fig. 1, and described as follows.

1. Given is the *RRI* series represented by $\mathbf{x}$. The anchor points (AP) are selected based on the condition $x_i < x_{i-1}$. These anchor points correspond to accelerations of the heart. Different conditions for the selection of AP can be used [5], however, in this study only the pre-ictal tachycardia, on a beat-to-beat basis, is considered.

2. A window of length $2L$ is defined around each AP. The AP that are at the border of the time series, and are not surrounded by a window of length $2L$ are discarded. A total of M anchor points remains. Note that most of the windows will overlap because most of the points in the time series are selected as AP. This becomes relevant when defining the parameter L, which should take into account the lower frequency one wants to detect. Since the presence of quasi-periodicities around epileptic seizures is currently unknown, this study aims to find an optimal value for L that can reveal important information before, during and after the ictal period.

3. An average curve $\mathbf{x}'$ is computed over all M windows. This curve now contains information of quasi-periodicities related to increases in heart rate. In other words, every time the heart is accelerated, this curve will provide information about autonomic responses and coherence in the *RRI* signal. Besides, it is also possible to see what happens after an increase in heart rate, and how long it takes for the heart to react to these accelerations.

The last three steps briefly described the general procedure to compute the PRSA curve of segments of heart rate, where the *RRI* is used as a trigger and a target simultaneously. However, a different approach can be considered, namely, the bivariate version BPRSA [11]. This approach can be used to study the interaction between two simultaneous time series. In this work, this is used to find inter-relations between the *EDR* signal, which is an estimation of the respiration, and the heart rate. Here, the anchor points are defined as decreases in the respiration $y_i < y_{i-1}$, with $\mathbf{y} = \{y_i\}_{i=1}^{N}$ representing the *EDR*. The reason to select decreases in the respiratory activity as AP, is due to the presence of apnea episodes during partial seizures [1]. In addition, other studies have shown that a reduction in respiratory rate might be associated with seizures, especially with those originated from the temporal lobe [1][2]. These changes in respiratory rate can be also detected from x'. Once the AP are identified in the *EDR*, M windows are selected from *RRI*.

C. Continuous detection of epileptic seizures

In order to perform *online* detection of epileptic seizures, a moving window of 80 heart beats with an overlap of 79 beats, is used to analyze the *RRI* and *EDR* signals. The length of the moving window was determined experimentally, as the length that allows to better differentiate between normal and pre-ictal/ictal activity. Each pair of signals is then used to extract two different PRSA curves, one where the *RRI* is used as trigger and target simultaneously, and one where the *EDR* triggers the *RRI*. This procedure is repeated every time a new heart beat is detected (see Fig. 1).

Different parameters can be used to quantify the PRSA curves [12]. For example, the slopes of the lines connecting the point before and the point after the AP in the PRSA curves. These features will be denoted as S_{RR} and S_{Resp} for the PRSA derived using only the *RRI* and using both the *EDR* and the *RRI*, respectively. These slopes will give an indication on how fast the heart reacts to accelerations, and how the reduction in respiratory amplitude is related to changes in the HRV on a beat-to-beat basis. In this study, it is hypothesized that during epileptic seizures, these reaction times will be affected due to sympathetic activations, or due to the involvement of the cardiorespiratory controls during the seizure. Besides, it is expected that the coherence times within the signal change due to the significant changes in HRV.

Once each PRSA curve is quantified, kernel spectral clustering (KSC) [13] is used to group events of different types. These groups are then labeled, and the cluster containing the epileptic seizures is identified using the position of the seizure onset in the EEG. The reason to use an unsupervised learning technique is that the labels are only known for the EEG signal, and early or late responses in the ECG are expected.

III. RESULTS AND DISCUSSION

All experiments were carried out in MATLAB R2012a on an Intel® Core™ i7, 3.4GHz, 7.8 GB RAM, running Ubuntu 12.04 LTS.

The dataset collected in UZ Leuven, was first used to train the learning algorithm, and to determine the features that best differentiate between normal and pre-ictal/ictal activity. Each ECG segment of 5 minutes was analyzed using the moving window of 80 heart beats as described above, and two PRSA curves were obtained for each heart beat. The parameter L was set to 20. This value was selected experimentally, as the length that allows to see changes in coherence times within the signal. Fig. 2 shows an example of a focal seizure originated from the temporal lobe, where clear changes in heart rate can be observed. These changes in temporal lobe seizures have already been reported in the literature [1][2].

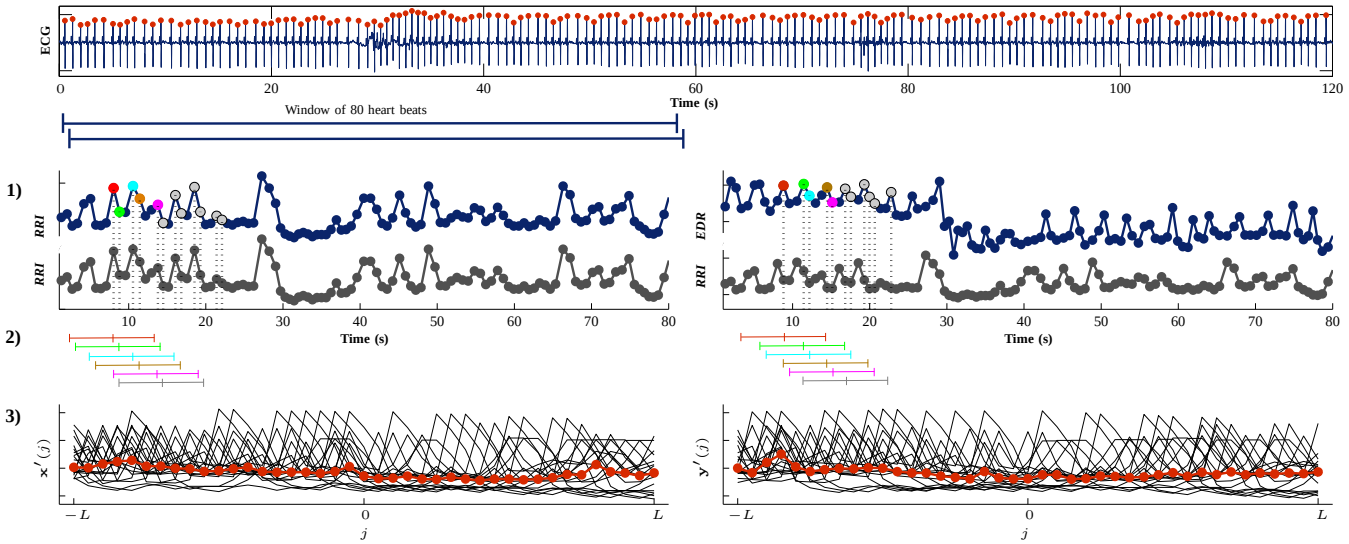


Fig. 1. Computation of the PRSA curves. A window of 80 heart beats in the ECG is used for the analysis. From each window two signals are computed namely *RRI* and *EDR*. 1) Selection of anchor points in the trigger signal *RRI* (left) and *EDR* (right). The first 12 AP are indicated. 2) Segmentation of the target signal *RRI*, using a window of length 2L around each anchor point. 3) Phase rectification and signal averaging of all extracted segments around AP. The average PRSA curves are indicated in red.

However, in this study changes in cardiorespiratory coupling around the seizures, were also observed and quantified.

One PRSA curve was computed for each new heart beat, and as can be seen from the bottom panels of Fig. 2, the shape of the curves changes around the seizure onset. Note that the time reversal symmetry of the curves around the anchor points ($j = 0$) is completely broken as the variability of the heart rate (HRV) is reduced. These changes in symmetry cannot be detected by any power spectral analysis [6], which makes PRSA a very powerful technique in this application. An important fact here is that the coherence time of the signal also changes. For instance, when the *RRI* starts to decrease dramatically, and the analyzed segment includes both pre-ictal and ictal periods, the predictive power of the signal is reduced. These changes are linked to the reduced standard deviation of the HR during seizures [2], [1], which on its turn can be explained by the propagation of the seizures to the central autonomic network [2]. An important contribution of this work is that these changes in coherence time and symmetry, proper of seizures, can be quantified using the slope of the line connecting the furthest points to the AP of both PRSA curves, $\Delta_{RR} = x'_L - x'_{-L}$, and $\Delta_{Res} = y'_L - y'_{-L}$, for $PRSA_{RR}$ and $PRSA_{Res}$ respectively. The panels in the 2^{nd} and 3^{rd} rows of Fig. 3 show these changes. In addition, this can also be quantified using the first point of the PRSA curves, namely, x'^k_{-L}, with $k = 1, 2, \ldots, M$, and M the total number of windows of 80 heart beats. This parameter indicates if the quasi-periodicities have already decayed or not when looking L heart beats in the past of the averaged AP. For normal activity, the values of x'^k_{-L} should be close to zero as seen in Fig. 3, 4^{th} row.

Another feature that varies around the seizure onset is the slope S_{RR} of the line connecting the point before x'_{-1} and the point after x'_1 the AP of the PRSA derived using *RRI* as target and trigger signals. Fig. 3, 2^{nd} row, show how

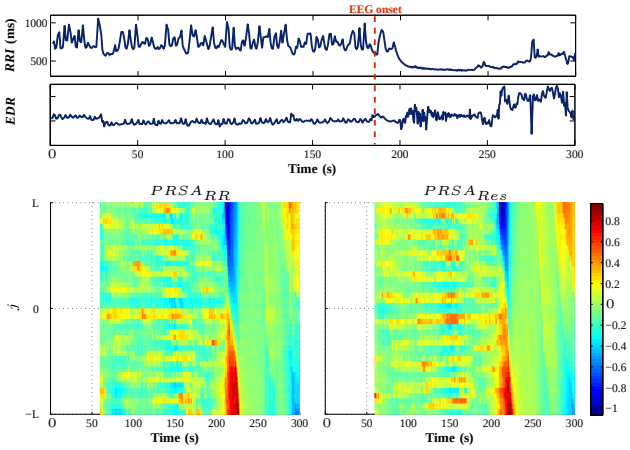


Fig. 2. (*top*) *RRI* and *EDR* signals. Note that the heart rate and respiration are significantly perturbed around the seizure onset. The PRSA curves are indicated in the lower panels, and it is important to keep in mind that the first 80 heart beats were used to compute the curves at the position of the 80^{th} R-peak. It is clear that the perturbations of the heart rate and respiration are captured by the dynamics of the PRSA curves around the EEG onset.

this slope becomes less negative during the ocurrence of the seizure. The reason for this is, again, the reduced variability of the heart rate during this period.

The four features described above were used to characterize each heart beat, and KSC was then implemented to group them into clusters containing similar activity. The algorithm was trained using 40 seizures, 20 focal and 20 generalized (no myoclonic included), and the other 40 were used as validation. It is important to keep in mind that KSC is an unsupervised learning algorithm, so no labels were used in training and validation. The optimal number of clusters and the optimal kernel parameter were selected using the balance line fit criterion described in [13]. The optimal number of clusters was found to be 3, and after analyzing each cluster separately, it was found that cluster number

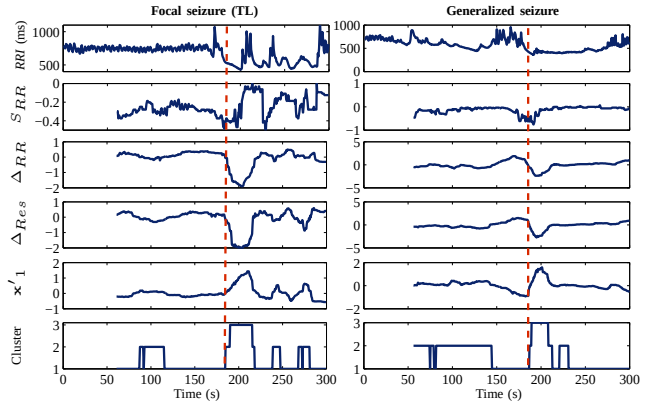


Fig. 3. Features extracted from the PRSA curves of a focal seizure originated in the left temporal lobe (*left*), and a generalized seizure (*right*). *From top to bottom*: RR-Interval time series; slope S_{RR} of the line connecting the point before x'_{-1} and the point after x'_1 the AP of $\mathbf{x}'$; Difference between the furthest points to the AP of both PRSA curves, $\Delta_{RR} = x'_L - x'_{-L}$, and $\Delta_{Res} = y'_L - y'_{-L}$; Variation of x'^k_1 as a function of time; and cluster memberships, where cluster 3 contains the epileptic seizures.

TABLE I

SEIZURE DETECTION RESULTS.

Dataset	Seizures	TP	FP	PPV
UZ Leuven	Focal	40	4	86.9%
	Generalized	27	5	84.3%
Physionet	Partial(Focal)	10	4	71.4%

3 contained most of the seizures of the whole set. The panels of the last row in Fig. 3 show the cluster membership as a function of time, and Table I indicates the positive predictive value (PPV) for each type of seizure. In order to determine the amount of TP, a window of 30s before and after the EEG onset was used. It is not a surprise that the results for generalized seizures are affected by myoclonic seizures, since they are brief, normally lasting no more than 2 seconds, and more importantly, they manifest themselves as rapid contraction/relaxation of a muscle. This implies motor involvement and very short changes (<2s). For this reason, the detection of these seizures remains a challenge. However, 9 of the 11 myoclonic seizures were detected, but 6 false positives were also included (PPV=60%). If these seizures are included in the generalized results, the total PPV was reduced to 76.5%. Therefore, other modalities like EMG or accelerometer data should be included in the analysis of myoclonic seizures. The results obtained for this dataset were compared with those reported in [4], which were obtained from the same dataset. Here an improvement in the PPV is achieved for both types of seizures, but what is more remarkable is that the algorithm proposed here reduces the amount of false positives by more than 50% for the generalized seizures.

After training and validating the KSC algorithm using the UZ Leuven, the resulting model was applied to the Physionet dataset. The PPV obtained for these partial seizures in adult epilepsy are indicated in Table I. Note that the model was trained in a completely different dataset, and still the algorithm is capable to detect all the seizures, and produce a relatively high PPV. A total PPV for focal seizures, including both datasets is 86.21%.

IV. CONCLUSION

The algorithm presented in this paper allows to detect epileptic seizures with PPV of more than 80%, in a window of 30s around the EEG onset . More importantly, this methodology is able to detect *both* focal and generalized seizures with a comparable positive predictive value, which until now was not achieved by any other algorithm. Another advantage of this algorithm is that it is easy to implement, and can be adapted to home monitoring systems, or online detection systems. These findings represent an important contribution to the development of closed-loop systems, where the aim is to abort epileptic seizures. However, it is important to consider training and validating the algorithm for each type of seizures, and to include different sources of data to be able to improve the performance for seizures with motor involvement.

REFERENCES

[1] M. E. O'Regan, J. K. Brown, Abnormalities in cardiac and respiratory function observed during seizures in childhood. Developmental Medicine and Child Neurology, vol. 47, pp. 4-9, 2005.

[2] K. Jansen, C. Varon, S. Van Huffel, L. Lagae, Ictal and interictal respiratory changes in temporal lobe and absence epilepsy in childhood. Epilepsy research, vol. 106, pp. 410-416, 2013.

[3] F. Leutmezer, C. Schernthaner, S. Lurger, K. Ptzelberger, C. Baumgartner, Electrocardiographic changes at the onset of epileptic seizures. Epilepsia, vol. 44, pp. 348-354, 2003.

[4] C. Varon, K. Jansen, L. Lagae, S. Van Huffel., Detection of epileptic seizures by means of morphological changes in the ECG. In Computing in Cardiology Conference (CinC 2013), IEEE, pp. 863-866, 2013.

[5] A. Bauer, J. W. Kantelhardt, A. Bunde, P. Barthel, R. Schneider, M. Malik, G. Schmidt, Phase-rectified signal averaging detects quasi-periodicities in non-stationary data. Physica A, vol. 364, pp. 423-434, 2006.

[6] J. W. Kantelhardt, A. Bauer, A. Y. Schumann, P. Barthel, R. Schneider, M. Malik, G. Schmidt, Phase-rectified signal averaging for the detection of quasi-periodicities and the prediction of cardiovascular risk. Chaos, vol. 17, 015112, 2007.

[7] A. Bauer, P. Barthel, A. Mller, J. Kantelhardt, G. Schmidt, Bivariate phase-rectified signal averaging-a novel technique for cross-correlation analysis in noisy nonstationary signals. Journal of Electrocardiology, vol. 42, pp. 602606, 2009.

[8] I. C. Al-Aweel, K. B. Krishnamurthy, J. M. Hausdorff, J. E. Mietus, J. R. Ives, A. S. Blum, D. L. Schomer, A. L. Goldberger, Post-Ictal Heart Rate Oscillations in Partial Epilepsy. Neurology, vol. 53(7), pp. 1590-1592, 1999.

[9] A. L. Goldberger, L. A. N. Amaral, L. Glass, J. M. Hausdorff, P. Ch. Ivanov, R. G. Mark, J. E. Mietus, G. B. Moody, C-K. Peng, H. E. Stanley, PhysioBank, PhysioToolkit, and PhysioNet: Components of a New Research Resource for Complex Physiologic Signals. Circulation vol. 101(23):e215-e220, 2000.

[10] D. Widjaja, C. Varon, A. Caicedo Dorado, J. A. K. Suykens, and S. Van Huffel, "Application of kernel principal component analysis for single lead ECG-derived respiration", *IEEE Trans. Biomed. Eng.*, vol. 59, pp. 1169–1176, 2012.

[11] A. Y. Schumanna, J. W. Kantelhardt, A. Bauer, G. Schmidt, Bivariate phase-rectified signal averaging. Physica A, vol. 387, pp. 5091-5100, 2008.

[12] E. A. Huhn, S. Lobmaier, T. Fischer, R. Schneider, A. Bauer, K. T. Schneider, G. Schmidt, New computerized fetal heart rate analysis for surveillance of intrauterine growth restriction. Prenat. Diagn, vol. 31, pp. 509-514, 2011.

[13] C. Alzate, J. A. K. Suykens, Multiway Spectral Clustering with Out-of-Sample Extensions through Weighted Kernel PCA. IEEE Trans Pattern Analysis and Machine Intelligence, vol. 32, pp. 335-347, 2010.