Epileptic Seizure Behaviour from the Perspective of Heart Rate Variability

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Abstract

Heart Rate Variability (HRV) analysis has gained much importance in recent years, as a technique to explore the activity of autonomic nervous system (ANS), and an important early marker for identifying different pathological conditions. Epilepsy is a disease which progressively involves cardiac autonomic activity.

Our studies indicate that time domain, frequency domain and some nonlinear measures of HRV would be able to provide valuable information regarding the autonomic dysfunction due to epileptic seizures. In this paper, we investigate the extracted features of heart rate variability for epileptic seizure detection and anticipation.

1. Introduction

The analysis of heart rate variation is becoming a powerful tool for evaluation of autonomic nervous system activities. Among the different available non-invasive techniques for assessing the autonomic status, HRV has emerged as a simple method to evaluate the sympatho-vagal balance at the sinoatrial level [1].

In normal subjects, both sympathetic and parasympathetic tone fluctuates throughout the day [2].

When vagal effects predominate, the heart rate is less than the intrinsic heart rate; when sympathetic effects predominate, the heart rate is greater than the intrinsic heart rate [2]. It is also rating dependent i.e. the HRV present higher values at lower heart rates [3].

HRV analysis has been used to investigate a variety of clinical situations including diabetic neuropathy, myocardial infarction, congestive heart failure and sudden death [1]. Abnormal non-linear HRV may predict sudden cardiac death [4].

Epileptic seizures are often accompanied by changes in various autonomic functions like heart rate (HR). HR, being measured relatively easily, may become interesting parameter for detecting epileptic seizures. Epileptic seizures affect ANS in a complex way. Changes in HR can occur prior, during or after clinical manifestations of the seizure.

Autonomic changes are common in epileptic seizures and may lead to sudden death in epileptic patients. These changes are not fully understood, but may be the result of increased motor activity, emotional distress or modulation of central autonomic circuitry [5-7].

The association between seizures and heart rate changes has been documented since thirty years ago in studies in patients with partial seizures [8, 9]. Several studies have demonstrated that HR usually increases during the seizures [5-7], but bradycardia [10] and even cardiac asystole [11] can occasionally occur during temporal lobe seizures.

In this study, we evaluated the HRV of pre-ictal phase in patients with epileptic seizures. We used time and frequency domain and nonlinear analysis to examine HRV changes during sympathetic and parasympathetic regulation in these patients.

Our long-term goal is to develop an algorithm based on ECG analysis which would be able to detect and predict epileptic seizures with high sensitivity and specificity.

Section 2 describes the data used for this study and methodological aspects related to HRV analysis. The results in a set of eight patients are presented in Section 3 and finally in Section 4 the main conclusions are drawn.

2. Methodology

2.1. Data

One lead ECG recordings of patients with pharmaco resistant focal epilepsies were compiled as part of the EPILEPSIAE project [12]. Recordings were obtained at the epilepsy units of the University Hospital of Freiburg, Germany; the Pitié-Salpêtrière Hospital of Paris, France; and the University Hospital of Coimbra, Portugal.

Patient characteristics are summarized in Table 1. Eight patients (five males and three females; mean age 37

years, SD: 17 years) affected by various kinds of epilepsy were selected for this study. In all cases EEG was recorded to confirm the seizure onset.

2.2. Time domain analysis

The HRV signals were analyzed using EPILAB; a MATLAB® toolbox, for epileptic seizure prediction that allows studying seizure prediction based on a high dimensional feature space [13]. A total of 1204 h of ECG data were collected and divided into different segments starting from three hours before the seizure onset. We analyzed the segments 180-90min, 90-30min, 30-10min, 10-5 min, and 5 -0 min before the seizure, to find changes in HRV signals. Two series of time-domain measures were extracted:

a) Mean HRV value
b) MBPM (Maximum of HRV)

2.3. Frequency domain analysis

The HRV is composed by multiple frequencies. The two main frequency components that represent ANS activity are the low frequency (LF) components (0.04 to 0.15Hz) and the high frequency (HF) components (0.15 to 0.4 Hz). Frequency domain analysis confirms that the LF and HF oscillatory components are relative indices of cardiac sympathetic and vagal activity respectively. In this research the LF/HF ratio was obtained based on frequency analysis.

2.3. Non-linear method- Poincare plot

Poincaré plots have been shown to be valuable in various studies [14]. Poincare plot analysis provides similar information to that obtained from spectral HRV analysis. However, Poincaré plot analysis is easier to use than spectral HRV as it does not need special assumptions and data filtering [15].

In HRV analysis, Poincaré plot is known as return maps or scatter plots where the current RR value (define here RR) is plotted against the following RR value. A graphical presentation of RR can be produced with SD1 as the short term variability and SD2 as the long term variability.

SD2 is defined as the standard deviation of the projection of the Poincaré plot on the line of identity ($y = x$), and SD1 is the standard deviation of projection of the Poincaré plot on the line perpendicular to the line of identity ($y = -x$) [16]. Both parameters can be defined as (1),

$$SD1 = \sqrt{\mathrm{Var}(x1)}, SD2\sqrt{\mathrm{Var}(x2)}[\mathrm{ms; ms}] \quad (1)$$

where $\mathrm{Var}(x)$ is the variance of x and

$$x_1 = \frac{\overrightarrow{RR_i} - \overrightarrow{RRi+1}}{\sqrt{2}}, x_2 = \frac{\overrightarrow{RRi} + \overrightarrow{RRi+1}}{\sqrt{2}}[\mathrm{ms; ms; ms}] \quad (2)$$

$\overrightarrow{RR_i}$ and $\overrightarrow{RR_{i+1}}$ are vectors defined as (3).

$$\overrightarrow{RR_{i+1}} = (RR_2, RR_3, \dots, RR_N)$$
$$\overrightarrow{RR_i} = (RR_1, RR_2, \dots, RR_{N-1}) \quad (3)$$

In other words, it means that x_1 and x_2 correspond to the rotation of $\overrightarrow{RR_i}$ and $\overrightarrow{RR_{i+1}}$ by $\frac{\pi}{4}\ rad$ as in (4):

$$\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} \cos\frac{\pi}{4} & -\sin\frac{\pi}{4} \\ \sin\frac{\pi}{4} & \cos\frac{\pi}{4} \end{bmatrix} \cdot \begin{bmatrix} RR_i \\ RR_{i+1} \end{bmatrix} \quad (4)$$

SD1 has been correlated with high frequency power while SD2 has been correlated with both low and high frequency powers.

In our research we want to use the combination of these two measures to form two additional Poincaré plots descriptors. These combinations are:

$S = \pi . SD1 . SD2$ and SD2/SD1 ratio.

S corresponds to the area of the ellipse fitted to the Poincaré plot, and, the ratio SD2/SD1 was defined, by analogy as LF/HF from spectral HRV analysis. There are some reasons indicate that S illustrates the total HRV and SD2/SD1 describes sympatho-vagal balance.

S and SD2/SD1, by analogy with LF/HF powers, help to derive additional information from SD1 and SD2 that is not available if these two descriptors are considered separately [16].

In this way the information obtained from Poincaré plot of HRV is richer than with SD1 and SD2 only, and similar to the one given by the spectral approach to HRV. This seems to be true for two reasons:

1) The influence of changing respiratory frequency on HRV is similarly detected by spectral and Poincaré plot analysis.
2) There are a number of significant correlations between the Poincaré plot descriptors and HRV as well as baroreflex sensitivity [16].

The highest correlation for S has been found with baroreflex sensitivity suggesting that the area of Poincaré plot represents the total variability of HRV and is under strong vagal influence [17]. SD2/SD1 is best correlated with LF/HF, which is believed to correspond to the sympatho-vagal balance [18].

It has been suggested that the SD2/SD1 ratio, which is a measure of the randomness in HRV time series, has the strongest association with mortality in adults [19]. However, the increased SD2/SD1 values over time suggest a higher level of randomness is present in HRV.

Table 1. Information of 8 studied patients

ID	Sex	Age	Sz. Type	Local. of Sz.	Number of Sz.	Recording Time (h)	Avg. Sz. Dur.(min)
1	F	2	UC	T	10	115.7	1.1
2	M	32	SG,SP,UC	T	5	169.6	1.6
3	M	42	CP,UC	T	6	93.7	1.57
4	M	52	CP,UC	T	6	260.9	1.33
5	M	51	SG,SP	T	6	118.5	2.1
6	F	46	CP,SG,UC	T	8	275.1	2.27
7	M	39	CP,SG,UC	N	9	143.2	0.8
8	F	32	CP,UC	O	9	143.3	1.8
Total					**59**	**1204**	**12.6**

- **Sz: Type of the clinical seizures; SG: Secondarily Generalized, SP: Simple Partial, CP: Complex Partial, UC: Un-Classified.**
- **Local. of Sz: Localization of seizures; T: Temporal, O: Occipital, N: Not defined.**
- **Avg. Sz. Dur. (min): Average seizure duration for each patient in minute.**

2.4. Statistical Analysis

We used ANOVA test to evaluate whether there was a significant relationship between the heart rate changes and pre-ictal phase during the event progression for each individual seizure, within each epoch. Differences were considered significant if $p<0.01$, 0.03 and 0.05.

3. Results

Time and frequency domain and nonlinear measures of HRV were computed for ECG of epileptic patients. Results of analysis are summarized in Tables 2.

It can be seen that the Mean HRV, MBPM and S (area of the ellipse) of the epochs near the seizure (5 min before) were significantly higher than those far from the seizure (180-10min before), ($p<0.05$). The significant changes for each feature are marked in bold.

Figure 1 represents a sample increase of Mean HRV between two seizures and Figure 2 is a sample representation of significant increase in Mean HRV for mentioned five epochs before the seizure. LF/HF and SD2/SD1 show any significant changes in some of the seizures during 5 min before the seizure (61.0% and 55.9% respectively).

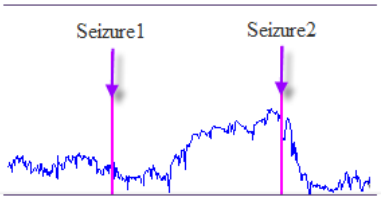

Figure 1. Increase of mean HRV in pre-ictal phase.

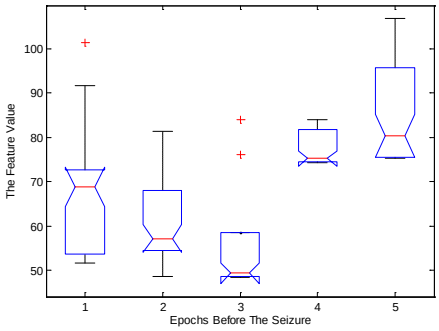

Figure 2. Mean HRV respectively from left to right for 180-90min, 90-30min, 30-10min, 10-5min, and 5 min before the seizure

4. Conclusion

Time and frequency domain and nonlinear analysis of HRV in epileptic subjects shows that there are significant differences in Mean HRV, MBPM and S for the time epochs far from the experienced seizures with respect to near epochs. Variation of the HRV parameters indicates changes in ANS activity of epileptic patients.

Although LF/HF and SD2/SD1 did not show significant changes in some of the seizures during 5 min before the seizure (16.9% and 25.4% respectively), 61.0% and 55.9% of them were increased, which is a proof of complexity and higher level of randomness in 5 min before the seizure.

As mentioned SD2/SD1 is best correlated with LF/HF, and corresponds to the sympatho-vagal balance.

The results showed the same behavior of them (increased 61.0% and 55.9% respectively) that confirm the correlation of these features.

	5min Before the Seizure				10min Before the Seizure	
Features	**Increase**	**Decrease**	**No Sig. Change**	**P-value**	**Increase**	**Decrease**
Mean HRV	**41/59 (69.5%)**	14/59 (23.7%)	4/59 (6.8%)	P<0.003	30/59 (50.8%)	5/59(8.5%)
MBPM	**40/59(67.8%)**	5/59(8.5%)	14/59(23.7%)	P<0.003	25/59(42.4%)	7/59(11.9%)
LF/HF	**36/59(61.0%)**	13/59(22.0%)	10/59(16.9%)	P<0.001	24/59(40.7%)	3/59(5.1%)
SD2/SD1	**33/59(55.9%)**	11/59(18.7%)	15/59(25.4%)	P<0.005	31/59(52.5%)	16/59(27.1%)
S	**38/59(64.0%)**	14/59 (23.7%)	7/59(11.9%)	P<0.005	25/59(42.3%)	8/59(13.6%)

Table 2. Overview of the heart rate characteristics during the seizures.

Moreover S, which represents the total variability of HRV and is under strong vagal influence, showed significant increase in 5 min before the seizure and can be as reflects of vagal behavior in this epoch.

These results can provide valid information regarding autonomic neuropathy in people with epilepsy. It may be noted that these features can detect HRV changes before seizure appearance. So we can expect that these measures enable early detection, anticipation or may be management of epileptic seizures. Prospective studies are necessary to confirm the present results and establish guidelines for combined analysis during EEG monitoring.

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