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2011 Physiol. Meas. 32 1425

(http://iopscience.iop.org/0967-3334/32/9/006)

IOP PUBLISHING PHYSIOLOGICAL MEASUREMENT

Physiol. Meas. **32** (2011) 1425–1437 doi:10.1088/0967-3334/32/9/006

The effect of orthostatic stress on multiscale entropy of heart rate and blood pressure

Zuzana Turianikova[1], Kamil Javorka[1], Mathias Baumert[2], Andrea Calkovska[1] and Michal Javorka[1,3]

[1] Department of Physiology, Jessenius Faculty of Medicine, Comenius University, Martin, Slovak Republic
[2] School of Electronic & Electrical Engineering, The University of Adelaide, Australia

E-mail: mjavorka@jfmed.uniba.sk

Received 28 January 2011, accepted for publication 4 July 2011
Published 28 July 2011
Online at stacks.iop.org/PM/32/1425

Abstract

Cardiovascular control acts over multiple time scales, which introduces a significant amount of complexity to heart rate and blood pressure time series. Multiscale entropy (MSE) analysis has been developed to quantify the complexity of a time series over multiple time scales. In previous studies, MSE analyses identified impaired cardiovascular control and increased cardiovascular risk in various pathological conditions. Despite the increasing acceptance of the MSE technique in clinical research, information underpinning the involvement of the autonomic nervous system in the MSE of heart rate and blood pressure is lacking. The objective of this study is to investigate the effect of orthostatic challenge on the MSE of heart rate and blood pressure variability (HRV, BPV) and the correlation between MSE (complexity measures) and traditional linear (time and frequency domain) measures. MSE analysis of HRV and BPV was performed in 28 healthy young subjects on 1000 consecutive heart beats in the supine and standing positions. Sample entropy values were assessed on scales of 1–10. We found that MSE of heart rate and blood pressure signals is sensitive to changes in autonomic balance caused by postural change from the supine to the standing position. The effect of orthostatic challenge on heart rate and blood pressure complexity depended on the time scale under investigation. Entropy values did not correlate with the mean values of heart rate and blood pressure and showed only weak correlations with linear HRV and BPV measures. In conclusion, the MSE analysis of heart

[3] Author to whom any correspondence should be addressed.

rate and blood pressure provides a sensitive tool to detect changes in autonomic balance as induced by postural change.

Keywords: complexity, heart rate variability, blood pressure variability, orthostasis, multiscale entropy

1. Introduction

The evaluation of cardiovascular autonomic function is a cornerstone in the clinical investigation of autonomic function (Freeman 2006). Analyses of spontaneous heart rate and blood pressure oscillations (heart rate variability (HRV) and blood pressure variability (BPV)) provide important information on the autonomic control of circulation in healthy and diseased subjects (Parati *et al* 2006). However, the physiological interpretation of these variables is still incompletely understood (Wessel *et al* 2007).

Modulations of the firing rate of cardiac pacemaker cells in the sinus node (i.e. heart rate) as well as blood pressure (via cardiac output and peripheral resistance) are thought to be predominantly nonlinear. Further, interactions between different control loops (e.g. the cardiac and vascular branch of the baroreflex loop and the coupling between cardiac and respiratory motor neurons within the medulla oblongata) introduce additional complexity. Linear models are often insufficient to describe these complex dynamics in the cardiovascular system adequately and nonlinear approaches are therefore used increasingly frequently (Eyal *et al* 2001). The complexity of short-term HRV and BPV results predominately from neuro-humoral autonomic control mechanisms and complexity analyses of HRV and BPV may consequently provide information about cardiovascular regulation (Porta *et al* 2007).

In healthy subjects, beat-to-beat R–R interval and blood pressure time series have complex temporal structures with correlations on multiple time scales (Costa *et al* 2008, Cerutti *et al* 2009). Thus, a comprehensive complexity analysis should take into account multiple time scales. Costa *et al* (2002) introduced a method to calculate entropy over multiple scales—multiscale entropy (MSE) analysis. MSE analysis of cardiovascular time series reveals features that are indiscernible by traditional linear measures (Costa *et al* 2008). In previous studies, MSE analyses of cardiovascular signals identified impaired cardiovascular control and increased cardiovascular risk in various pathological conditions, including fetal distress (Cao *et al* 2006, Ferrario *et al* 2006), chronic heart failure (Lee *et al* 2005), atrial fibrillation (Costa *et al* 2002), phobia (Bornas *et al* 2006), critical post trauma state (Norris *et al* 2008) and type 1 diabetes mellitus (Trunkvalterova *et al* 2008).

Despite the increasing acceptance of the MSE in clinical research, its physiological meaning is hardly understood, in particular the involvement of autonomic nervous system in the MSE of heart rate and blood pressure.

The aim of this study is to investigate the effects of the autonomic nervous system on the MSE of HRV and BPV, by means of orthostatic challenge. Orthostatic challenge is a well-described autonomic stress paradigm that is characterized by an immediate reduction in vagal outflow to the sinus node and an increase in skeletal-muscular sympathetic nerve activity (Paton *et al* 2005). Further, we explore correlations between MSE and linear standard measures of HRV and BPV.

2. Materials and methods

2.1. Subjects

In this study, we included 28 healthy young subjects (21 females, 7 males) with a median age of 20.4 years (interquartile range 19.9–21.0 years). All subjects were normotensive, non-obese (body mass index: median 21.6, interquartile range 19.7–23.6 kg m^{-2}) and were not taking any medication at the time of study. All subjects gave their informed consent prior to examination. The study was approved by the Ethics Committee of Jessenius Faculty of Medicine, Comenius University.

Subjects were instructed not to use substances influencing cardiovascular system activity (caffeine, alcohol, tobacco) for at least 12 h prior to examination.

2.2. Procedures

All subjects were investigated under standardized conditions in a quiet room during morning hours (8 am to 12 am). The subjects were resting for 10 min before the actual recording started, allowing the cardiovascular system to reach equilibrium, i.e. a quasi-stationary condition. Recordings of R–R intervals, systolic and diastolic blood pressure (SBP, DBP, respectively) were obtained simultaneously and continuously during an orthostatic stress test that consisted of 20 min in the supine position followed by 15 min of active standing. Recording during the standing position commenced after 90 s allowing the cardiovascular system to approach a steady-state level. R–R intervals (the reciprocal value of heart rate (HR)) were obtained from a one-lead ECG (Cardiofax ECG-9620M, Nihon Kohden, Tokyo, Japan). The SBP and DBP recordings were obtained using a beat-to-beat blood pressure monitor (Finapres, Ohmeda, USA). All analog signals were transmitted to a PC using an analog–digital converter (Advantech PCL 711, Taiwan) at a sampling rate of 500 Hz.

2.3. Data analysis

HRV and systolic and diastolic BPV (SBPV and DBPV) analyses were performed on time series of 1000 beats from each condition (supine position—*L*, standing—*S*) using a custom-made computer software package.

2.3.1. Multiscale entropy. The MSE was computed according to the procedure published by Costa *et al* (2002). From one-dimensional discrete time series, $\{x_1, \ldots, x_i, \ldots, x_N\}$, we constructed consecutive coarse-grained time series $\{y^{(\tau)}\}$ determined by the scale factor τ, according to the equation

$$y_j^{(\tau)} = 1/\tau \sum_{i=(j-1)\tau+1}^{j\tau} x_i,$$

where τ represents the scale factor and $1 \leqslant j \leqslant N/\tau$. The length of each coarse-grained time series is N/τ. For scale 1, the coarse-grained time series is simply the original time series. We calculated sample entropy (SampEn) (Richman and Moorman 2000) for each of the coarse-grained time series as a function of the scaling factor.

SampEn quantifies the irregularity of a time series and estimates the conditional probability that two sequences of m consecutive data points, which are similar to each other (within a given tolerance r) will remain similar when one consecutive point is included. The SampEn algorithm underlying the MSE computation comprises two degrees of freedom: the tolerance

level r and the pattern length m. According to previous studies, we have chosen a tolerance level of $r = 0.15^*$ standard deviation of the time series to avoid distortion of SampEn values by changes in the signal magnitude. Because of the relatively short data (1000 beats), we computed SampEn values for $m = 1$ and for scales τ up to 10. MSE analysis was performed on HRV, SBPV and DBPV signals separately for both body postures (supine, standing).

2.3.2. Linear analysis. Linear measures were obtained in accordance with the recommendations of Task Force (1996).

Time domain analysis. HRV analysis. For time domain HRV analysis, we computed the three most commonly used measures: *MeanNN*—the mean length of the beat-to-beat interval of normal heart beats (NN intervals), *SDNN*—standard deviation of NN intervals, reflecting the overall variability magnitude and *RMSSD*—the root-mean-square of successive beat-to-beat differences, reflecting the average magnitude of changes between two consecutive beats, which is regarded to be a marker of vagal heart rate control.

BPV analysis. From SBP and DBP signals, we computed the following linear measures:

For SBP: *Mean SBP*—mean systolic blood pressure value, *SD SBP*—standard deviation of systolic blood pressure values, *RMSSD SBP*—root-mean-square of successive differences in SBP values.
For DBP: *Mean DBP*—mean diastolic blood pressure value, *SD DBP*—standard deviation of diastolic blood pressure values, *RMSSD DBP*—root-mean-square of successive differences in DBP values.

SD SBP and *SD DBP* measures reflect the overall magnitude of BPV, whereas *RMSSD SBP* and *RMSSD DBP* quantify the beat-to-beat variability of the respective signals.

Frequency domain analysis. Spectral analysis of HRV, SBPV and DBPV was performed to obtain power values in the low- and high-frequency bands. Time series were interpolated at 500 ms in order to obtain equidistant time series, using cubic splines. As we were interested in oscillations between 0.04 and 0.5 Hz that are mediated by vagal and sympathetic efferents, we eliminated the slower oscillations and trends using the detrending procedure of Tarvainen *et al* (2002). Subsequently, the power spectrum was repeatedly estimated, using fast Fourier transform and the Hanning window with a length of 1024 samples and a shift of ten samples. The average power spectrum was computed and the following measures were derived for all three analysed signals (HRV, SBPV, DBPV):

LF—low-frequency power (0.04–0.15 Hz);
HF—high-frequency power (0.15–0.4 Hz).

2.4. Statistics

Due to the non-Gaussian distribution of several variables (validated by the Lilliefors test), nonparametric tests were used. The Wilcoxon signed-rank test was applied to test the differences in MSE values of HRV, SBPV and DBPV between the supine and standing positions. In addition, we generated surrogates of all HR, SBP and DBP time series by shuffling all samples in order to destroy temporal structures. This way, we were able to test whether MSE values of measured data were different from those of completely uncorrelated data. Correlations between variability measures were assessed by Spearman correlation coefficients. A p-value <0.05 (two-tailed) was considered statistically significant and the

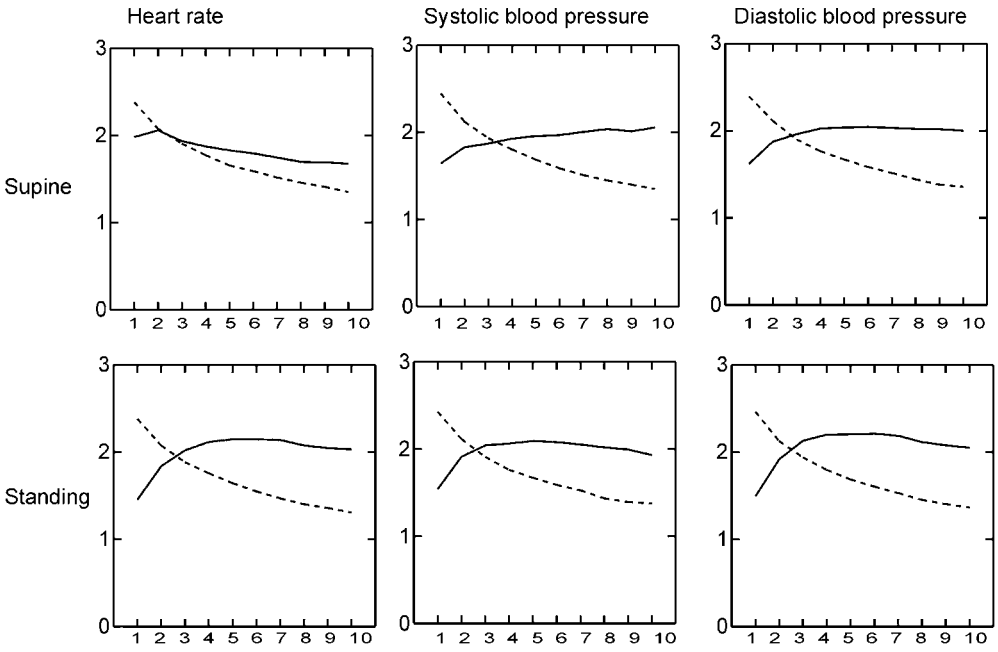

Figure 1. MSE analysis of heart rate (first column), systolic (second column) and diastolic blood pressure (third column) in the supine (first row) and standing (second row) positions. Mean values of SampEn values for scales 1–10 are presented for measured signals (full line) and randomized surrogate data (dashed lines).

Bonferroni correction was used to address the problem of multiple comparisons. All variables were presented as medians and interquartile ranges.

3. Results

3.1. MSE of randomized HR and BP time series

MSE analysis of randomized time series, independent of the body posture and the signal under investigation (i.e. heart rate or blood pressure), showed the same typical pattern of decreasing SampEn values with increasing scales (figure 1). The coarse-graining algorithm leads to a loss of entropy on higher scales (Costa *et al* 2002) while relatively stable values of SampEn were found on higher scales in real data.

3.2. MSE analysis of HR

The MSE functions of HR recorded in the supine position showed a continuous reduction in entropy values with increasing scales except from scale 1 (figures 1 and 2). Compared to the surrogate data, supine HR entropy values were higher than those from noise on scales >3. On scale 1, entropy was lower than that of random data but on scales 2–3 the entropy was not significantly different (figure 1).

In the standing position, HR entropy values initially increased and remained stable on scales >5. Compared to the surrogate data, HR entropy values were lower on scales 1–2 and significantly higher on scales >3 (figure 1).

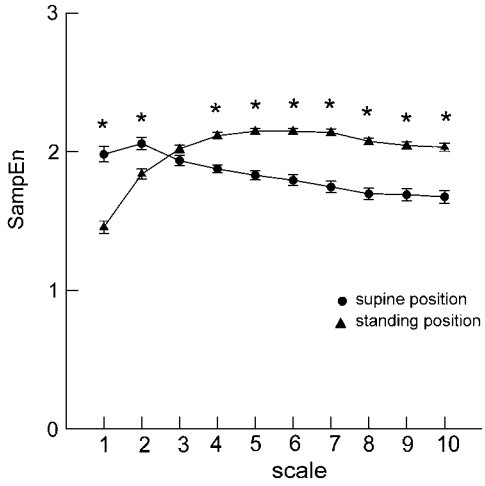

Figure 2. ME analysis of heart rate. Significant differences between supine and standing positions were detected on all scales with the exception of scale 3. For scales 1 and 2, the entropy of heart rate was lower in standing position, whereas for scales 4–10, entropy was higher in the standing position. The circles/triangles represent mean values and error bars indicate the standard error of the mean.

When comparing the MSE function obtained in the supine position with that in the standing position (figure 2), significant differences were found on all scales with the exception of scale 3, on which a cross-over of entropy values was observed. On smaller scales (1 and 2) significantly lower values of SampEn were found in the standing position compared to the supine position ($p = 0.000\,06$ and $p = 0.0002$ for scales 1 and 2, respectively). Conversely, on scales >3 the complexity of HR was significantly higher in the standing position compared to the supine position (p values ranging from 0.000 004 to 0.000 03).

Individual-specific analysis of the cross-over phenomenon showed that the 'cross-over scale' was 3 in 14 subjects (50%), 2 in 6 subjects (21%), 4 in 6 subjects (21%) and 9 in 1 subject.

3.3. MSE analysis of BP

In the supine position, SampEn values of SBP as well as DBP increased with increasing scales, where the biggest changes occur on small scales. Similar to the HR data, initial entropy values (scales 1 and 2) of SBP and DBP were smaller than those of randomized data and entropy values of larger scales (>4 for SBP and >3 for DBP) were higher (figure 1).

In the standing position, SampEn values initially increased with increasing scales and showed a slight reduction on higher scales. Compared to randomized data, SBP entropy values were significantly different on all scales, i.e. significantly lower on scales 1–2 and significantly higher on scales >2 (figure 1).

When comparing MSE results of SBP obtained in the supine with those obtained during the standing position (figure 3), significantly higher values of SampEn in the standing position were found on scales 3 and 4. On the remaining scales (scales 1, 2 and 5–10) no differences between body postures were found (figure 3).

The effect of body position on MSE analysis measures was more prominent in the DBP signal than in the SBP signal. SampEn values of DBP for five out of ten scales (scales 3–7) were significantly higher in the standing position (figure 4).

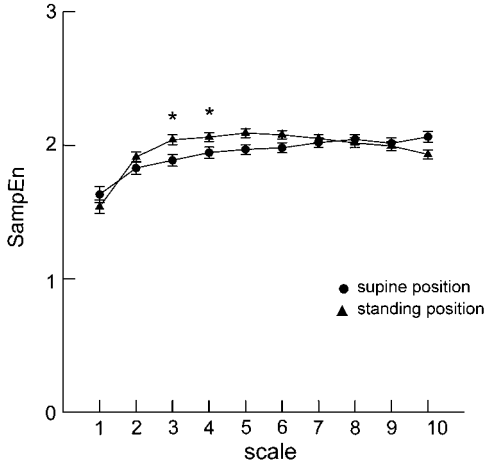

Figure 3. MSE analysis of systolic blood pressure. Significant differences between supine and standing positions were observed on scales 3 and 4. The circles/triangles represent mean values and error bars indicate the standard error of the mean.

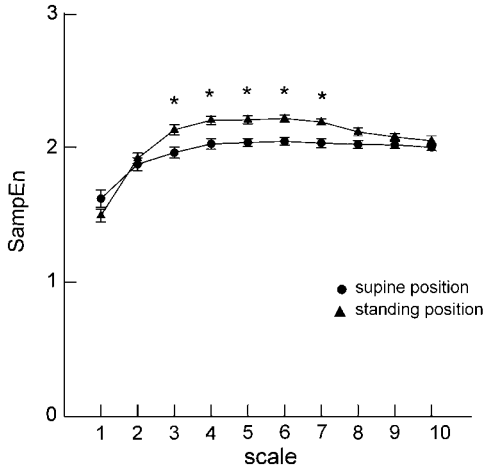

Figure 4. MSE analysis of diastolic blood pressure. Significant differences in SampEn values between supine and standing positions were found on scales 3–7. The circles/triangles represent mean values and error bars indicate the standard error of the mean.

3.4. Standard linear HRV and BPV analysis (table 1)

Significant decreases were found in all time and frequency domain HRV parameters (except the power in the LF band) in the standing position compared to the supine position. Conversely, an increase in overall as well as beat-to-beat SBPV and DBPV was detected during standing.

3.5. Correlation analysis of the MSE versus linear measures

HRV. None of the SampEn values correlated with MeanNN (table 2(A)). While no significant correlation between linear HRV measures and results of MSE were found in the standing position, time and frequency domain HRV measures showed significant

Table 1. Linear analysis of heart rate and blood pressure variability.

	Supine (*L*)	Standing (*S*)	*P*
HRV			
MeanNN (ms)	865 [811–984]	651 [621–790]	<0.001*
SDNN (ms)	57 [39–88]	43 [35–56]	0.001*
RMSSD (ms)	53 [27–84]	19 [15–26]	<0.001*
LF–HRV (ms^2)	459 [167–1233]	570 [211–794]	0.690
HF–HRV (ms^2)	851 [221–1957]	149 [87–277]	<0.001*
SBPV			
Mean SBP (mmHg)	112 [100–120]	145 [131–163]	<0.001*
SD SBP (mmHg)	6.4 [4.7–7.9]	8.7 [7.2–10.6]	<0.001*
RMSSD SBP (mmHg)	2.9 [2.4–3.4]	3.3 [3.0–4.3]	<0.001*
LF–SBPV (ms^2)	3.5 [2.1–4.9]	13.2 [8.5–19.5]	<0.001*
HF–SBPV (ms^2)	2.3 [1.3–3.0]	4.8 [3.2–6.8]	<0.001*
DBPV			
Mean DBP (mmHg)	47 [41–54]	83 [74–89]	<0.001*
SD DBP (mmHg)	3.2 [2.7–4.0]	5.5 [4.6–6.5]	<0.001*
RMSSD DBP (mmHg)	1.7 [1.5–2.5]	2.2 [1.9–2.7]	0.001*
LF–DBPV (ms^2)	1.6 [1.2–2.5]	9.0 [6.7–11.9]	<0.001*
HF–DBPV (ms^2)	0.7 [0.4–1.4]	1.6 [0.9–2.3]	<0.001*

Linear time and frequency domain measures computed for heart rate variability (HRV), and systolic and diastolic blood pressure variability (SBPV and DBPV) time series in the supine (*L*) and standing (*S*) positions. The values are presented as median [interquartile range]. The *p*-values were obtained using the Wilcoxon test. Asterisks indicate significant between-groups differences ($p < 0.05$). For a more detailed description of the variables see section 2.

negative correlations with SampEn values on higher scales (scales 5–10) in the supine position.

SBPV. None of the SampEn values correlated with Mean SBP values (table 2(B)). In the supine position, several significant correlations between SBPV magnitude and SampEn values on lower scales (1–3) were detected.

DBPV. None of the SampEn values correlated with Mean DBP values (table 2(C)). Similarly, no correlations were observed between SampEn values of any scale and SD DBP values (a measure of the overall DBPV magnitude) in either position. There were only a few significant correlations between SampEn values and spectral indices of DBP in the supine position.

4. Discussion

The major finding of our study is that MSE analysis of heart rate and blood pressure is sensitive to changes in autonomic balance as induced by postural change from the supine to the standing position. We also demonstrated that the effect of orthostatic challenge on heart rate and blood pressure complexity depends on the time scale under investigation. Further, MSE values do not correlate with the mean values of heart rate and blood pressure and show only weak correlations with standard linear time and frequency measures.

Table 2. Correlation of multiscale entropy and linear measures.

		Multiscale entropy analysis: *SampEn for scale*									
		1	2	3	4	5	6	7	8	9	10
					(A)						
Supine position	*MeanNN*	0.194	−0.096	−0.171	−0.203	−0.329	−0.324	−0.201	−0.343	−0.195	−0.165
	SDNN	0.109	0.217	0.105	−0.128	−0.416	−0.513	**−0.588****	**−0.724****	**−0.691****	**−0.594****
	RMSSD	0.300	0.246	0.070	−0.163	**−0.523****	**−0.622****	**−0.712****	**−0.765****	**−0.764****	**−0.693****
	LF	−0.038	0.162	0.232	0.075	−0.233	−0.377	−0.442	**−0.616****	**−0.606****	**−0.532****
	HF	0.318	0.372	0.207	−0.081	−0.468	**−0.562****	**−0.664****	**−0.716****	**−0.752****	**−0.697****
Standing position	*MeanNN*	0.339	0.425	0.306	0.112	0.174	0.091	0.090	−0.342	−0.123	−0.169
	SDNN	0.007	0.194	0.318	0.216	0.333	0.033	0.159	−0.292	−0.112	−0.088
	RMSSD	0.241	0.332	0.419	0.313	0.403	0.077	0.153	−0.236	−0.099	−0.165
	LF	−0.059	0.152	0.344	0.360	0.460	0.188	0.197	−0.138	0.037	−0.143
	HF	0.200	0.346	0.445	0.316	0.332	0.096	0.142	−0.283	−0.210	−0.168
					(B)						
Supine position	*Mean SBP*	0.240	0.192	0.206	0.080	−0.036	−0.037	0.083	0.017	−0.074	−0.041
	SD SBP	**−0.802****	**−0.585****	−0.377	−0.371	−0.312	−0.198	−0.448	−0.333	−0.120	−0.109
	RMSSD SBP	0.264	0.356	0.102	−0.159	−0.228	−0.171	−0.109	−0.110	−0.204	−0.186
	LF	**−0.640****	−0.299	0.103	0.131	0.178	0.209	−0.032	0.049	0.344	0.330
	HF	0.294	0.501	0.068	−0.203	−0.243	−0.212	−0.168	−0.114	−0.166	−0.035

Table 2. (Continued.)

		Multiscale entropy analysis: *SampEn for scale*									
		1	2	3	4	5	6	7	8	9	10
Standing position	*Mean SBP*	−0.007	−0.028	0.008	−0.014	0.089	−0.007	−0.052	0.031	0.050	0.331
	SD SBP	−0.471	−0.340	−0.246	−0.252	−0.284	−0.471	−0.132	−0.157	−0.184	−0.102
	RMSSD SBP	0.444	0.455	0.270	0.188	0.194	0.444	0.058	−0.082	0.051	0.079
	LF	−0.208	0.053	0.314	0.301	0.200	−0.208	0.296	−0.083	0.019	0.062
	HF	0.386	0.432	0.255	0.165	0.125	0.386	0.079	−0.112	−0.032	−0.105
					(C)						
Supine position	*Mean DBP*	−0.347	0.112	0.233	0.372	0.349	0.147	0.147	−0.063	0.379	0.323
	SD DBP	0.081	−0.214	0.036	−0.014	−0.085	−0.163	−0.086	−0.205	0.023	−0.147
	RMSSD DBP	0.741	0.274	0.171	−0.063	−0.106	−0.269	−0.295	−0.143	−0.185	−0.425
	LF	−0.023	0.167	0.454	**0.518****	0.485	0.227	0.215	−0.038	0.137	0.063
	HF	**0.804****	0.415	0.192	−0.086	−0.106	−0.275	−0.351	−0.160	−0.200	−0.421
Standing position	*Mean DBP*	−0.173	−0.200	−0.100	0.001	−0.141	0.295	0.165	0.059	0.005	−0.167
	SD DBP	−0.360	−0.227	−0.143	−0.180	−0.205	0.012	0.041	−0.060	0.296	0.107
	RMSSD DBP	0.475	0.366	0.246	0.105	0.054	0.138	0.027	0.095	0.349	−0.069
	LF	−0.181	0.162	0.361	0.349	0.184	0.437	0.192	0.001	0.309	−0.077
	HF	0.323	0.166	0.069	−0.122	−0.122	−0.181	0.033	0.082	0.396	−0.083

Values are Spearman correlation coefficients calculated between sample entropy values of scales 1–10 (columns) and linear measures of heart rate variability (A), systolic (B) and diastolic blood pressure variability (C). Significant correlations are highlighted in bold. Single asterisks indicate correlations significant at the 0.05 level (two-tailed). Double asterisks indicate correlations significant at the 0.01 level (two-tailed).

Fluctuations in cardiovascular signals exhibit complex structures that have received attention only recently (Peng *et al* 2009). Understanding the mechanisms leading to this natural complexity is not only important at the basic scientific level, but also at the clinical level to understand the degradation of dynamical complexity that is commonly observed with disease and aging (Norris *et al* 2008, Peng *et al* 2009). In clinics, complexity measures are not used yet, as they are often difficult to interpret. The literature on the relationship between complexity measures, clinical correlates and standardized autonomic reflex tests is scarce (Kuusela *et al* 2002, Raab *et al* 2006, Baumert *et al* 2009). This is unfortunate as studies have repeatedly demonstrated that complexity measures provide information that is independent of the magnitude of cardiovascular oscillations as traditionally quantified by linear measures in the time and frequency domains (Costa *et al* 2008, Javorka *et al* 2008, 2009, Cerutti *et al* 2009, Voss *et al* 2009, Bornas *et al* 2006).

Cardiovascular regulation in the healthy human body is mediated by a variety of neural, hormonal, genetic and external interactions that operate across multiple time scales ranging from seconds to years (Costa *et al* 2008). Insight into the dynamics of biological control systems can be gained by studying the complexity of cardiovascular signals over multiple time scales (Angelini *et al* 2007).

In our study, we employed MSE analysis to investigate the effect of a shift in sympathovagal balance toward sympathetic predominance on heart rate and blood pressure complexity. In the supine as well as the standing position, we observed that entropy values of heart rate and blood pressure change as a function of the time scale. On small scales, the entropies of heart rate and blood pressure are lower than those of randomized data, demonstrating that beat-to-beat fluctuations follow regular patterns. These are mostly likely the result of regular breathing patterns and associated control mechanisms (cardio-respiratory coupling, baroreflex, hemodynamic coupling). On larger scales, the entropies of heart rate and blood pressure oscillations are larger than those of random data. This apparent paradox can be explained as follows: the coarse-graining procedure reduces the information content of random data when the scales increase. In HR and BP time series, the structure is more complex than uncorrelated noise and therefore results in higher entropy values after coarse graining.

In previous studies, the effect of orthostasis on HR complexity was predominantly assessed on the beat-to-beat time scale, ignoring the multiscale nature of cardiovascular fluctuations. In line with our MSE analysis, orthostatic challenge was reported to be accompanied by a decrease in SampEn (scale 1) of HRV (Vuksanovic and Gal 2005, Porta *et al* 2007). Our results further show that this reduction in HR entropy extends to scale 2. In contrast to that, HR entropy values on scales above 3 were consistently higher during orthostasis than in the supine position. A similar finding (i.e. a reduction in heart rate entropy on scales 1–2 and an increase on scales above 4) was described during wakefulness compared to sleep (Costa *et al* 2005), which is characterized by a similar shift in sympathovagal balance. It is noteworthy that the cross-over scale (below this scale, SampEn during orthostasis values were lower than in the supine position and above this scale, SampEn values were higher) of the heart rate signal was close to 3 in the majority of subjects. We suggest that the decrease in HR entropy on scales below 3 primarily corresponds to a decrease in respiratory sinus arrhythmia contribution due to parasympathetic inhibition during standing.

With regard to the complexity of blood pressure fluctuations, even less information is available than for heart rate. Animal studies on the effect of pharmacological blockades and acute haemorrhage showed no changes in blood pressure entropy (Beckers *et al* 2006, Batchinsky *et al* 2007). In our study, we found that scales above 3 showed the biggest differences in BP complexity caused by orthostasis (this difference was more expressed in

the diastolic BP signal), suggesting that those scales are of significance for the detection of changes in autonomic nervous system activity. Presumably, those scales reflect sympathetic activity in the vasculature that gives rise to Traube–Mayer–Herring blood pressure waves (Julien 2006). A similar pattern of changes in MSEs of SBP and DBP was found in patients with chronic heart failure and might result from elevated sympathetic nerve activity (Angelini *et al* 2007). This observation further stresses the importance of the multiscale approach in the analysis of blood pressure oscillations.

In a previous study on heart rate and blood pressure complexity in diabetic patients, we have shown that heart rate and blood pressure dysregulation was most prominent on time scales 2–4. However, these changes were only subtle compared to those observed in this study as a result of orthostatic challenge. This suggests that cardiovascular dysregulation in young diabetics is not comparable to a reciprocal shift in sympathovagal balance as occurs during orthostasis (Paton *et al* 2005). The assessment of MSE changes during maneuvers with nonreciprocal changes in autonomic nervous components balance or with directly measured sympathetic activity (Baumert *et al* 2009) could provide additional insight into MSE analysis.

4.1. Study limitations

We assessed MSE in the supine and standing positions. Our results might not be fully comparable to those obtained with a standard head-up tilt test, as active standing involves leg muscle pump action. Another limitation of our study is the relatively short duration of recording, which limited MSE analysis to scales 1–10.

5. Conclusion

MSE analysis of heart rate and blood pressure is sensitive to changes in autonomic balance as induced by postural change. The change in entropy depends on the time scale under investigation, emphasizing the importance of a multiscale approach for the analysis of cardiovascular signals analysis.

Acknowledgments

This study was supported by project of Centre of Excellence for perinatological research (CEPV II) no. 26220120036, grants VEGA no. 1/0073/09 and 1/0033/11, grant VVZ MSMT 0021622402. Dr Baumert was supported by a fellowship and project grant from the Australian Research Council (DP 110102049).

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