Correlations between Spectral Measures of Baroreflex Sensitivity Variability and HRV during Supine Position, Paced Breathing, Standing and Exercise

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Abstract

We assessed the relations between spectral and temporal measures of baroreflex sensitivity variability (BRSV) and heart rate variability (HRV) during four maneuvers that induce distinctive vagal activity. From the time-frequency distribution (TFD) of RR intervals (RR) and systolic arterial pressure (SAP), low-frequency power of RR (LF_{RR}), high-frequency power of RR (HF_{RR}), low-to-high-frequency ratio (LF_{RR}/HF_{RR}) and low-frequency power of SAP (LF_{SAP}) were computed. BRS instantaneous values, obtained by the alpha index from the low-frequency band, can be separated into a non-fluctuating part, mean BRS (BRS_m), and a variable part, BRSV. The TFD of BRSV showed a single component in the very low-frequency band (VLF_{BRS}). Correlations of both HF_{RR} and mean RR (RR_m) with VLF_{BRS} and BRS_m ranged from 0.89 to 0.90. RR_m-BRS_m correlation was greater ($p<0.01$) than the non-significant RR_m-LF_{RR}/HF_{RR} correlation (-0.38±0.39). BRS_m and VLF_{BRS} power are strongly correlated to each other and to vagal activity, and are better indexes of sympathovagal balance than the usual LF_{RR}/HF_{RR} ratio.

1. Introduction

Baroreflex sensitivity (BRS) is usually obtained from stationary recordings with suitable spectral estimation techniques such as Fourier-based methods and autoregressive models. Only a few studies have computed BRS in an instantaneous mode, employing techniques such as time-frequency wavelet transform [1] and time-frequency distributions (TFD) [2].

The fluctuating nature of BRS during daily activities has been documented [3]. Moreover, there is some evidence that BRS presents variability that is not a procedural artifact but may be an intrinsic property of cardiovascular control mechanisms [4]. However, the association between autonomic activity and the highly dynamic features presented by BRS is poorly understood. To provide insight on this issue, we assessed the relations between spectral and temporal measures of BRS variability (BRSV) and heart rate variability (HRV) during four maneuvers that induce distinctive vagal activity levels.

2. Methods

2.1. Subjects

Thirty young, healthy, nonsmoking, normotensive and sedentary subjects, 17 men and 13 women, participated. Their age, height and weight were 22.6±2.2 years, 164±9 cm and 61.4±11.2 kg respectively. Their written informed consent was requested to participate. The present study was approved by the ethics committee of our university.

2.2. Protocol

In a first visit to the laboratory, the health status and anthropometric characteristics of the volunteers were evaluated, and in a second visit the experimental stage was carried out. Four 5-min maneuvers inducing supposedly stationary state and distinctive changes in the cardiac autonomic activity were performed [5]. These were: Supine position (SP), considered as control state; controlled breathing (CB) at 0.2 Hz, which increases HRV; standing (S), which rises sympathetic activity, and a single bout of 100W cycle exercise (E), which causes an important HRV reduction. ECG and noninvasive arterial pressure were recorded during each condition.

2.3. Recorded variables and acquisition

ECG was detected at the CM5 lead using a bioelectric amplifier (Biopac Systems). None of the participants presented ectopic beats. Noninvasive arterial pressure was measured with Finapres (Ohmeda). Both signals were digitized at a sampling rate of 500 Hz via an acquisition and display system (Biopac Systems).

2.4. Data processing

All data processing was performed offline. Maximum values of R waves and systolic arterial pressure (SAP) were detected from ECG and arterial pressure traces to generate R-R intervals (RR) and SAP series, which were cubic-spline interpolated, resampled at 8 Hz and detrended using the smoothness priors method.

Auto- and cross-spectra of RR and SAP series were estimated with the smoothed pseudo-Wigner-Ville TFD to compute instantaneous values of: low-frequency power of RR (LF_{RR}), high frequency power of RR (HF_{RR}), low to high frequency ratio (LF_{RR}/HF_{RR}), low frequency power of SAP (LF_{SAP}), BRS obtained by alpha index in the low frequency band, and coherence between LF_{RR} and LF_{SAP}. Time-frequency coherences greater than 0.5 were considered significant. The trend of RR and BRS instantaneous values series were obtained from smoothness priors filters with cutoff frequencies of 0.04 and 0.003 Hz and were considered as mean RR (RR_m) and mean BRS (BRS_m) values respectively. Additionally, standard deviation (BRS_{SD}) and time-frequency spectra of BRS instantaneous values were computed. Indexes dynamics were segmented into 50-s epochs and integrated to obtain a mean value per epoch. For visualization purposes, the individual continuous dynamics were ensemble-averaged.

2.5. Statistical analysis

Data are expressed as means ± SD. Using the mean values of the epochs, linear correlations and regressions between the spectral measures of HRV, BRS_m and the temporal and spectral indexes of BRSV were computed for each subject. Comparisons of the measures between maneuvers were tested by ANOVA for repeated measures with post-hoc pairwise comparisons by the Tukey test. Statistical significance was accepted at $p<0.05$.

3. Results

$LnHF_{RR}$ decreased progressively from a maximum in CB to a minimum in E, with significant differences among maneuvers ($p<0.001$). RR_m was not different ($p>0.05$) in SP and CB but decreased gradually in S and E conditions. LF_{RR}/HF_{RR} was minimal in CB, increased in S but decreased in E, with similar mean value ($p>0.05$) to that of SP (Fig. 1).

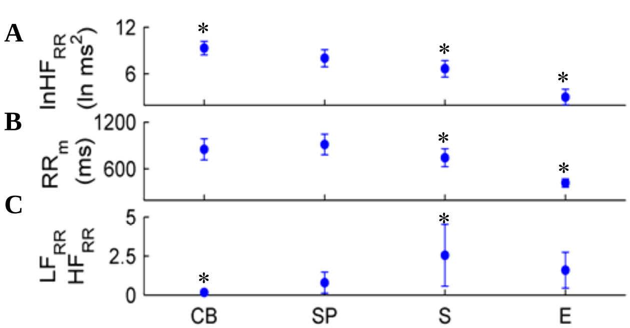

Figure 1. Means ± SD of (A) $lnHF_{RR}$ power, (B) RR_m and (C) LF_{RR}/HF_{RR} during the 4 maneuvers. *p<0.01 vs. SP condition.

Mean LF_{RR}-LF_{SAP} coherence, pooled for all subjects and maneuvers was 0.77±0.07.

BRS instantaneous values displayed low frequency oscillations whose amplitudes were affected by the maneuvers; being maximal during CB, gradually decreasing in SP and S, and reaching a minimum in E condition (Fig. 2).

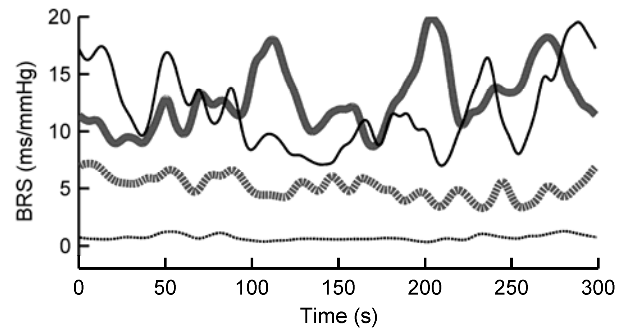

Figure 2. Representative example of the instantaneous BRS values computed by alpha index based on a TFD during the four conditions: CB: thick solid line, SP: thin solid line, S: thick dashed line, E: thin dashed line.

BRSV time-frequency spectra showed a single component in the very low frequency band (VLF_{BRS}) whose power was maximal in CB, reduced progressively in SP and S maneuvers, and minimal in E (Fig. 3).

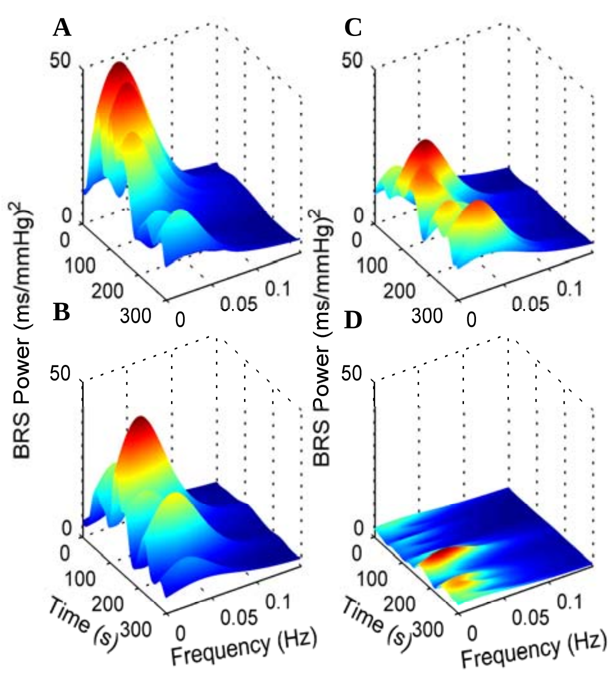

Figure 3. Representative example of BRSV time-frequency spectra during: (A) CB, (B) SP, (C) S and (D) E maneuvers.

VLF_{BRS} power, BRS_m and BRS_{SD} changed in similar direction throughout the four conditions. These measures presented significant differences ($p<0.001$) in accordance to the inequality CB>SP>S>E, except for BRS_{SD} in CB (Table 1, Fig. 4). Mean values of the instantaneous frequency of VLF_{BRS} were similar ($p>0.05$) in the four maneuvers (Table 1, Fig. 4).

Table 1. Means ± SD of the mean values of the dynamics of BRS_m, VLF_{BRS} power and instantaneous frequency as well as BRS_{SD} during the four maneuvers. N=30.

	CB	SP	S	E
BRS_m (ms/mmHg)	14.5±5.0*	12.1±5.2	7.1±1.9*	0.8±0.3*
VLF_{BRS} $(ms/mmHg)^2$	19.8±14.4*	16.0±13.7	5.7±4.6*	0.1±0.1*
VLF_{BRS} (mHz)	20.5±0.7	20.5±0.8	20.7±0.6	20.4±0.6
BRS_{SD} (ms/mmHg)	4.2±2.0	3.3±1.2	2.1±0.8*	0.3±0.2*

*$p<0.001$ vs. SP condition.

Figure 4 depicts the instantaneous dynamics of BRS_m and VLF_{BRS} power and frequency during the four maneuvers. While BRS_m attained different levels for each maneuver (Fig. 4A), VLF_{BRS} power fluctuated with amplitude dependent of the maneuver (Fig. 4B) and VLF_{BRS} frequency remained around 0.02 Hz in the four maneuvers (Fig. 4C).

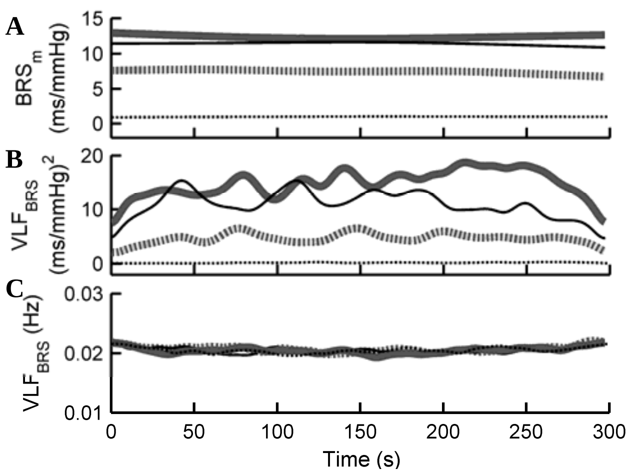

Figure 4. Ensemble averages of the dynamics of (A) BRS_m (B) VLF_{BRS} power and (C) VLF_{BRS} frequency during the four maneuvers: CB: thick solid line, SP: thin solid line, S: thick dashed line and E: thin dashed line.

Correlations of VLF_{BRS} power and BRS_m with both $lnHF_{RR}$ and RR_m were nearly 0.90 (Fig. 5). Correlation between BRS_m and VLF_{BRS} was 0.89±0.04 (Fig. 5G). Correlations of BRS_{SD} with $lnHF_{RR}$ and RR_m were about 0.72. LF_{RR}/HF_{RR}-RR_m correlation was non-significant ($p>0.05$).

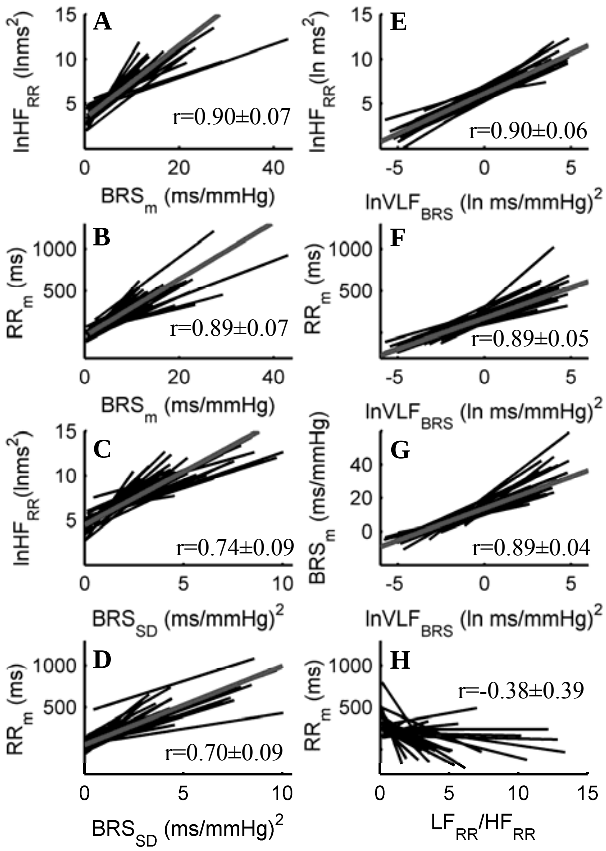

Figure 5. Individual (black lines) and mean (grey thick lines) regressions of: VLF_{SRB} and (A) $lnHF_{RR}$, (B) RR_m and (C) BRS_m; BRS_m and (E) $lnHF_{RR}$ and (F) RR_m; BRS_{SD} and (G) $lnHF_{RR}$ and (H) RR_m; (D) LF_{RR}/HF_{RR} and RR_m.

4. Discussion and conclusions

BRS instantaneous values, obtained by the alpha index computed with a TFD, can be separated into a level and variability, both showing similar changes to the maneuvers employed. Our specific findings are: (1) time-frequency spectra of BRSV instantaneous values show a single component, VLF_{BRS}, whose power, just as BRS_m, is strongly correlated to HRV measures. VLF_{BRS} frequency is centered in 0.021±0.001Hz, with no significant changes among the four maneuvers. (2) Correlations of RR_m with both BRS_m and VLF_{BSR} power are greater than those with LF_{RR}/HF_{RR} ratio. This last index fails to indicate the sympathetic activity increase produced by E condition.

BRS_m values obtained during the different maneuvers are similar to the values reported for the same maneuvers but computed using the Welch periodogram method for stationary series: the greatest values correspond to CB and the smallest to E [5]. However, TFDs present two advantages when computing BRS: because they do not require stationarity, testing it is no longer necessary; and, given their ability to provide instantaneous power and frequency values, they yield further information, such as the novel time-frequency spectra of BRSV found in the present study. Therefore, we suggest using TFDs instead of stationary spectral techniques when computing BRS_m and BRSV.

Only LF_{RR} and LF_{SAP} powers can be used to compute BRS by alpha index, because the BRS values found in the high frequency band are inconsistent due to respiratory influences [5]. The high coherences found between LF_{RR} and LF_{SAP} fulfilled the coherence requirement for the validity of BRS values.

Each maneuver produced distinctive effects on HF_{RR} power: high vagal outflow in CB, intermediate in S and very low in E [5]. LF_{RR}/HF_{RR} is not a consistent marker of sympathovagal balance because it fails to indicate the increase of cardiac sympathetic activity during E, established by the lack of differences between E and SP conditions (Fig. 1).

BRS dynamics, resolved by the alpha index in the low frequency band estimated by a TFD, can be separated into a non-fluctuating portion, BRS_m, and a fluctuating portion, BRSV. Analogously to the use of RR_m as a gross marker of autonomic activity tone [6] and of HF_{RR} as a satisfactory index of vagal modulation [7], BRS_m indicates the tone and VLF_{BRS} power the modulation. Both tone and modulation of BRS changed in the same direction throughout the maneuvers. BRS describes the ability of baroreflex to change heart period in response to a change in arterial pressure [4], with a quantitative level associated to a specific functional state. According to our findings, this conception can be refined by incorporating the notion that BRS itself presents variability, with a rhythm quasi fixed at the very low frequency band whose amplitude is linearly related with its tone (BRSm) and with the vagal activity level. The single BRSV spectral component, centered around 20.5 mHz in all the studied conditions, underlies to and interplays with the dynamic sympathetic and vagal activity rhythms, whose central frequencies fluctuate over the narrow low frequency band and the wider and respiratory-coherent high frequency band respectively. It has been reported that BRSV presents a frequency of 0.012±0.003 Hz, estimated by autoregressive modeling [8]. In our study the instantaneous central frequency of VLF_{BRS} was about twice as large as the reported one. The maneuvers we used produce characteristic inputs that determine specific baroreflex responses. The resulting degree of BRS tone-modulation drives the degree of autonomic tone-modulation, in direct relation with vagal activity and inverse relation with sympathetic outflow. When BRS increases, as in CB maneuver → ↑BRS_m and ↑VLF_{BRS} power → ↑vagal and ↓sympathetic outflows → HRV increase. When BRS diminishes, as in S and even more in E condition → ↓BRS_m and ↓VLF_{BRS} power → ↑sympathetic and ↓vagal outflows→ HRV decrease.

BRS_m and VLF_{BRS} power could be used as more consistent indexes of sympathovagal balance than LF_{RR}/HF_{RR}, as supported by: (1) the distinctive values presented by both measures in response to each maneuver; (2) the non-significant correlations found between RR_m and LF_{RR}/HF_{RR}; (3) the inability of the latter to indicate the sympathetic increase during exercise, and (4) the strong correlations of BRS_m and VLF_{BRS} power with vagal activity measures.

In conclusion: (1) BRS instantaneous values can be separated into a tone, represented by BRS_m, and a modulation, indicated by VLF_{BRS}, both of which are linearly related to each other and to the tone (RR_m) and modulation (HF_{RR}) of vagal outflow; (2) both BRS_m and VLF_{BRS} power can be employed as better measures of sympathovagal balance than the usual LF_{RR}/HF_{RR}, and (3) the use of TFDs to compute BRS by the alpha index is better than the usual methodologies because they do not require stationary series and can provide instantaneous values that yield further functional information.

References

[1] Keissar K, Maestri R, Pinna G, La Rovere M, Gilad O. Non-invasive baroreflex sensitivity assessment using wavelet transfer function-based time-frequency analysis. Physiol Meas 2010;31:1021-36.

[2] Orini M, Laguna P, Mainardi L, Bailón R. Assessment of the dynamic interactions between heart rate and arterial pressure by the cross-time frequency analysis. Physiol Meas 2012;33:315-31.

[3] Parati G. Arterial baroreflex control of heart rate: determining factors and methods to assess its spontaneous modulation. J Physiol 2005;565:706-7.

[4] Karemaker J, Wesseling K. Variability in cardiovascular control: the baroreflex reconsidered. Cardiovasc Eng 2008;8:23-9.

[5] Carrasco-Sosa S, Gaitán-González M, González-Camarena R, Yáñez-Suárez O. Baroreflex sensitivity assessment and heart rate variability: relation to maneuver and technique. Eur J Appl Physiol 2005;95:265-75.

[6] Palatini P. Heart rate and the cardiometabolic risk. Curr Hypertens Rep 2013;15:253-9.

[7] Parati G, Mancia G, Di Rienzo M, Castiglioni P. Point:counterpoint: cardiovascular variability is/is not an index of autonomic control of circulation. J Appl Physiol 2006;101:676-8.

[8] Eckberg D, Kuusela T. Human vagal baroreflex sensitivity fluctuates widely and rhythmically at very low frequencies. J Physiol 2005;567:1011-9.

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