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Potential force dynamics of heart rate variability reflect cardiac autonomic modulation with respect to posture, age, and breathing pattern

Faizal Mahananto, Tomohiko Igasaki*, Nobuki Murayama

Department of Information Technology on Human and Environmental Science, Graduate School of Science and Technology, Kumamoto University, 2-39-1 Kurokami, Chuo ward, Kumamoto 860-8555, Japan

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ABSTRACT

Rationale: Various physiological and pathological conditions are correlated with cardiac autonomic function. Heart rate variability is a marker of cardiac autonomic modulation and can be measured by several methods. However, the available methods are sensitive to breathing patterns.
Objectives: To quantify cardiac autonomic modulation by observing the potential force dynamics of the R-R interval time series in healthy individuals.
Methods: We propose two "potentials of unbalanced complex kinetic" (PUCK) parameters to quantify the characteristics of the potential force dynamics of R-R interval time series: potential strength (slope) and fluctuation size (slope standard deviations [SSD1, SSD2]). We applied this method to the series of R-R intervals obtained from 30 healthy subjects in an experimental condition that elicited cardiac autonomic (i.e., sympathetic and vagal) activation (in supine, sitting, and standing positions). Subjects were categorized into three groups by decade (i.e., 20 s, 30 s, and 40 s) to verify the cardiac autonomic differences by age. Two respiration patterns were introduced to check the influence of the pattern into the analytical results.
Measurements and main results: Sympathetic modulation activation significantly increased the slope and reduced SSD1 and SSD2; these trends were confirmed in all groups. The slope is concordant with the result of the low frequency/high frequency (LF/HF) ratio in frequency components as an indicator of sympathetic modulation. No trend was observed in slope among age groups. However, SSD1 and SSD2 in the 40 s group were significantly decreased in the supine and sitting positions. The results with respect to respiration frequency showed lower sympathetic modulation as shown in the LF/HF ratio and slope, whereas higher vagal modulation as shown in the HF appeared with a longer breathing rate.
Conclusions: PUCK can quantify the cardiac autonomic modulation in the experimental conditions of different postures. SSD1 and SSD2 are more sensitive to age than frequency components and are unaffected by breathing patterns. This method may be an alternative method for observing cardiac autonomic modulation in clinical practice.

1. Introduction

Cardiac autonomic dysfunction is one of the determinants of the development of cardiovascular diseases [1–3]. Cardiac autonomic imbalances and reduction of its modulation are signs of disorders and conditions. Heart rate variability (HRV), a promising marker of those autonomic activities, can be measured non-invasively in order to observe the influence of the cardiac autonomic system on sinus node activity through changes in the cyclic variations of beat-to-beat (R-R) intervals. The physiological correlations of HRV and standards for its measurement have been proposed [4]. An important marker is the frequency domain representation; however, the result of the high-frequency (HF) component might be influenced by breathing pattern [5–8]. Therefore, additional methods have been proposed to obtain more accurate estimates.

HRV is evaluated by observing R-R interval variations. The simplest method is to calculate the time domain of the mean R-R interval and its standard deviation. The more complex evaluation method, which involves quantifying frequency domain representation, is the most widely accepted method by both researchers and medical practitioners. In addition, the non-linear characteristics that

* Corresponding author.
E-mail address: iga@cs.kumamoto-u.ac.jp (T. Igasaki).

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accommodate the non-stationary phenomenon underlying the R-R interval time series have been reported [9–11]. Moreover, physiological interpretation and the relationship with the cardiac autonomic activity of non-linear methods have also been studied intensively [12–14].

As the R-R interval time series is non-linear, it is necessary to quantify it in a non-linear manner. Therefore, we proposed a non-linear method called the "potentials of unbalanced complex kinetics" (PUCK) to observe the potential force of the R-R interval time series. The potential force is the moving potential of the time series, with its center given by the moving average of its own trace. The observation of potential forces has been used in the econophysics field to analyze the fluctuation of foreign exchange prices [15]. Meanwhile, such a complex and non-stationary fluctuation has also been found in the R-R interval time series variability caused by cardiac autonomic regulation [16]. Several non-linear methods for HRV analysis are reportedly applicable in econophysics [17–19]. The present study addresses the implementation of this method for HRV analysis.

Several methods have been proposed to elicit the influence of sympathetic and vagal tone on heart rate [20,21]. Medication or changes in body position or posture can be used to alter the activity of sympathetic or vagal influence on the heart rate. For example, head-up tilt position elicits sympathetic activation, whereas the rest position has the reverse effect [4,22].

The present study aimed to quantify cardiac autonomic modulation by observing the potential force dynamics of the R-R interval time series in healthy individuals using different postural gravitational stimuli to increase sympathetic modulation. The subjects were also divided into three age groups to determine the effect of age on method performance. Two respiration patterns were introduced to examine the influence of respiration pattern on the method results. The results were then compared with the HRV time-frequency and the non-linear measures.

2. Methods

2.1. Subjects

Thirty healthy men (23–49 years old) participated in this study. The subjects were divided into three groups by age: group I ($n=10$; age range, 21–26 years), group II ($n=10$; age range, 30–39), and group III ($n=10$; age range, 40–49 years) [23]. The subjects had no reported heart-related or internal diseases. The subjects were asked to refrain from taking any medication in the morning prior to the experiment. The subjects were instructed not to consume alcohol-containing beverages the day before the experiment. All subjects provided informed consent to participate. We excluded individuals with observed arrhythmias such as premature ventricular contractions.

2.2. Experimental protocol

The experiments were started between 8:00 and 8:30 AM and finished at around 11:00 AM to minimize the effect of circadian rhythm on HRV measurements [24,25]. The subjects were asked to maintain supine, sitting, and standing postures for 20 min and were not allowed to talk or move during observation. The task sequences were randomized for each subject, with a 5-min rest period scheduled between tasks. Each task was performed twice under 3-s (20 breaths/min) and 5-s (12 breaths/min) breathing interval patterns. The order of breathing patterns in each task was also randomized. A special electronic metronome was used to maintain the subjects' breathing patterns. This study complied with the principles of the Declaration of Helsinki and was granted full ethical approval by the Ethics Committee of Kumamoto University.

2.3. Data acquisition

Electrocardiography (ECG) signals were recorded using a single-lead ECG recorder following the standard limb lead II. ECG data were sampled at 1000 Hz. The R-wave peaks of the ECG were detected using a moving average threshold algorithm [26] and manually checked to ensure a lack of misdetections or missed beats. The R-R interval time series was estimated as the time between two consecutive R-wave peaks. Each R-R interval time series was then linearly interpolated and resampled at 1 Hz to obtain 1200-point equidistant data samples. Resampling the signal below the original ECG sample interval will produce significant systematic errors, especially if there are several missing beats [27]. Resampling the R-R interval time series into 1 Hz is widely accepted and reduces computation time [28,29]. In addition, only data with no missing beats were used to reduce such systematic errors.

2.4. HRV analysis

To compare the performance of the PUCK analysis method on the R-R interval time series, the standard HRV analysis methods, which included time domain, frequency domain, and non-linear analyses, were also performed. Time domain analysis provides statistical values of the R-R time series. The mean of all R-R intervals (MeanRR), standard deviation of all R-R intervals (SDRR), and root-mean-squares of the successive differences in the R-R intervals (RMSSD) were calculated.

In the frequency domain, the power spectrum density was measured by discrete Fourier transformation of the R-R interval time series. Four components were considered: the low frequency (LF) (area under 0.04–0.15 Hz), high frequency (HF) (area under 0.15–0.4 Hz), total power (TP) (area under 0.01–0.4 Hz), and LF/HF ratio [4]. Frequency domain quantification provides an understanding of cardiac autonomic modulation. The LF component is influenced by both sympathetic and vagal modulation, while the HF component is only influenced by vagal activity. Therefore, the LF/HF ratio is considered to indicate the sympathovagal balance reflecting sympathetic modulation. The TP component represents the variance of the R-R interval [4].

Three non-linear analyses were employed: sample entropy (SampEn) [10], Poincaré plot analysis [30], and detrended fluctuation analysis (DFA) [9]. The SampEn analysis parameters, similarity tolerance r and epochs length m, were set at 2 and $0.2\times$ SDRR, respectively [10]. The pSD1 and pSD2 components in the Poincaré plot analysis were calculated from the plot as the standard deviation of the lines $y=x$ and $y=-x+2$MeanRR, respectively [30]. Two features from the DFA were obtained from the slope of the scaling exponent at <11 beats (DFA $\alpha 1$) and >11 beats (DFA $\alpha 2$) [9]. As a limitation of the Poincaré plot analysis as non-linear tool, the result statistic is not independent of other time domain measures [31].

2.5. Potential force dynamics (PUCK analysis)

The observation of potential force dynamics has been studied for market foreign exchange data [15]. A moving average model (optimal moving average [OMA]) was introduced, and a noiseless R–R interval time series was considered.

$$\overline{RR_t} = \sum_{n=1}^{k} w_n RR_{t-n} \tag{1}$$

The variable w_n as the autoregressive coefficient was estimated using the Yule–Walker equation.