Entropy characteristics of heart rate wavelet multiscale components in epileptic children before and after seizures*

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***Abstract*— In this work, we analyze the information content of the multiple time scale components of heart rate variability (HRV) in children with focal epilepsy. HRV components are extracted from 30 pediatric patients, monitored 10 min and 10 s before and after focal epileptic seizures, using wavelet multiscale decomposition (with 5, 15, 30, 60, 120, 180 s time scale), and then characterized computing Entropy (E), permutation entropy (PE), conditional entropy (CE) and information storage (IS). Moving from preictal to postictal windows, we find statistically significant differences in the CE and IS values of HRV components at short time scales, which reflect autonomic imbalance and appear as potential candidates of descriptive features for HRV monitoring in epilepsy.**

I. Introduction

While the origin of epilepsy and its main symptoms are connected to the functioning of the brain, it is known that epileptic seizures have an impact on the cardiorespiratory and autonomic function as well [1]. In fact, dysfunction of the cardiovascular regulation in epilepsy has long been reported, encouraging research on the connections between epilepsy and heart rate variability (HRV), especially related to the detection and prediction of epileptic seizures [2, 3]. To quantify the characteristics of heart functioning in epileptic patients, time and frequency domain measures and nonlinear parameters have been proposed (see, e.g., [4-6]). More recently, the multiscale analysis of HRV has been proposed to account for the multiple time scales inherent in the heart rate dynamics of healthy and pathologic physiologic states. In this context, the most widespread measure is the Multiscale entropy (MSE) [7], a tool able to assess the complexity of time series across multiple temporal scales. After its formulation, MSE has been refined and extended in various forms, for instance using linear models to allow its reliable computation over the data sequences of limited duration typical of short-term HRV [8], also accounting for long-range correlations [9].

In this work, a similar approach for the analysis of HRV at multiple time scales in epileptic children before and after seizures is proposed. The approach is based on using the wavelet transform [10] followed by the computation of different entropy measures. The wavelet transform is exploited to decompose the heart beat-to-beat intervals (HBIs) time series into components at different time scales. Afterwards, four different information measures are considered to characterize the information content and complexity of the HBIs at each specific time scale: entropy (E), measuring the information content of an HBI sequence [11]; permutation entropy (PE), capturing the order relations between consecutive HBI values [12]; and conditional entropy (CE) and information storage (IS), quantifying respectively complexity and regularity of an HBI sequence through the information-theoretic analysis of the dependencies between past and present HBI values [11]. The aim of the present study is thus to analyze the multiscale behavior of these information indexes applied to HRV time series measured in different preictal and postictal epochs from children suffering from focal epilepsy.

II. Materials and Methods

A. Patients and Data Measurement

This study uses the data from 30 pediatric patients suffering from focal epilepsy, diagnosed according to common clinical and electroencephalographic criteria at the TMO "Psychiatry" clinic of Kyiv (Ukraine). From these patients, a total of 93 seizures was considered for the analysis.

HBIs were measured as sequences of the RR intervals measured in four time windows (four different conditions): the windows ending 10 min and 10 s before the onset of a seizure (preictal) and the windows starting 10 s and 10 min after termination of the seizure (postictal). The duration of each window was set to obtain HBIs sequences of 300 HBIs (corresponding to about 5 minutes depending on HBI duration). The choice of 300 HBIs is typical of short-term heart rate variability analysis and allowed us to have equal number of samples for estimating the information measures.

B. Wavelet-based multiscale analysis

In wavelet decomposition [13], the time course of the values of the relevant coefficients is a measure of the presence of the time-domain fragments of particular duration T_a^*, with the shape of scaled wavelet $\psi(t)$, in the signal. We propose to extract and further analyze a single component from the full decomposition $WT_\psi(a,\tau)$ using the corresponding scale coefficient a^*:

$$X_{a^*}(t) = \frac{1}{C}\int_0^\infty WT_\psi(a^*,\tau)\psi\left(\frac{t-\tau}{a^*}\right)d\tau, \qquad (1)$$

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where C is a constant dependent on the properties of mother wavelet and the decomposition scale.

In this work, the continuous wavelet transform using Daubechies 4th order mother wavelet function was applied to the each analyzed HBI time series to obtain the decomposition coefficients. After that, the time scales of the processes of interest were defined by selecting specific durations (i.e., 5, 15, 30, 60, 120, and 180 seconds), and the corresponding components $X_a(t)$ were obtained by applying (1) to each scale. More details of the procedure can be found in [10].

C. Information-theoretic measures

After wavelet decomposition, the following information measures were applied to the time series corresponding to each derived wavelet component $X_a(t)$ (we refer to [11,12] for details about computation of the measures): E, quantifying entropy intended as the average uncertainty about the time series samples; PE, quantifying the joint entropy of rank vectors of length m+1 extracted from the time series; CE, quantifying the entropy of the present value of the time series when the past m values are known; IS, quantifying the mutual information between the present and the past m values of the time series. E, CE and IS were computed on normalized time series using both linear (lin) parametric models and nonlinear kernel (ker) estimators. Computations were performed using standard parameter settings (m=2, kernel threshold r=0.2).

D. Statistical analysis of PE, E, CE, and IS

Since each patient contributed with a different number of seizures, the information-theoretic analysis of HBIs was performed averaging the values of each considered index across the different seizures of the same patient. This averaging procedure led to obtain, for each index and wavelet component, a set of (27, 29, 30, 30) values in the 10-m pre-ictal, 10-s preictal, 10-s postictal and 10-m postictal conditions (HBIs could not be acquired in 3 patients in the 10-m pre-ictal and 1 patient in the 10-s pre-ictal conditions). Then, the statistical significance of each index across the four conditions was tested using the Kruskal-Wallis non-parametric ANOVA, followed by post-hoc two-sided Wilcoxon rank sum test. Finally, p-values relevant to the Wilcoxon pairwise test were analyzed only when the ANOVA test indicated statistically significant variations across the four conditions (significance p<0.05).

III. Results and Discussion

The following two measures were defined as different between the corresponding conditions:

1. Conditional entropy (CE(lin) index), computed 10 s before and after seizure for 15 s time scale, increased significantly (p=0.0052).
2. Information storage (IS(lin) index), computed 10 s before and after seizure for 15 s time scale, decreased significantly (p=0.0052).

These measures can thus be assumed as potential candidates of descriptive features for HRV monitoring in the transition from preictal to postictal states. These results suggest a lower regularity and higher complexity of the HRV dynamics in the period following focal seizures. Since they are obtained at time scales compatible with the respiratory influence on HRV, they may indicate a lower involvement of the parasympathetic system after seizures. The unbalance of the autonomic nervous system suggested by these results is in line with the activation of the sympathetic nervous system activity related to epilepsy suggested in a recent study [5]. On the other hand, no statistically significant differences (p>0.05 in each case) were obtained for the comparison of the HBI measures at longer time scales, and for nonlinear information-theoretic indexes. More types of entropy descriptors and other refined nonlinear measures should be challenged using larger datasets. The effects on the statistical analysis of including windows far away in time from the seizures (10 min) should be also investigated.

IV. Conclusion

The first attempt to analyze the entropy characteristics of the wavelet-based multiscale components of heart rate in epileptic children allowed to identify measures that appear as promising candidates for distinguishing the HBI before and after epileptic seizures. The approach may be further explored in future studies, on more subjects and datasets, to prove whether it could provide useful information about the disease management based on autonomic dysfunction reflected by the cardiovascular oscillations probed at various time scales. Moreover, it should be combined with measurements of central nervous system activity such as those based on EEG (e.g., studying brain-heart interactions), to yield a more general and comprehensive understanding of the nature of epileptic disorders.

V. References

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