A Comparison Study between Fainter and Non-fainter Subjects during Head-Up Tilt Test using Reconstructed Phase Space

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Abstract

The analysis of cardiac dynamics based on time series extracted from cardiovascular signals (e.g. electrocardiogram, blood pressure) is relevant for differentiating between normal and pathological cases with feasible functions in the diagnosis and risk estimation. In this study, the dynamic behavior of cardiovascular time series is analyzed using reconstructed phase space to identify differences between subjects who developed syncope during head-up tilt test (fainters) and others who did not (non-fainters). Electrocardiogram and arterial blood pressure were recorded from 29 non-fainter and 28 fainter subjects. RR-interval, Amplitude of Systolic blood pressure (AmpS), peak amplitude of the first derivative of blood pressure (dPdt_max) and Pulse Transit Time (PTT) were extracted. Different features, such as the phase space density and indices derived from the recurrence quantification analysis, were computed from the phase space area of the above cited time series. In order to identify fainter and non-fainter groups, we selected the most pertinent parameters using Relief method to be used for further classification by K-nearest neighbor. The results show that the performance of the classification is approximately the same in all these time series with sensitivity (Se) near to 66.5% and specificity (Sp) around 62% during the first 5min of supine position. These values increase in the first 15min of tilted position to Se= 67% and Sp= 73%. Using an optimal fusion node, we demonstrate that the joint analysis of RR and dPdt_max provides a sensibility around 95% and a specificity of 87%. This analysis suggests that a bivavariate analysis enhances the classification performance, and help predict the outcome of the HUTT.

1. Introduction

Syncope is a sudden and transient loss of consciousness and postural tone [1] usually known as fainting. It is a common problem for 3% of emergency room visits. Vasovagal syncope is one of the most common types of syncope and can happen at any age. It occurs due to a malfunction of the autonomic nervous system responsible for the regulation of heart rate and blood pressure, and it is characterized by peripheral vasodilation and drop in blood pressure along with bradycardia. Although syncope is not life threatening but it decreases the quality of life of patients (up to 35% of people who have syncope injure themselves [2]), in addition to its economic impact on the health care system. Head-Up Tilt Test (HUTT) is a commonly diagnostic test for evaluating patients with syncope. The main problem of this test is in its duration, which is unsuitable for patients and for clinical practitioners as well.

The objective of this study is to develop and test an algorithm based on ECG and blood pressure time series that can provide information about an impending syncope during HUTT. Recently, several methods have been developed to compute dynamical features from time series. Reconstructed phase space (RPS) is a powerful tool to characterize system's behavior. Based on RPS, a large amount of information on the dynamics of the system can be extracted and analyzed. In addition, it is suitable for physiological signals, which are generally non-stationary. Some of its application are ECG abnormalities classification [3] and EEG recording analysis [4].

In this paper, we assess the difference of the dynamical behavior of time series extracted from cardiovascular signals between subjects who developed syncope during HUTT (fainters) and others who did not (non-fainters). A combination of RPS analysis and *K*-nearest neighbors algorithm was used. Such analysis could reduce the test duration and avoid patients to develop syncope during HUTT. The rest of this paper is organized as follows, in the methods section; we describe the population study and the clinical procedure. After that, we present the signal preprocessing followed by the reconstructed phase space algorithm. Then we report the feature selection and classification methods that have

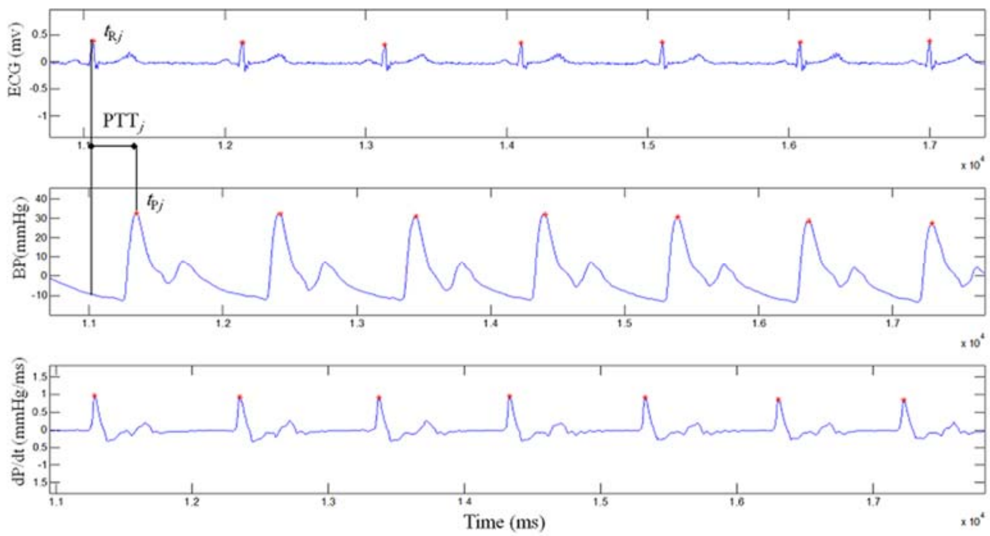

Figure 1. Example of Electrocardiogram (ECG), Blood Pressure (BP) and the first derivative of BP (dP/dt) signals. The R-wave peaks, systolic wave peaks and the peak amplitude of dP/dt are marked by red dots in ECG, BP and dP/dt respectively.

been used. Results are presented in the results section and interpreted in the conclusion.

2. Methods

2.1. Subjects

Subjects enrolled in the study are non-smoker men from 18 to 35 years, they weren't taking cardioactive medication and they didn't have any other disorders. All participants signed a consent form before performing the HUTT. They were asked to avoid physical activity 24 hours and abstain from consuming stimulating beverages (e.g. alcohol and coffee [5]) 12 hours before the test, and to have a light or no breakfast on the day of the test. Tilt test was performed in the university hospital of Rennes-France, in 57 subjects, 29 had a negative response to HUTT (non-fainter subjects) and 28 have developed syncope during the test (fainter subjects). All participants signed a consent form and performed the HUTT.

2.2. Clinical procedure

Acquisitions were performed in a quiet room, without provocative drugs. Subjects underwent a familiarization 2 to 6 days before the HUTT. The HUTT started with 12 min of resting in a supine position, after that, the table (Sissel, Sautron, France), that had a foot-board support was tilted at 80° for 45 min. HUTT was considered as positive if the subject developed syncope or intolerable presyncope associated with significant arterial hypotension, in this case the table was immediately returned to its initial position, and the test was terminated.

During the HUTT, ECG (standard limb lead configurations), continuous blood pressure (BP) using non-invasive finger sensors and heart rate variability were monitored with Task Force Monitor® (CN Systems, Graz, Austria).

2.3. Signal preprocessing

We acquired one lead ECG with sampling frequency 1000 Hz. Electrocardiogram signal were processed with a validated software DELICE (LTSI, UMR 1099, Rennes), which provides a fully automatic segmentation of all heart beats based on wavelet decomposition [6]. The BP signals were interpolated to have the same sampling frequency of ECG. Then, the first derivative of the BP (dP/dt) was estimated. After that, several feature points were extracted from these signals as shown in figure 1. Finally the following time series were constructed: ***RR***-interval (the time between the R-peaks in the ECG of two consecutive heart beats), ***AmpS*** (the amplitude of systolic wave in BP), ***PTT*** (the time between the R-wave and its corresponding systolic wave), ***dPdt_max*** (the peak amplitude of dP/dt). Figure 2 illustrates an example of these time series for a non-fainter subject during supine position.

2.4 Reconstructed Phase Space algorithm

Given a time series: $x(t_i)$ where t_i =0,..,T, the reconstructed phase space vector can be represented as:

$$X(t_i)= [x(t_i)\ \ x(t_i+\tau) \ \ldots \ x(t_i+(d\text{-}1)\tau)\ ]$$

with τ is the time delay between the points of the time series and where d is the embedding dimension which defines the number of phase space coordinates.

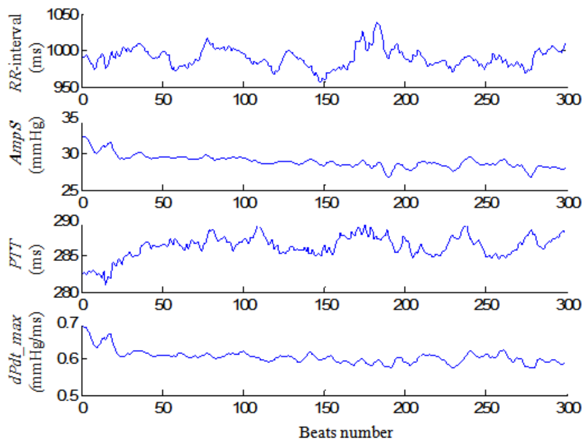

Figure 2. Example of ***RR***, ***AmpS***, ***PTT*** and ***dPdt_max*** series of a non-fainter subject during supine position

Eckman et al have proposed a method to visualize the recurrence of states in phase space [7]. This representation is called *recurrence plot (RP)* and can be mathematically expressed as:

$$R_{i,j} = \Theta(\varepsilon_i - \|x(t_i) - x(t_j)\|, \quad i,j=1\ldots T$$

To predict the outcome of the HUTT (subject will develop syncope or not) two methods were evaluated. The first one requires the normalization of the reconstructed phase space to have all values within the range [0,1], divides it into 1000 equal sized cells [8] and then estimates the distribution of points in each cell. In the rest of this paper each cell is mentioned by an attributed number according to its bounds in the 3 axes (*i.e.* the bounds of cells number 1 and 2 are 0-0.1 in the 1st axis; 0-0.1 in the 2nd axis and respectively 0-0.1 and 0-0.2 in the 3rd axis). The second method computes new measures of complexity based on RP extended by [9] and used in [10].

In this study, we computed the aforementioned parameters from the different constructed time series: ***RR***, ***AmpS***, ***PTT*** and ***dPdt_max***, in different conditions (in supine and tilted position). To do that, we set the values of RPS parameters based on the average mutual information method and the false nearest neighbor algorithm for time delay τ and embedding dimension d respectively.

2.5. Feature selection and classification

In order to separate patients into two classes (fainters and non-fainters), the K-nearest neighbor algorithm [11] was employed. A large number of features were extracted from the phase space (such as the phase space density, Correlation Dimension, Shannon Entropy) and they exceed the number of subjects in the database. Thus the use of all the descriptors is not feasible. Hence, a selection of the most relevant descriptors that can help in the classification of subjects according to the results in HUTT was done using Relief method [12].

2.6. Optimal fusion rule

After univariate analysis, a bivariate one was performed using a data fusion technique. It aims to evaluate the performance of the combination of the different time series. It produces a new statistical decision based on the association of a set of local decisions (derived from different sources, here they are derived from different time series) in which the weights are defined as a function of the detection performance of each individual time series. More details are reported in [13].

3. Results

Classification results of univariate time series analysis is reported in figure 3 and figure 4 in terms of sensitivity (Se) and specificity (Sp) in the first 5min of supine position (Supine5) and the first 15min of tilted position (Early15) respectively.

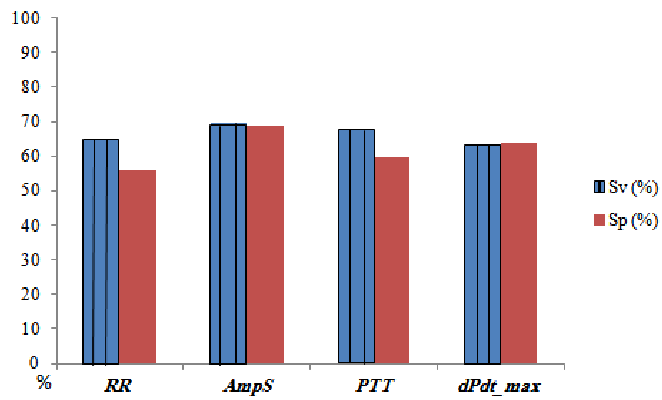

Figure 3: Results of classification for different time series in Supine5

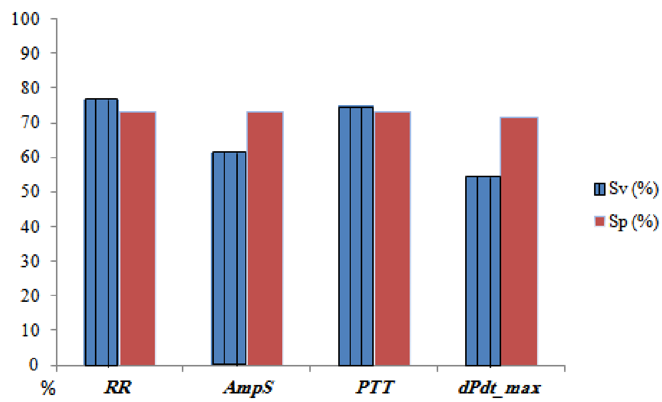

Figure 4: Results of classification for different time series in Early15

By looking for the best couples of time series using an optimal fusion node, we find that the joint analysis of ***RR*** and ***dPdt_max*** provides high values of sensibility and specificity. Table 1 reports the performance of classification when the ***RR*** and ***dPdt_max*** time series are jointly analysis.

Table 1. Classification results of the joint analysis of ***RR*** and ***dPdt_max*** time series.

Condition	Sensitivity	Specificity
Supine5	71.4%	60%
Early15	**92.8%**	**86.7%**

4. Conclusion

The aim of this study is to compare the difference between fainter and non-fainter subjects during head-up tilt test. For this reason, time series from different cardiovascular signals were analysed in the reconstructed phase space. The results indicate a difference between fainter and non-fainter subjects reflected by non-similar dynamical behaviours of cardiovascular system. This difference appears more significantly during the first minutes of tilting position, which indicates an abnormal response of cardiovascular system to postural change in fainters group. Results also show that the bivariate analysis of cardiovascular "time series can better discriminate between the two groups than univariate analysis. These findings, that reach 92,8% of sensitivity and 86,7% of specificity when using ***RR*** and ***dPdt_max*** together during the first 15 min of tilted position demonstrate that the complexity of the cardiovascular system can be better reflected through multiple source analysis than within univariate source analysis. In clinical practice, this high performance can help to reduce the duration of the tilt test.

Acknowledgments

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References

[1] Moya A et al. 2009. Guidelines for the diagnosis and management of syncope (version 2009). The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC) Eur. Heart J.

[2] St-Jean K, Kus T, Dupuis G, Lévesque K, Thibault B, Guerra P G, Nadeau R, D'Antono B. 2008. Quality of life in patients with recurrent vasovagal or unexplained syncope: Influence of sex, syncope type and illness representations. Appl. Res. Qual.

[3] Roberts F M, Povinelli R J, Ropella K M. Identification of ECG Arrhythmias Using Phase Space Reconstruction. In: Proceedings of the 5th European Conference on Principles of Data Mining and Knowledge Discovery. London, UK, UK, 2001, p. 411–423.

[4] Ouyang G, Li X, Dang C, Richards D A. Using recurrence plot for determinism analysis of EEG recordings in genetic absence epilepsy rats. In: Clin. Neurophysiol. vol. 119, nº 8, p. 1747‑1755, août 2008.

[5] Karapetian G K, Engels H J, Gretebeck K A, Gretebeck R J. Effect of caffeine on LT, VT and HRVT . In: Int. J. Sports Med. vol. 33, nº 7, p. 507‑513, juill. 2012.

[6] Dumont J, Hernandez A I, Carrault G. Improving ECG Beats Delineation With an Evolutionary Optimization Process. In: IEEE Trans. Biomed. Eng. vol. 57, nº 3, p. 607‑615, mars 2010.

[7] Eckmann J.-P, Kamphorst S. O, Ruelle D. Recurrence Plots of Dynamical Systems. In: EPL Europhys. Lett. vol. 4, nº 9, p. 973, nov. 1987.

[8] Srinivasan N, Wong M T, Krishnan S M. A new phase space analysis algorithm for cardiac arrhythmia detection. In: Proceedings of the 25th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2003. vol. 1, p. 82‑85 Vol.1.

[9] Marwan N, Wessel N, Meyerfeldt U, Schirdewan A, Kurths J. Recurrence-plot-based measures of complexity and their application to heart-rate-variability data. In: Phys. Rev. E. vol. 66, nº 2, p. 026702, août 2002.

[10] Khodor N, Carrault G, Matelot D, Amoud H, Ville N, Khalil M, Carre F, Hernandez A. A new phase space analysis algorithm for the early detection of syncope during head-up tilt tests. In: Computing in Cardiology Conference (CinC), 2014, p. 141‑144.

[11] Duda R O, Hart P E. Pattern Classification and Scene Analysis. 1 edition. New York: Wiley, 1973.

[12] Kenji Kira L A R. « The Feature Selection Problem: Traditional Methods and a New Algorithm. p. 129‑134, 1992.

[13] Hernandez A I, Carrault G, Mora F, Thoraval L, Passariello G, Schleich J-M. Multisensor fusion for atrial and ventricular activity detection in coronary care monitoring. In: IEEE Trans. Biomed. Eng., vol. 46, nº 10, p. 1186‑1190, oct. 1999.

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