Performance of the Low Frequency Power of Pulse Pressure Variability as a Sympathetic Activity Measure during Supine Rest, Controlled Breathing, Standing and Exercise

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Abstract

In 28 healthy volunteers, we assessed the effects of 5-min maneuvers that provoke different sympathetic and respiratory activities (supine rest (SR), controlled breathing (CB), standing (S) and exercise (E)) on the instantaneous low (LF) and high frequency (HF) powers of pulse (LF_{PP}, HF_{PP}), systolic (LF_{SP}, HF_{SP}), and diastolic pressures (LF_{DP}, HF_{DP}), to associate physiological correlates to LF_{PP} and HF_{PP}, and to test the interchangeability of those of systolic and diastolic pressures. Except for LF_{DP} in E, LF_{PP}, LF_{SP} and LF_{DP} powers increased progressively from CB to SR, S and E. LF_{SP} and HF_{SP} powers were greater than LF_{DP} and HF_{DP}. Correlations of both LF_{PP} and HF_{PP} were greater with LF_{SP} and HF_{SP}. Instantaneous coherences of respiration with HF_{PP}, HF_{SP} and HF_{DP} were greater than 0.76. Sympathetic modulation is greater in LF_{SP} than in LF_{DP} and is smaller in LF_{PP} than the respiratory modulation in HF_{PP}. LF_{PP} adequately marks the progressive sympathetic increases evoked by the maneuvers, mainly due to its greater resemblance with LF_{SP}. LF_{DP} is not a satisfactory sympathetic index. LF_{SP} and HF_{SP} are not interchangeable with LF_{DP} and HF_{DP} respectively.

1. Introduction

Pulse pressure (PP) is considered a risk predictor of a wide variety of cardiovascular diseases, independent from systolic pressure (SP) and diastolic pressure (DP) [1]. Moreover, it has been found to be an index of arterial stiffening, pulse wave velocity and stroke volume magnitude [2, 3].

It has been reported that PP exhibits variability (PPV) and that its frequency spectrum presents components in the same standard low (LF) and high frequency (HF) bands as other cardiovascular variables [2]. The LF power of PPV (LF_{PP}) has been associated with baroreflex sensitivity (BRS) [2], and its HF power (HF_{PP}) has been related to respiration in ventilated patients [3].

After some evidence supporting the similarity between the frequency spectra of SP variability (SPV) and DP variability (DPV) was provided several decades ago [4], there were no further studies to corroborate it, and hence their spectral components have been used indistinctly, being referred to by the imprecise term “blood pressure variability” [5, 6]. Of the SPV and DPV spectral components, the most studied and used one is the LF power of SP (LF_{SP}), which, by the available evidence, is considered a suitable noninvasive marker of sympathetic activity [7, 8].

It is still unclear if maneuvers that modify autonomic and respiratory activities affect the spectral powers of SPV and DPV similarly. Furthermore, given that PP series, which is formed by subtracting DP from SP series, presents a power spectrum, SPV and DPV must therefore be necessarily different. Considering these notions, we examined: 1) the effects of four maneuvers that elicit different respiratory and sympathetic activity levels on the spectral powers of PPV, SPV and DPV, and 2) the relations among them and with measures of heart rate variability (HRV).

2. Methods

2.1. Subjects

Twenty-eight healthy, normotensive, nonsmoking and sedentary subjects, 16 male and 12 female, were studied. Mean age, height and weight were 22.5±2.2 years, 164±8 cm and 60.4±10.3 kg respectively. Their written informed consent was requested to participate.

2.2. Protocol

Volunteers visited the laboratory twice. The first time, their health status and anthropometric variables were evaluated, and in the second visit the experimental stage was carried out. The 5-min-long maneuvers employed to induce specific changes in the sympathetic and respiratory activities were: supine rest (SR) with spontaneous breathing as control condition; postural change from SR to standing position (S); lying with controlled breathing (CB) at 0.2 Hz with tidal volume of about 1.5 liters, and one bout of 100W cycling exercise (E). Resting periods between maneuvers were 5 min long.

2.3. Signal recording and acquisition

ECG was detected at the CM5 bipolar lead using a bioelectric amplifier (Biopac Systems). Noninvasive arterial pressure (AP) was measured by Finapres (Ohmeda). The respirogram (Res) was obtained with a stretching pneumograph (Nihon Kohden). ECG, AP and Res signals were digitized at a sampling rate of 1 kHz via an acquisition and display system (Biopac Systems).

2.4. Data processing

R-wave peaks, SP and DP values were detected from ECG and AP waveforms respectively to form the corresponding time series. DP series were beat-by-beat subtracted from SP series to generate the PP series. All time series, including Res, were cubic-spline interpolated, resampled at 4 Hz and separated into levels (RR_L, SP_L, DP_L and PP_L) and oscillations by the smoothness priors method with a cutoff frequency of 0.03Hz. Time-frequency spectra of the oscillations series, estimated with the smoothed pseudo-Wigner-Ville distribution, were integrated to compute their LF (LF_{RR} and LF_{DP}) and HF powers (HF_{RR}, HF_{SP}, HF_{DP} and HF_{Res}). Time-frequency coherences of HF_{Res} with HF_{PP}, HF_{SP} and HF_{DP} were obtained. Coherences greater than 0.5 were considered significant. Indexes dynamics were ensemble-averaged for visualization, and were segmented into 50-s epochs for statistical purposes.

2.5. Statistical analysis

Data are expressed as mean ± SD. Inter- and intra-maneuver indexes differences were tested by ANOVA for repeated measures. Post-hoc pairwise comparisons were performed by the Tukey test. Pooled means of the 50-s segments of the indexes dynamics of the four maneuvers were used to compute linear regressions and correlations for each subject. Statistical significance was accepted at $p<0.05$.

3. Results

In relation to SR (Fig.1): $\ln HF_{RR}$ power was maximal in CB and gradually decreased in S and E ($p<0.001$); RR_L progressively decreased in CB, S and E ($p<0.001$); SP_L, DP_L and PP_L increased in E condition ($p<0.001$); and respiratory frequency (RF) decreased in CB ($p<0.001$) and increased progressively in S and E ($p<0.001$).

In the time-frequency spectra of PPV and SPV, the LF power gradually rose in S and E, becoming maximal in the latter, but that of DPV did not. The HF power was different for each pressure series in each condition and greatest in E (Fig. 2).

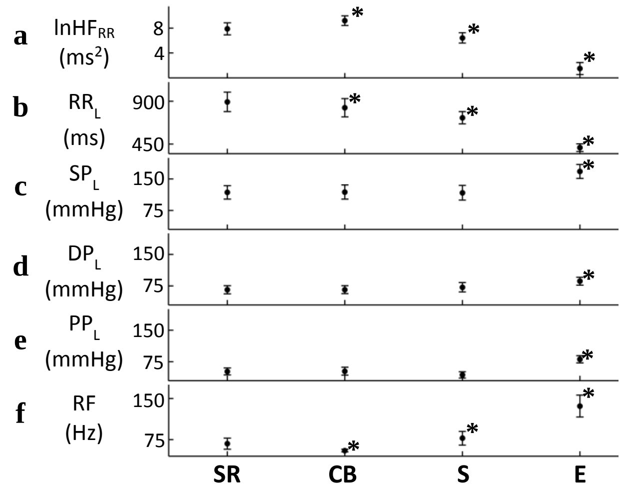

Fig. 1. Pooled means±SD of the dynamics of: a) $\ln HF_{RR}$, b) RR_L, c) SP_L, d) DP_L, e) PP_L and f) RF during the four maneuvers. *$p<0.001$ vs. SR, control condition.

Important fluctuations of instantaneous power were noticeable in both frequency bands in each maneuver.

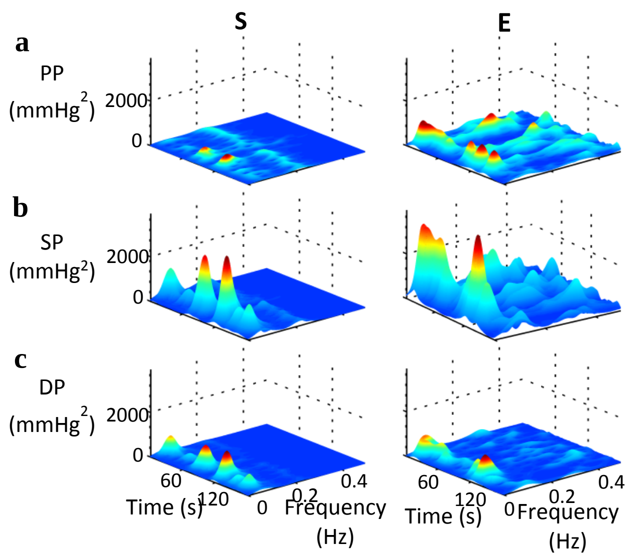

Fig. 2. Representative examples of time-frequency spectra of: a) PP, b) SP and c) DP series during S (left column) and E (right column) conditions.

In all maneuvers, pooled means of the LF powers dynamics of the three pressures were different ($p<0.001$), greatest for LF_{SP}, intermediate for LF_{DP} (around half of LF_{SP} power), and smallest for LF_{PP}, except for SR, in which LF_{DP} and LF_{PP} were similar (Fig. 3). In relation to SR, mean values of LF powers of the three pressures decreased in CB ($p<0.01$) and increased progressively in

S and E conditions ($p<0.001$), except LF_{DP} in E (Fig. 3).

In CB, S and E conditions, HF_{SP} power was greater ($p<0.03$) than HF_{PP}, and this component was in turn greater ($p<0.015$) than HF_{DP} (Fig. 3). In SR condition, only HF_{SP} was greater ($p<0.001$) than HF_{DP}. HF powers of the three pressures were maximal in E. Except in CB, LF_{SP} power was greater ($p<0.001$) than HF_{SP}. LF_{DP} was greater ($p<0.009$) than HF_{DP} in SR and S. HF_{PP} was greater ($p<0.001$) than LF_{PP} in CB, S and E.

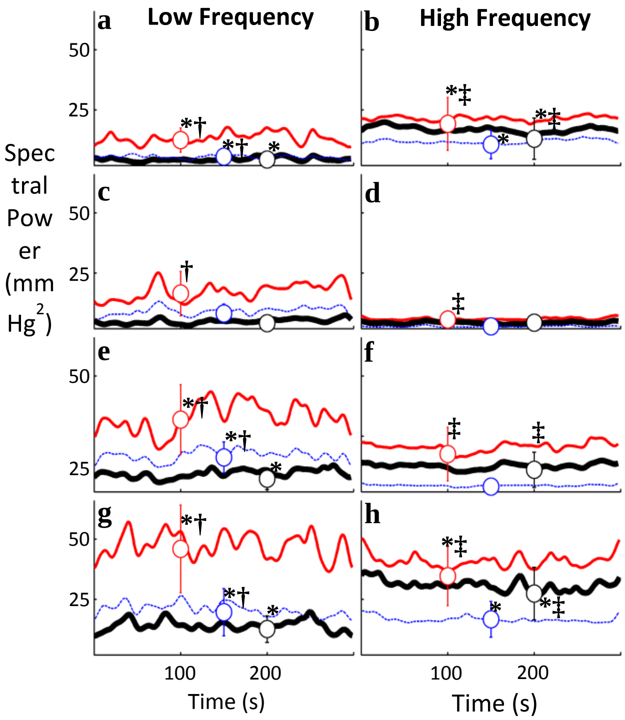

Fig. 3. Ensemble averages and pooled means±SD of instantaneous dynamics of LF and HF powers of SP (thin line), DP (dotted line) and PP (thick line) in: CB (a and b), SR (c and d), S (e and f) and E (g and h). *$p<0.01$ vs SR, †$p<0.001$ vs. LF_{PP}, ‡$p<0.015$ vs. HF_{DP}.

In the four maneuvers, pooled means of the time-frequency coherences of HF_{Res} with HF_{SP} were greater than 0.92, with HF_{PP} ranged from 0.86 to 0.96 and with HF_{DP} ranged from 0.76 to 0.96 (Fig. 4).

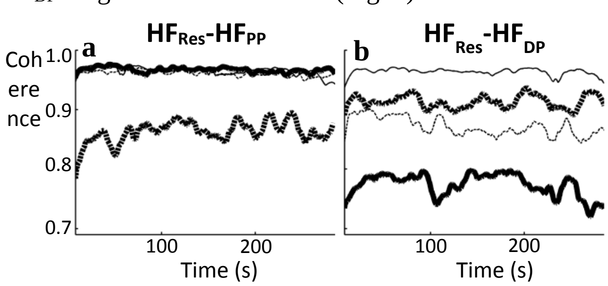

Fig. 4. Ensemble averages of (a) HF_{Res}-HF_{PP} and (b) HF_{Res}-HF_{DP} time-frequency coherences obtained in: SR (thin dotted line), CB (thin solid line), S (thick solid line) and E (thick dotted line).

While the mean correlation of LF_{PP} with LF_{SP} was 0.88±0.06 (Fig. 5a), its correlations with LF_{DP} (Fig. 5b), $lnHF_{RR}$ and RR_L ranged from -0.60 to 0.73. The correlations of HF_{PP} with HF_{SP} and HF_{DP} ranged from 0.79 to 0.84 (Fig. 5 c-d). While HF_{SP}-HF_{DP} correlation was 0.72±0.33, LF_{SP}-LF_{DP} correlation was 0.92±0.04.

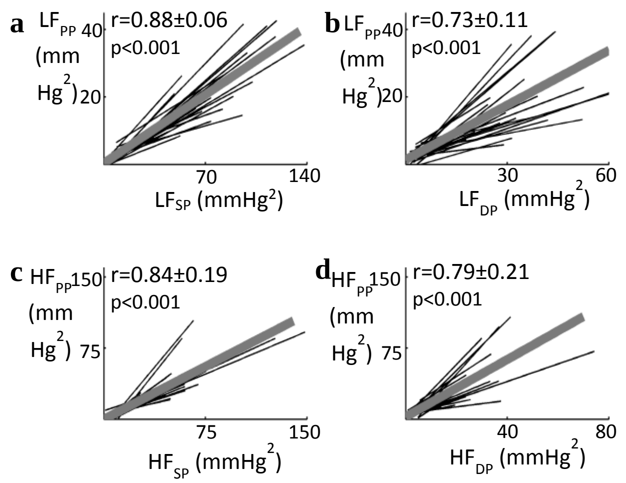

Fig. 5. Individual (black lines) and mean (thick grey lines) linear regressions of: a) LF_{PP} vs. LF_{SP}, b) LF_{PP} vs. LF_{DP}, c) HF_{PP} vs. HF_{SP}, d) HF_{PP} vs. HF_{DP} powers.

4. Discussion

This study establishes that, in healthy subjects, the time-frequency distributions (TFD) of SP and DP series are not interchangeable, and those of their difference, the PP series, are associated to sympathetic and respiratory activities. These notions are supported by the following findings: 1) LF_{PP}, LF_{SP} and LF_{DP} powers increased progressively from a minimum in CB to SR, then S and to a maximum in E, except for LF_{DP} in E, being the LF_{SP} powers nearly double those of LF_{DP}, and those of LF_{PP} the smallest. 2) Correlation of LF_{PP} with LF_{SP} was very strong, and with LF_{DP}, $lnHF_{RR}$ and RR_L were lower. 3) HF_{SP} was greater than HF_{DP} in all maneuvers, and HF_{PP} power was of intermediate value. Similarly, coherences with HF_{Res} were very high for HF_{SP} and smaller for HF_{PP} and HF_{DP}. 4) HF_{PP}-HF_{SP} correlation was strong and greater than HF_{PP}-HF_{DP}. HF_{SP}-HF_{DP} correlation was lower than that of LF_{SP}-LF_{DP}.

The progressive sympathetic activity increase and vagal withdrawal elicited by CB, SR, S, and E, were indicated by $lnHF_{RR}$ power and RR_L, and the different respiratory activities were reflected in RF (Fig.1).

The few studies that have performed spectral analysis of PPV associated LF_{PP} with BRS in subjects in supine position [2], and HF_{PP} with respiratory activity in mechanically ventilated patients [3]. These studies did not assess the close relation among the spectra of the three pressures series; specifically, they did not deal with the notion that, for PPV to present a meaningful power spectrum, SPV and DPV must be different. Moreover, it has not been clearly established how different the spectra of SPV and DPV are from one another. Based on fragile evidence, a prestigious study established that they were similar [4], and subsequently LF_{SP} and LF_{DP} powers have been indistinctly employed as sympathetic markers, the former more frequently than the latter [5].

In our study, in response to all maneuvers, both LF and HF powers of SPV are around double those of DPV; therefore, their differences necessarily generate the LF and HF powers of PPV. To the best of our knowledge, this is the first study to: 1) explore the effects of sympathetic maneuvers on the TFD of PPV, associating the sympathetic activity to its LF power and the respiratory influence to its HF power as physiological correlates, and, in consequence 2) document the non-interchangeability of the TFD of SPV and DPV.

LF_{SP} power is an adequate noninvasive sympathetic marker with enough supporting evidence published [6, 8]. In contrast, the evidence that supports the performance of LF_{DP} as sympathetic activity marker is rare. Our finding that LF_{SP} power is around two times larger than LF_{DP} indicates that the sympathetic activation elicited by the maneuvers affect SPV and DPV differently. The greater increments of LF_{SP} and its better correlation with LF_{PP} during the maneuvers, suggest that LF_{PP} is more influenced by LF_{SP} than by LF_{DP} power. While both LF_{SP} and LF_{PP} powers discriminated the progressively raising sympathetic activation in CB, SR, S and E, LF_{DP} was unable to indicate the greater sympathetic activation provoked by E (Fig. 3); therefore, its performance as sympathetic activity marker is not acceptable. The similar performance of LF_{PP} and LF_{SP}, and their moderate correlation with HRV measures, which disagrees with the reported lack of correlation [2], support that LF_{PP} is a suitable noninvasive index of sympathetic activity.

Our findings that HF_{SP} is greater than HF_{PP} and this is in turn greater than HF_{DP} (Fig. 3) disagree with the reported results [2]. Their different coherences with HF_{Res}, together with the diverse correlations between HF_{PP}, HF_{SP} and HF_{DP}, suggest that HF power of each pressure is influenced differently by Res, with a greater effect in SPV than in DPV. That the respiratory effect on the three pressures is maximal in E and prominent in S, the maneuvers that course with minimal vagal modulation, suggest that it is mechanically mediated. While in SR and CB, the respiratory effect may also be produced by vagal modulation, which is maximal in the last maneuver (Fig. 1). Thus, the physiological correlate of the resulting HF_{PP} power must be the respiratory activity, mediated by both vagal and mechanical effects. The greater powers and correlations of LF_{SP} and LF_{DP} than those of HF_{SP} and HF_{DP} suggest that the sympathetic modulatory effect is greater and more uniform than the respiratory one, and that it is the main source of variability for SP and DP (Fig. 5). In contrast, the result that HF_{PP} is greater than LF_{PP} in all maneuvers suggests that respiratory activity is the main source of PPV.

In conclusion, the sympathetic and respiratory activities elicited by the maneuvers provoke a modulation nearly double in SPV than in DPV, yielding the PPV. The progressive sympathetic increases evoked by the maneuvers, estimated by HF_{RR} power and RR_L, are adequately marked by LF_{PP}, mainly due to its greater resemblance with LF_{SP} than with LF_{DP}. The performance of LF_{DP} as sympathetic index is not adequate. The respiratory modulation, mechanical and vagally mediated and indicated by the HF powers, affects the three pressures series differently. Furthermore, it is smaller than the sympathetic modulation in SPV and DPV but greater in PPV. Thus, LF_{SP} and HF_{SP} are not interchangeable with LF_{DP} and HF_{DP} powers respectively.

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