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Joint symbolic analyses of heart rate, blood pressure, and respiratory dynamics

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Abstract

Introduction: The dynamics of cardiovascular variables are modulated by respiration. The aim of this study was to assess baroreflex function in normal subjects based on the joint symbolic dynamics of heart rate, blood pressure and respiration.

Methods: ECG, continuous blood pressure and respiration were recorded in ten healthy subjects during rest in the supine position and upon standing. Beat-to-beat time series of heart rate, systolic blood pressure and respiratory phase were extracted and transformed into binary symbol sequences. Words of length two that were reflective of baroreflex activity were statistically analysed with respect to the respiratory phase.

Results: Symbolic analysis showed a significant influence of the respiratory phase on the occurrence of baroreflex patterns. Upon standing, the frequency of baroreflex words increased and the effect of respiration appeared to be reduced.

Conclusions: Symbolic dynamics provide a simple representation of cardiovascular dynamics and may be useful for assessing baroreflex function.
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Keywords: Baroreflex; Heart rate variability; Blood pressure variability; Symbolic dynamics

Introduction

Heart rate and blood pressure fluctuate spontaneously from beat to beat. Assessment of those spontaneous fluctuations is thought to provide insight into cardiac baroreflex control. Traditionally, assessment of spontaneous baroreflex activity has been carried out in the time and frequency domains, employing the sequence technique and the alpha index.[1] Both techniques provide indices of baroreflex sensitivity, i.e. the magnitude of the RR interval prolongation as a response to systolic blood pressure drop and vice versa. Other indices of baroreflex function include baroreflex effectiveness[2] and information transfer based measures.[3,4] We have previously developed an approach based on symbolic dynamics to quantify patterns in heart rate and blood pressure changes and demonstrated its usefulness for baroreflex assessment.[5,6] We later adopted this approach to quantify cardio-respiratory coupling and developed a measure of respiratory sinus arrhythmia.[7,8]

As the interplay between blood pressure and heart rate is overarched by respiration,[9] its incorporation into the analysis has been proposed to obtain more reliable indices of baroreflex control. Using autoregressive models, distinct transfer functions for the relationships between respiration, heart rate and blood pressure have been delineated.[10]

In this paper we propose a model-free approach for the joint assessment of heart rate, blood pressure as well as respiration based on symbolic dynamics. We applied this technique to study the effect of orthostasis on baroreflex control in healthy subjects and hypothesized that it provides detailed information on the coupling between blood pressure and heart rate with regard to the respiratory phase.

Methods

Subjects

Ten healthy athletes (5 males and 5 females) participated in this study. None of the subjects were taking medication before or during the study. Anthropometric data and peak oxygen uptake are shown in Table 1. The study conformed to the principles outlined in the Declaration of Helsinki. All

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Table 1
Anthropometric data and peak oxygen uptake of the athletes presented as medians and interquartile ranges (IQR).

Gender	Men		Women	
	Median	IQR	Median	IQR
Age (y)	26.6	26.5–28.8	24.8	24.7–26.4
Body Mass (kg)	72.0	69.0–86.8	54.8	50.4–61.8
Height (cm)	181	181–182	163	162–168
VO_2 peak (ml/[kg*min])	65.9	61.4–74.6	51.1	48.9–52.2

participants provided written informed consent. More details on the study group have been published elsewhere.[11,12]

Data and pre-processing

High resolution (1600 Hz) ECG, respiration (piezo sensor belt, placed around the chest) and non-invasive continuous blood pressure (Portapres M2, TNO Biomedical Instrumentation, The Netherlands) were recorded simultaneously for 30 minutes under standardized resting conditions in the supine position and subsequently for 20 minutes upon standing. Custom-written computer software was used for the detection of ECG R-peaks, systolic blood pressure and inspiratory/expiratory onsets of respiratory signal. The R-R time series, obtained from the time intervals between consecutive R-peaks, were visually scanned for artefacts and, if necessary, manually edited. Systolic blood pressure (SBP) was determined as the peak amplitude of the continuous blood pressure signal between two consecutive R-peaks. The respiratory signal was low-pass filtered at 0.5 Hz using a zero-phase forward and reverse digital filter. The respiratory phase (RP) was measured at the time instants of R-peaks, using the Hilbert transform. The R-R time series were aligned to the SBP time series such that the nth R-peak with corresponding R-R interval (time distance from R_n to R_{n+1}) is the one that follows the nth SBP (i.e. the cardiac cycle following the systolic blood pressure pulse). The n^{th} respiratory phase was measured at R_{n-1}.

Joint symbolic dynamics

From the time series of R-R interval, SBP and RP we established three symbolic sequences, s^H (H denoting the heart rate − reciprocal of R-R interval) s^S and s^R, based on the differences between successive R-R intervals, SBP values and R-instant respiratory phases, respectively, as described previously[7]:

$$s_i^H = \begin{cases} 0 \text{ if} RR_{i+1} - RR_i > 4 \\ 1 \text{ if} RR_{i+1} - RR_i \leq 4 \end{cases} \quad (1)$$

$$s_i^S = \begin{cases} 0 \text{ if} SBP_{i+1} - SBP_i \leq 0 \\ 1 \text{ if} SBP_{i+1} - SBP_i > 0 \end{cases} \quad (2)$$

$$s_i^R = \begin{cases} 0 \text{ if } |RP_{i+1}| - |RP_i| > 0 \\ 1 \text{ if } |RP_{i+1}| - |RP_i| \leq 0 \end{cases} \quad (3)$$

Using these symbolic time series, words of length two were formed for each series and denoted as H, S and R, resulting in four different word types each. The interactions between heart rate, blood pressure and respiration were quantified by measuring the joint occurrences of word types across the three domains.

Surrogate analysis

R-R interval and SBP time series were randomly shuffled to test whether symbolic encoding and word formation are able to capture non-random features. Respiratory phases were measured at the time instants of the cumulated surrogate R-R interval time series. Ten sets of surrogate data were generated for each of the ten subjects' recordings during rest. Thus, symbolic analysis was performed for 100 surrogate data. Relative word frequencies were subsequently averaged for each of the ten surrogates, originating from the same recording.

Baroreflex pattern analysis

Combinations of word types where the symbol pattern in S is the inverse of H, i.e. S00H11, S01H10, S10H01, and S11H00 were regarded as baroreflex activity and considered for analysis.

Statistics

Relative frequencies of all 64 word type combinations of S, H and R were considered for statistical analysis. The distributions of word types were quantified using Shannon entropy. The student's t-test was used to compare entropy values obtained in supine position, during standing and from surrogate data. Distributions of relative frequencies of baroreflex word types with respect to the respiratory phase were compared between the supine measurement and surrogate data and between supine data and recording obtained during standing, respectively; using a two-way ANOVA repeated measurement design. Data are presented as mean ± standard deviation. Values of p 0.05 were considered to be statistically significant.

Results

Surrogate analysis

The relative frequencies of word types that occurred in the supine position during rest as well as those of randomized surrogates are shown in Fig. 1 (top panel). The Shannon entropy of surrogate data was significantly higher than those of original data, indicative of non-random dynamics captured by symbol analysis (5.79 ± 0.04 vs.4.90 ± 0.31, p 0.0001). The word distribution of surrogate data appears to be different from uniform distribution and follows a specific pattern.

The percentage of baroreflex patterns in the supine position was 27 ± 16% and not significantly different from surrogate data (28 ± 1%).

Distributions of baroreflex words with respect to the respiratory phase are displayed in Fig. 1 (bottom panel). During respiratory phase pattern R11 (inspiration) word type S00H11 occurred significantly more frequently in the supine measurement compared to surrogate data (ANOVA: group

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