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Recurrence plot of heart rate variability signal in patients with vasovagal syncopes

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ABSTRACT

Currently, heart rate variability (HRV) is commonly evaluated using time and frequency domain analysis in the clinical practice. Due to the fact that cardiovascular system is regulated by the autonomic nervous system (ANS) that also influences HRV, however exhibits rather nonlinear behaviour, it appears more appropriate to apply nonlinear methods to evaluate functioning of ANS. This study presents recurrence analysis as a tool to test the presence of ANS dysfunction that is responsible i.e. for orthostatic (vasovagal) syncope by which abnormal HRV has been demonstrated in the past.

Study included 18 patients that experienced vasovagal syncope (mean age 23.7 ± 5.2 years) and 18 healthy subjects (mean age 24.5 ± 3.2, $p = 0.85$). In all tested subjects, ECG recording was performed during active orthostatic test that comprised two phases (5 min of resting in a supine position and 5 min of active standing). Sequence of R-R intervals (time intervals between two consecutive heart beats derived from ECG) was analysed using standard time (mean *RR*, mean *HR*, *SDNN*, *SDHR*, *RMSSD*, *NN*50 and *pNN*50) and frequency domain (*LF*, *HF* and *LF*/*HF* ratio) analysis. Moreover, recurrence analysis was performed (*RATIO*, *DIV*, *AVDL*, *MAXV*, *DET*, *ENTR*, *LMAX*, *TT* and *LAM*).

Frequency domain analysis did not demonstrate significant difference between the two groups in any of the parameters during both phases of the test. On the contrary, both time domain analysis and recurrence analysis showed comparable findings in both groups during resting phase of the orthostatic test with a significant change of most tested parameters after stand-up.

As the use of time domain HRV may be perceived as problematic regarding their interpretation in short ECG recordings, recurrence analysis appears to be a sensitive tool for detecting ANS dysfunction in patients with vasovagal syncope.

1. Introduction

Currently, the field of medicine is experiencing a rising tendency towards the use of nonlinear methods derived from chaos theory [1–3] that describe the dynamics of a system [4]. What makes nonlinear methods so widely used nowadays is their ability to describe certain ongoing processes in the organism more precisely than a range of other methods [5] that are currently used in medicine.

Every living organism shows signs of chaotic behaviour ranging from sub-cellular level to vital regulations, such as heart rate and blood pressure [4]. Since dysregulation of the latter may prove pathological and yields significant clinical consequences, measurement and evaluation of heart rate and blood pressure behaviour are particularly instrumental and important in clinical practice. Their dysregulation may be caused by abnormal autonomic

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nervous system (ANS) regulation, as in the case of vasovagal syncopes [6]. Dysregulated oscillation activity of ANS in vasovagal syncopes is related to hemodynamic changes that lead to sudden occurrence of bradycardia and hypotension resulting in loss of consciousness and collapse of a patient although there is no structural heart disease present. The most frequent provoking factor resulting in syncopes is orthostasis that leads to blood concentration in lower limb vessels in sensitive individuals. This blood redistribution in the vascular space causes lower blood filling of the heart with resulting activation of baroreceptors in the aortic arch and carotic sinus. Consequently, sympathetic division of ANS is activated, which results in increased heart rate and diastolic pressure [7]. However, in patients with vasovagal syncopes, no increase of sympathetic division activity occurs. Thus blood pressure decreases as a result of diminished ventricular filling and excessive activity of parasympathicus (the other part of ANS) causes bradycardia through mechanoreceptors in pulmonary artery, atrial walls and left ventricle [8]. In fact, vasovagal syncope is not a rare disease and falls among the most common causes of fainting, black-outs, sudden falls and short term loss of consciousness.

Autonomic nervous system, perceived as a fine example of nonlinear deterministic system [4,9,10], influences heart rate and blood pressure in order to secure proper functioning of all organs based on the state of the body. A constant and balanced tone between sympathicus and parasympathicus is responsible for adequate blood pressure and heart rate that reflects an actual hemodynamic need. Thus, ANS functioning can be partly studied using heart rate variability (HRV), an analysis of heart rate changes over time, which reflects the heart's ability to react to the changes of ANS tone [11].

Clinical assumption on vasovagal aetiology of syncope is verified in a defined test that aims to de-mask presence of ANS dysfunction under the heading of so-called orthostatic test. There are two different methods of orthostatic testing, first is active standing and second is head-up tilt test (HUTT) [12,13].

ANS system dysfunction is believed to be present when blood pressure and/or heart rate suddenly decreases during stand-up phase of the test which is usually associated with manifestation of typical clinical symptoms/syncope. However, HRV analysis has proven to better identify and measure autonomic dysregulation responsible for heart rate and blood pressure changes before they manifest themselves in the form of a syncope. Actually, HRV has been known to be an effective tool for the prediction of cardiovascular morbidity and mortality [14–16]. For HRV evaluation, there are commonly used linear methods of analysis (based on time and frequency domain analysis) as well as nonlinear methods [14,17,3,18]. However, linear methods that are based on fast Fourier transform and autoregressive model proved to have a number of disadvantages [10]. Frequency domain also yields disadvantages such as long sessions of obtaining data, non-stationarity, lower sensitivity as well as high sensitivity to noise. On the other hand, recurrence analysis as a new and promising approach to HRV assessment seems to be able to tackle these obstacles relying on the observation that a healthy subject's ANS immediately responds to impulses of the organism resulting in lower occurrence of the same or similar states. In contrast, since autonomic dysfunction causes a significant simplification of bodily functions control (including heart rate variability), similar states recur more frequently. Recurrence analysis seemed to be promising in pilot studies as an effective nonlinear technique capable of presenting discrete abnormalities in heart rate regulation in earlier stages of the autonomic dysfunction [9,19–23].

This work primarily aims to verify relevance of recurrence analysis in the detection of ANS regulation disorders that result in vasovagal syncopes.

Table 1
Study groups characteristics.

	Control group	Syncope group	The significance level
Mean age (years)	24.5 ± 3.2	23.7 ± 5.2	0.8493
Maximal age (years)	33	33	–
Minimal age (years)	20	15	–
Sex (male/female)	9/9	2/16	0.0477

2. Methods

2.1. Participants and measuring procedure

Two groups were formed with the total of 36 subjects. Eighteen patients, 16 women and 2 men, aged 15–33 years (mean age 23.7 ± 5.2 years), suffering from vasovagal syncope comprised the Syncope group. The second, Control group comprised of 18 healthy subjects. 9 women and 9 men, aged 20–33 years (mean age 24.5 ± 3.2 years), see Table 1. None of the subjects had history of cardiovascular disease or other disorders. All subjects participating in this study gave their informed consent with the examination.

Active standing test (including resting supine position phase lasting 5 min and standing position phase of the same duration) was used for this study. Subjects were instructed to avoid alcohol, caffeine and nicotine consumption for at least 12 h prior to examination. In our autonomic laboratory, heart rate variability recordings were assessed under standard conditions. We assessed short-term recordings between 10 a.m. and 12 a.m., and patients remained in supine rest 15 min before recording. Then the 5 min supine rest phase was recorded. For the standing phase, patients were instructed to stand up. To prevent artifacts from muscular contraction, the stand-up phase measurement was initiated after the patient was fully adapted to standing position (usually 10–15 s after standing up) and then the 5 min standing phase was recorded. We did not use paced breathing as it was considered less physiological than normal breathing, however, patients were instructed to breath comfortably a without changing breathing frequency after changing the position of their body. According to literature [24,25], we absolutely agree that short term heart indices are subject to high variation and their reliability is still discussed in literature. We are trying to achieve similar conditions (i.e. time of examination, room temperature, humidity, absence of unwanted noise, etc.) to minimize those variations. During the entire test, ECG and blood pressure were recorded in both phases and sequence of R-R intervals (intervals between two consecutive heart beats) was subsequently derived from ECG recording. This series of R-R intervals was then analysed using Schwarzer FAN Study (FAN®, Schwarzer, Germany) system and HRV analysis was performed in accordance with standard measurement techniques and algorithms [26–28].

2.2. Data analysis

Specifically, sequence of R-R intervals has been analysed using standard time and frequency domain analysis. In addition, recurrence analysis was subsequently performed. In case of the former, following parameters were calculated: mean R-R, mean heart rate (*HR*), standard deviation for R-R intervals (*SDNN*), standard deviation for heart rate (*SDHR*), root mean square of the successive differences for R-R intervals (*RMSSD*), the sum of all R-R intervals occurring more than 50 ms from each other (*NN*50), percentual representation of *NN*50 occurrence in the total sum of R-R intervals (*pNN*50). Parameters derived from geometric methods (Triangular interpolation of N-N intervals and HRV triangular index) were not evaluated, as they are not suitable for short-term 5-min records [14,29].