On the viability of ECG features for seizure anticipation on long-term data

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***Abstract*— Besides the evident brain state alterations present in electroencephalogram (EEG), epileptic seizures are also associated with changes in the cardiovascular status. In particular, heart rate (HR) has become an important autonomic biomarker in seizure prediction. Based on that, a preliminary study is here proposed in order to inspect the behaviour of electrocardiogram (ECG) derived features in the period preceding epileptic seizures. The study took place using data from 1275 seizures collected from a set of 167 patients available in EPILEPSIAE database. The analysis was conducted considering three different variables: seizure type, seizure hour onset and vigilance state.**

The results did not reveal a clear effect of any of the three variables, assessed individually, in entire seizure set. Nevertheless, some evidence has been found that, for some seizures, it was possible to detected a consistent pattern of increase/decrease in feature magnitude before the onset. These patterns were revealed using the mean of RR intervals and the mean of the number of beats per minute.

***Keywords*—epilepsy; seizure; anticipation; electrocardiogram.**

I. Introduction

The management of refractory epileptic patients requires systems able to provide warning before seizures onset to the patients during their everyday life.

The vast majority of epileptic seizure prediction studies available in literature has been proposed using information from electroencephalogram (EEG), which is composed of a mixture of different cerebral activities. Due to EEG complexity no mathematically sensible features to the pre-seizure period were developed until now [1], [2]. In recent years, however, a great focus has been put in other seizure extracerebral manifestations including the often reported changes in the cardiovascular status. In fact, the autonomic function is affected during seizures, subsequently triggering the parasympathetic and sympathetic system responses which in turn will be responsible for modulation of cardiac parameters such as heart rate and blood pressure [3], [4], [5]. An increase in heart rate (HR) and blood pressure, possible occurrence of tachycardia, atrio-ventricular conduction and ventricular excitability are the result of the sympathetic nervous activity. On the other hand, the effect of the parasympathetic response can be detected when there is a decrease in the heart rate and blood pressure [4], [5], [6], [7], [8].

HR was reported to increase during seizures, being typically associated with high variability regarding its magnitude, velocity and duration depending for example on the vigilance state (sleep versus awake) [3]. In face of these observations, new studies were proposed addressing the differences in HR across the periods preceding, during and after the seizure [4], [9]. Results from 30 refractory epilepsy patients have shown statistically significant differences among different seizure stages [9]. Furthermore, HR variations related to the occurrence of epileptic seizures, besides the vigilance state, can also be influenced by other aspects such as the type of epilepsy, location of seizure onset, seizure type, patients' age and gender and time to diagnosis [3], [10].

Apart from the refereed HR variations, the morphology of the electrocardiogam (ECG) also depicts changes that typically occur before the EEG onset, making the former useful for seizure early detection [5], [11]. For example, it was observed that the QT interval diminished during the early post-ictal period in patients diagnosed with refractory epilepsy whereas in the pre-ictal phase, a T wave inversion and ST elevation or depression happened [5], [7], [11].

Varon et al. achieved a positive predictive value of 80% in a 30s window near EEG onset using HRV and also the changes in the ECG morphology, obtained from 37 patients [11]. A sensitivity of 91% and false-positive rate (FPR) of 0.7 times per hour was obtained by Fujiwara et al. using HRV features from 14 patients [12]. Behbahani et al. obtained accuracies of 86.74% and 79.41% when classifying 86 left-sided and 84 right-sided seizures, respectively, using HRV collected from 16 patiets [13].

Based on the aforementioned, the current work was developed in order to understand which variables, including seizure type, lateralization, location, among others, can contribute to discriminate between the different set of seizures identified in a specific patient and for different patients. Towards that end, information from ECG features will be analysed and interpreted in light of the metadata available, for each seizure and patient. Long-term continuous ECG data and associated metadata are provided by the European Epilepsy Database (EPILEPSIAE).

II. Material and Methods

A. Data

The study was conducted using ECG information from the European Epilepsy Database, also known as the EPILEPSIAE database (http://epilepsy-database.eu). The database

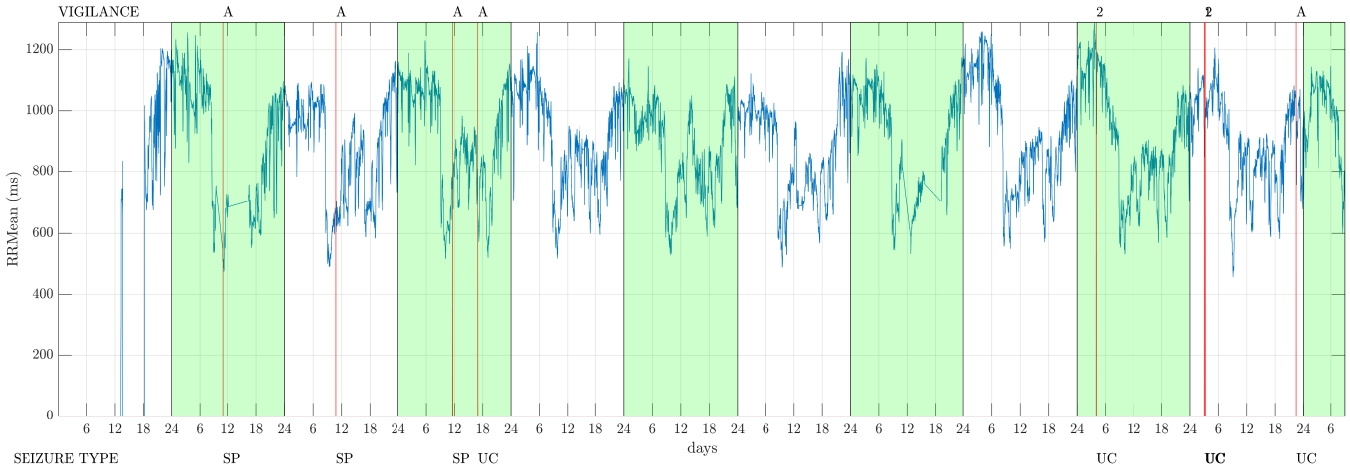

Fig. 1: RRMean feature computed for a single patient. Days are separated by different colors. Seizures are indicated in red. Information is provided regarding the seizure type (SP: simple partial seizure, UC: unclassified seizure) and the vigilance state (A: awake, 2: NonREM stage II). Seizures that are not separated by at least 240 min from the preceding seizure are not analysed.

contains long-term (165 h on average per patient) and simultaneous EEG and ECG recordings of 275 refractory epilepsy patients acquired in the epilepsy centres of the University Hospital of Freiburg, Germany, of the University Hospital of Coimbra, Portugal, and of the Hôpital de la Pitié-Salpêtrière of Paris, France [14], [15]. The majority of EEG data was acquired non-invasively (217 patients). The number of seizures per patient can go from 3 up to 94. Information about the etiology of the epileptic patient, seizure type (e.g., simple partial, complex partial, secondarily generalized), seizure localization (temporal, frontal, occipital, parietal), seizure vigilance state, and medication, among other variables is also available. Most of the recorded seizures have been doubly annotated, which means that two types of annotations are provided: electrographic changes in EEG and clinical changes detected by video-EEG analysis [14]. The results present in this work are provided by the analysis of 1275 seizures from 167 patients (accounting for 1260 days of ECG signal) having information regarding vigilance state, seizure type and seizure onset hour.

B. Methods

Time-domain features were obtained from the ECG signals using a 5-min window and a 98% overlap. The feature set comprises:

- The minimum, maximum, mean and variance of RR intervals (RRMin, RRMax, RRMean and RRVar).
- HR statistics: minimum (BPMMin), maximum (BPMMax), mean (BPMMean) and variance (BPMVar) of the number of beats per minute (BPM).
- A measure of complexity of a time series given by approximate entropy (AppEn).

Another four features were obtained from the frequency spectrum analysis of the ECG data and stand as frequency-domain measures of HRV:

- The power in the very-low-frequency (VLF) range: 0.003–0.04 cycles/interval.
- The power in the low-frequency (LF) range: 0.04–0.15 cycles/interval.
- The power in the high-frequency (HF) range: 0.15–0.4 cycles/interval.
- The ratio of the low-frequency-range power to that in the high-frequency range (LF/HF).

An example of the obtained features is depicted in Figure 1 for the RRMean, where it is possible to observe a recurrent pattern defined by an increase in average of the RR intervals during the night, which manifestly corresponds to periods when the patient is at rest.

In order to inspect the behaviour of the ECG features four hours before the seizure happens, the correlation between the ECG feature and the time sequence corresponding to that period was obtained using the Pearson correlation coefficient (as can be seen in Figure 2) and named *CorrCoef*. According to this procedure, a value of correlation is obtained for each seizure and the idea was to analyse those correlation values in light of the metadata characterizing each seizure (vigilance state, seizure type and occurrence hour). An example is depicted in Figure 3. For each seizure data, correlation is performed first for an increasing time vector and secondly for a decreasing time vector. The final value of correlation considered for that seizure will correspond to the maximum of the two correlation values. When maximum corresponds to the correlation with the decreasing time vector, the final correlation value is defined to have negative sign. in this way, it is possible to distinguish between an increase or a decreased in feature magnitude before seizure arising.

III. Results and Discussion

The analysis of the plots of the correlation between the features and the corresponding regression line for each of the 1275 seizures (take the example of Figures 3, 4 and 5) allowed us to conclude that, even though a high correlation

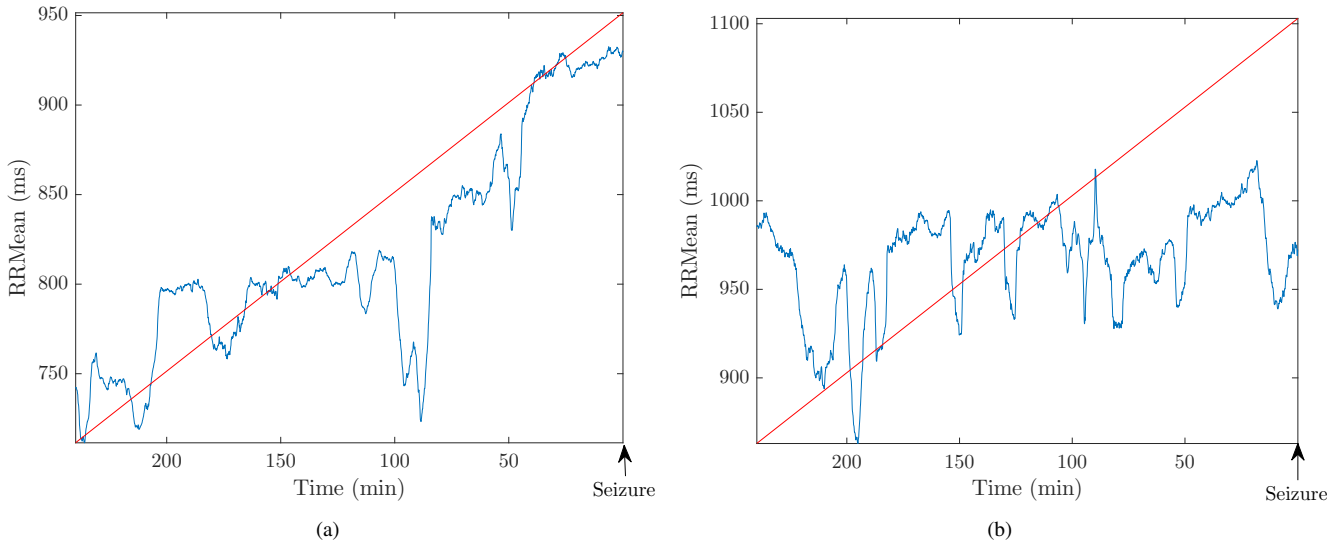

Fig. 2: (a) Example of high correlation between feature RRMean obtained from seizure 190 and the time vector, with $CorrCoef = 0.88$. (b) Example of low correlation between feature RRMean obtained from seizure 193 and the time vector, with $CorrCoef = 0.39$.

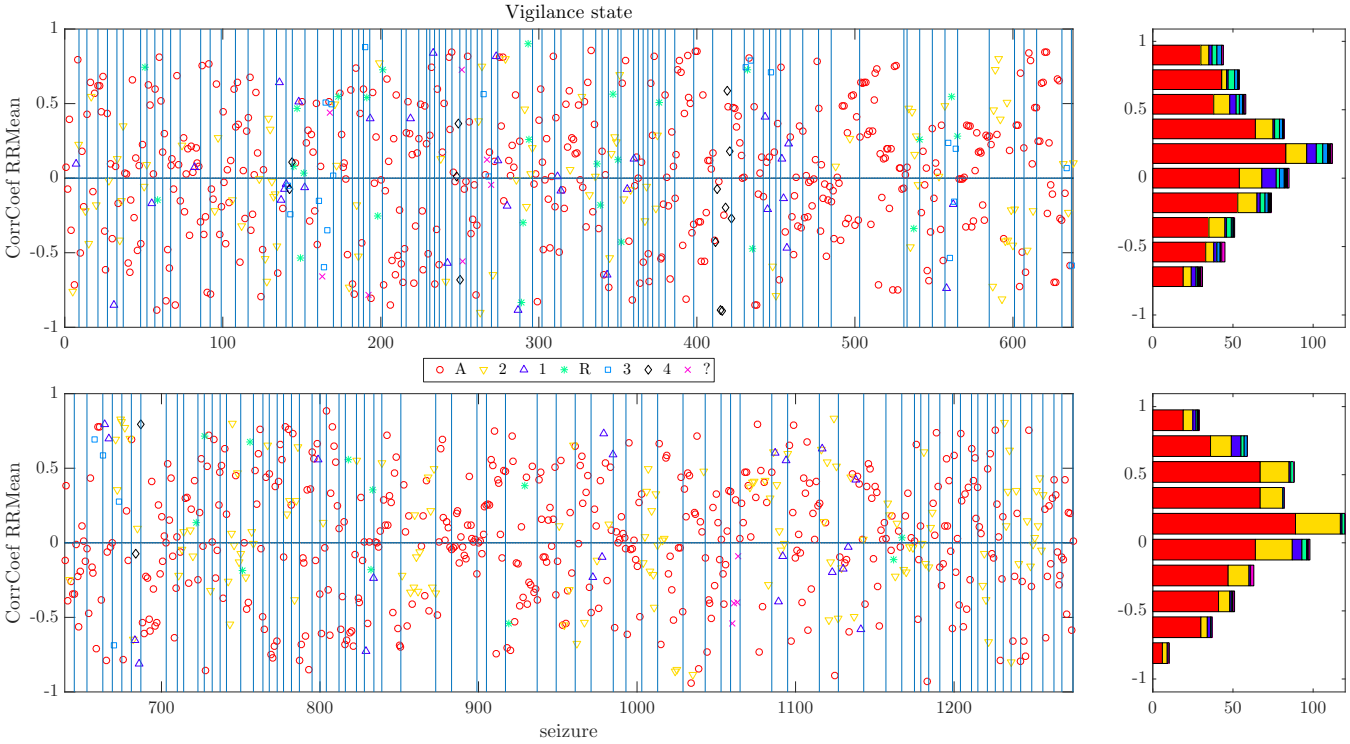

Fig. 3: Results for RRMean feature regarding the vigilance state variable. A: awake state, 2: NonREM sleep stage II, 3: NonREM sleep stage III, 4: NonREM sleep stage IV, R: REM sleep stage, ?: unknown. Results for the seizures (each point) referring to a given patient are delimited by two vertical lines.

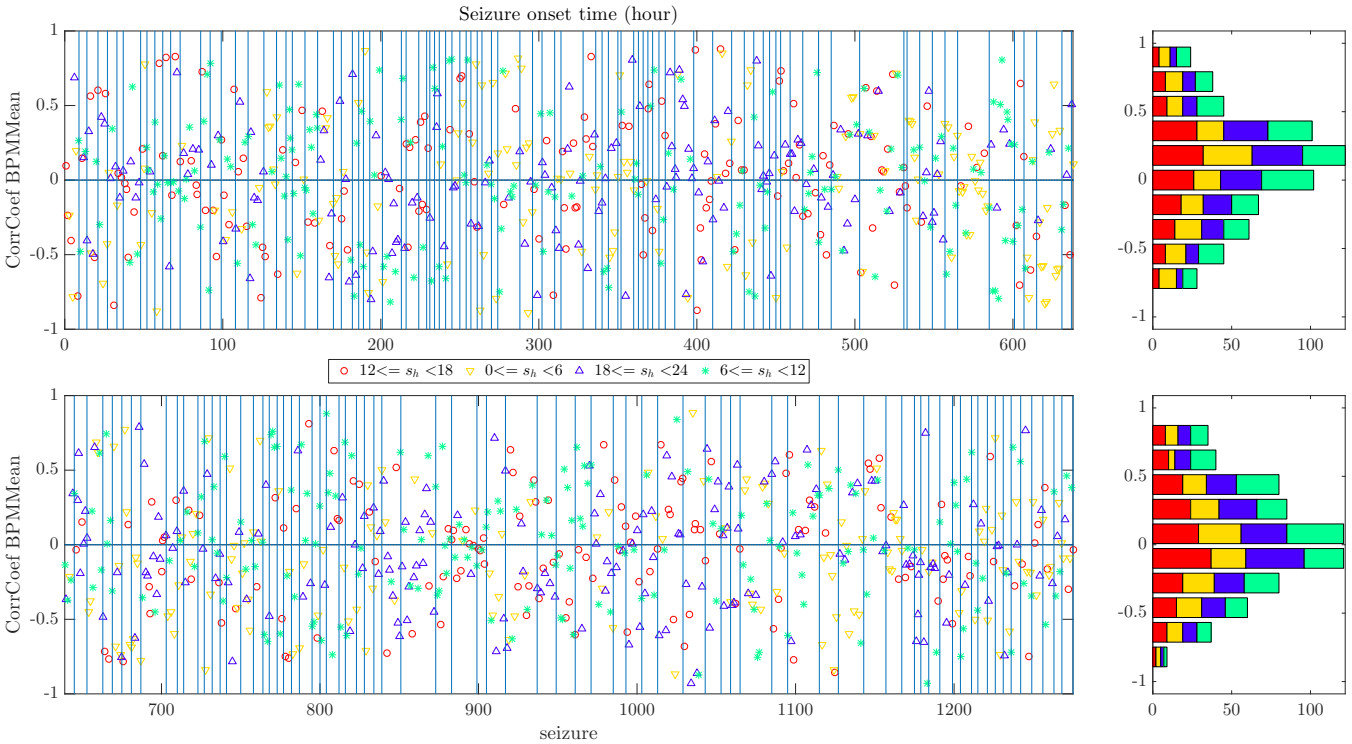

Fig. 4: Results for BPMMean feature regarding the seizure onset hour variable. Results for the seizures (each point) referring to a given patient are delimited by two vertical lines.

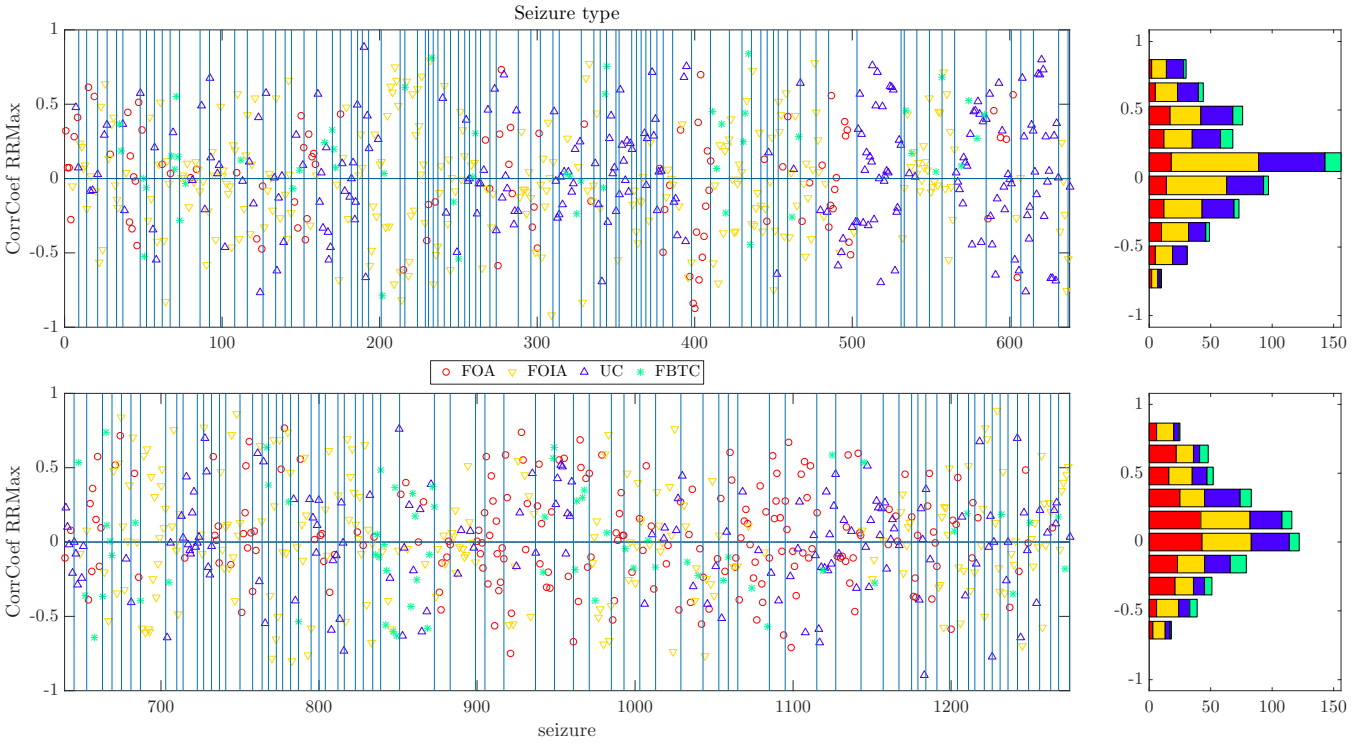

Fig. 5: Results for RRMax feature regarding the seizure type variable. FOA: focal onset aware, FOIA: focal onset impaired awareness, UC: unclassified, FBTC: focal to bilateral tonic-clonic. Results for the seizures (each point) referring to a given patient are delimited by two vertical lines.

has been obtained for some seizures that variation was not associated with a particular vigilance state, seizure onset hour or seizure type. In other words, a coherent incremental evolution (sometimes increase other times decrease) of the feature magnitude until the seizure occurrence has been noticed in only a few seizures not being associated to any of the tested variables.

However, it was possible to observe that, in general, higher values of correlation were obtained for features such as RRMax, RRMean, BPMMean and BPMMin, indicating that these features have more potential to exhibit a consistent pattern of transition from normal to seizure state.

IV. Conclusions

The present study represents a preliminary study of the potential of ECG features for seizure prediction. It was possible to observe a coherent behaviour of increasing or decreasing feature magnitude for some seizures whereas for others such pattern was not present. The variables vigilance state, seizure type and seizure occurrence hour were not specifically associated to an increase or decrease in feature magnitude as the temporal distance to the seizure diminishes. Average of RR intervals and average of the number of beats per minute were the ECG features that best described an increment/decrement in magnitude before the seizure onset. The period preceding the seizure must be extensively studied taking into account the peculiarities of seizure occurrence in a given patient and in a specific epilepsy population. To that end, more studies regarding the circumstances characterizing each seizure must be undertaken.

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