Central Frequency of Low Frequency Component of HRV Estimates Sympathetic Activity during Dynamic Exercise, Standing and Paced Breathing Maneuvers

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Abstract

In 25 healthy subjects we assessed the effects of the maneuvers supine position (S), dynamic exercise (DE), standing (ST), controlled breathing (CB) and DE recovery (DER) on the time-courses of: central frequencies and powers of the low and high frequency components of RR ($\text{LF}_{\text{RR}}$, $\rho_{\text{LF}_{\text{RR}}}$, $\mu_{\text{HF}_{\text{RR}}}$), systolic ($\text{LF}_{\text{SP}}$, $\rho_{\text{LF}_{\text{SP}}}$) and diastolic ($\text{LF}_{\text{DP}}$, $\rho_{\text{LF}_{\text{DP}}}$) pressures, estimated by a time-frequency distribution, and of $\rho_{\text{LF}_{\text{RR}}}$/$\mu_{\text{HF}_{\text{RR}}}$ and $\text{CF}_{\text{LF}_{\text{RR}}}$/$\mu_{\text{HF}_{\text{RR}}}$ ratios. Relative to S, significant means changes ($p<0.03$) were: $\text{CF}_{\text{LF}_{\text{RR}}}$ and $\mu_{\text{HF}_{\text{RR}}}$ increased in CB and decreased distinctively in ST, DE and DER; $\rho_{\text{LF}_{\text{RR}}}$/$\mu_{\text{HF}_{\text{RR}}}$ decreased in CB and increased distinctly in ST, DE and DER; $\rho_{\text{LF}_{\text{RR}}}$ only decreased pronouncedly in DE. $\rho_{\text{LF}_{\text{RR}}}$/$\mu_{\text{HF}_{\text{RR}}}$ means were similar in ST, DE and DER. In S, CB, ST and DER, $\text{CF}_{\text{LF}_{\text{RR}}}$ was greater ($p<0.005$) than $\text{CF}_{\text{LF}_{\text{DP}}}$ and $\text{CF}_{\text{LF}_{\text{SP}}}$.

Correlations of $\text{CF}_{\text{LF}_{\text{RR}}}$ with $\rho_{\text{HF}_{\text{RR}}}$ and mean RR were $0.78\pm0.07$ and $0.64\pm0.12$ respectively. That $\text{CF}_{\text{LF}_{\text{RR}}}$ estimates the sympathetic activity (SA) level of each maneuver, is strongly correlated with $\rho_{\text{HF}_{\text{RR}}}$ improving the estimating capability of the ratio in DE, and is greater than $\text{CF}_{\text{LF}_{\text{DP}}}$, strengthen our previous reports that $\text{CF}_{\text{LF}_{\text{RR}}}$ is a trustable SA indicator, relevantly in DE, and that the sympathetic modulatory frequency of the cardiac branch is greater than the vasomotor one.

1. Introduction

The leftward shift of the central frequency of the low-frequency component ($\text{CF}_{\text{LF}}$) of RR series ($\text{CF}_{\text{LF}_{\text{RR}}}$) as an effect provoked by maneuvers that increase sympathetic activity (SA) has been poorly studied. Active orthostatic test, head-up tilt and dynamic exercise (DE) are the provocative maneuvers more frequently used to study autonomic cardiovascular function; they cause SA increment with vagal activity (VA) reduction [1]. The leftward shift of $\text{CF}_{\text{LF}_{\text{RR}}}$ was first reported during standing condition (ST) with autonomic blockade [2]. The relation of $\text{CF}_{\text{LF}_{\text{RR}}}$ leftward shift produced by head-up tilt with the arterial pressure was studied with autoregressive modeling [3]. In a study about the effect of steady-state DE on HRV spectrum a $\text{CF}_{\text{LF}_{\text{RR}}}$ leftward shift was found [4]. In none of the previous studies, or in the 1996 Task Force report on HRV [5] or a recent review of methods to study the autonomic cardiovascular function [1] the possible use of $\text{CF}_{\text{LF}_{\text{RR}}}$ as an autonomic activity spectral estimator has been considered. Conversely, in a study about the effects of continuously increasing static exercise on $\text{CF}_{\text{LF}_{\text{RR}}}$ and on the $\text{CF}_{\text{LF}_{\text{SP}}}$ and diastolic pressure ($\text{CF}_{\text{LF}_{\text{DP}}}$), we provided evidence that support the performance of all $\text{CF}_{\text{LF}}$ as adequate SA spectral estimators [6]. Additionally, in that same study we documented that $\text{CF}_{\text{LF}_{\text{RR}}}$ was of greater value than $\text{CF}_{\text{LF}_{\text{SP}}}$ and $\text{CF}_{\text{LF}_{\text{DP}}}$, finding attributed to functional differences between the cardiac and vasomotor sympathetic branches [6]. It has been reported that, during DE, total HRV and the powers of the high frequency ($\rho_{\text{HF}_{\text{RR}}}$) and low frequency ($\rho_{\text{LF}_{\text{RR}}}$) components of RR are reduced; therefore, $\rho_{\text{LF}_{\text{RR}}}$ and the derived $\rho_{\text{LF}_{\text{RR}}}$/$\mu_{\text{HF}_{\text{RR}}}$ ratio fail to mark the SA increment elicited [4, 7]. We assume that: a) the maneuvers supine position (S), controlled breathing (CB), ST and DE elicit different degrees of SA; b) SA can be assessed by the usual autonomic activity indexes; c) the study of recovery from DE (DER) allows documenting the reversibility of the effects of DE; d) the maneuvers considered affect $\text{CF}_{\text{LF}_{\text{RR}}}$, $\text{CF}_{\text{LF}_{\text{SP}}}$ and $\text{CF}_{\text{LF}_{\text{DP}}}$; e) $\text{CF}_{\text{LF}_{\text{RR}}}$ is strongly correlated with other autonomic activity measures; f) and that in all the maneuvers studied $\text{CF}_{\text{LF}_{\text{RR}}}$ is greater than $\text{CF}_{\text{LF}_{\text{SP}}}$ and $\text{CF}_{\text{LF}_{\text{DP}}}$. To provide further support to our aforementioned previously reported findings, our aims were, in 25 healthy subjects, to assess the effects of S, DE, ST, CB and DER –each maneuver lasting 5 min– on the time-courses of $\text{CF}_{\text{LF}_{\text{RR}}}$, $\text{CF}_{\text{LF}_{\text{DP}}}$, $\rho_{\text{LF}_{\text{RR}}}$, $\rho_{\text{HF}_{\text{RR}}}$, all estimated by a time-frequency distribution, and of the computes $\rho_{\text{LF}_{\text{RR}}}$/$\mu_{\text{HF}_{\text{RR}}}$ and $\text{CF}_{\text{LF}_{\text{RR}}}$/$\mu_{\text{HF}_{\text{RR}}}$ ratios. Comparisons and correlations among spectral measures will be obtained.

2. Methods

2.1. Subjects

Twenty five healthy, nonsmoking and sedentary subjects, 14 men and 11 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. This study was
approved by the ethics committee of our university.

2.2. Protocol

In the first visit to the laboratory, the 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 changes in SA were: S with spontaneous breathing, considered the control condition; ST, change from S to erect position; CB in S position at 0.2 Hz with increased tidal volume of around 2.0 liters; DE, a single bout of 100W cycling exercise, and DER, sitting quietly. ECG, arterial pressure (AP) and respiration were recorded all over the session.

2.3. Signal recording and acquisition

ECG was detected at the thoracic bipolar lead CM5 using a bioelectric amplifier (Biopac Systems). Non-invasive AP was measured by Finapres (Ohmeda). Respirogram was obtained by a stretching pneumograph (Nihon Kohden). All signals were digitized at a sampling rate of 1 kHz via an acquisition and display system (Biopac Systems).

2.4. Data processing

Fiducial points of ECG and AP recordings were detected to construct the RR, systolic pressure (SP) and diastolic pressure (DP) time series, which were cubic-spline interpolated, resampled at 4 Hz and detrended. Time-frequency spectra of the series were estimated with the smoothed pseudo-Wigner-Ville distribution and their first two-order moments were computed in the standard low and high frequency bands to obtain the instantaneous time courses of low frequency power of SP (pLFSP), and of DP (pLFDP), LFRR, HFRR, LFSP, and LFDP. LFRR/pHFRR and LFRR/pHFRR ratios were computed.

2.5. Statistical analysis

Data are expressed as mean±SD. Inter-manuever and inter-variable means comparisons were performed with ANOVA for repeated measures. Post-hoc pairwise comparisons were performed by the Tukey test. 50-s epochs of variables dynamics were used to compute subject-by-subject correlation and regression of LFRR with HFRR and mean RR (RRm). Statistical significance was set at p<0.05.

3. Results

Relative to S, mean values of: LFRR increased in CB (p<0.03) and decreased in ST (p<0.001) and DE (p<0.001) but were similar in DER (Fig. 1A), with a shift range across maneuvers of 25 mHz; LFSP and LFDP showed similar changes across the maneuvers, increasing in CB, ST and DER (p<0.003, Fig. 1B-C), with a shift range of 5 mHz. The mean values of LFRR were greater (p<0.003) than those of LFDP in S (10±5 mHz), CB (15±5 mHz), ST (3±3 mHz) and DER (4±4 mHz), but were similar in DE (0±3 mHz) (Fig. 1).

Fig. 1. Mean±SD of: A) LFRR, B) LFSP, C) LFDP during the 5 maneuvers. * p<0.05 vs. S.

Relative to S condition, mean values of: LFRR only decreased pronouncedly in DE (p<0.001, Fig. 2A), LFSP and LFDP displayed parallel changes across maneuvers, no change in CB, increase in ST, DE and DER (p<0.03, Fig. 2B-C); HFRR increased in CB and decreased in ST, DE and DER (p<0.001, Fig. 2D).

Fig. 2. Mean±SD of: A) LFRR, B) LFSP, C) LFDP, D) HFRR during the 5 maneuvers. * p<0.05 vs. S.
With respect to S, mean values of RR_m decreased in CB, ST, DE and DER (p<0.01, Fig. 3A); pLF_RR/ LF_HF decreased in CB (p<0.01) and increased in ST, DE and DER (p<0.005), but similar in ST and DE (Fig. 3B); cLF_RR/ LF_HF decreased in CB (p<0.03) and increased in ST (p<0.01), DE (p<0.001) and DER (p<0.001) (Fig. 3C).

Fig. 3. Mean±SD of: A) RR_m, B) pLF_RR/ LF_HF, C) cLF_RR/ LF_HF during the 5 maneuvers. *p<0.05 vs. S.

For cLF_RR, LF_HF, LF_SP, RR_m and cLF_RR/ LF_HF, all of the paired mean comparisons among the five maneuvers were different (p<0.01). The mean values of all measures presented large SD values, indicative of the high intersubject response variation.

Mean correlation of cLF_RR with LF_HF was 0.78±0.07 (p<0.001, Fig. 4A) and with RR_m was 0.64±0.12 (p<0.01, Fig. 4B).

Fig. 4. Mean linear regression (red) computed from the individual regressions (black) between cLF_RR and: A) LF_HF, B) RR_m.

4. Discussion

Using five maneuvers that provoke distinct degrees of SA as estimated by the usual robust autonomic indexes, LF_HF and RR_m, we provide evidence that cLF_RR, in a relevant fashion and, to a lesser degree, cLF_SP and cLF_DP, present distinctive changes that are inversely proportional to the SA level, which makes their use as quantitative SA estimators feasible. Our main findings are: 1) with respect to S, the mean values of: cLF_RR and LF_HF increase in CB and decrease distinctively in ST and DE (Fig. 2A and 3D); pLF_RR only decreases pronouncedly in DE; cLF_SP and cLF_DP augment in CB, ST and DER (Fig. 2B-C); cLF_RR/ LF_HF ratio decrease in CB and increase distinctively in ST and DER (Fig. 4C); LF_RR/ LF_HF ratio increased in ST, DE and DER but with similar mean values (Fig. 4B); LF_SP and LF_DP increased distinctively in S, DE and DER (Fig. 3B-C). 2) cLF_RR presents strong correlations with LF_HF and RR_m (Fig. 5). 3) cLF_RR mean values are greater than those of cLF_DP in S, CB, ST and DER but similar in DE (Fig. 2).

CB at 0.2 Hz elicits, possibly via central command, an increase of VA [1], although the associated SA degree has not been reported. In our study and in relation to S, considered as the baseline condition for SA and cLF_RR, CB shifted cLF_RR 11 mHz to the right, raising its level to a maximum, without significantly changing pLF_RR, which, associated to the also maximal LF_HF, suggests that CB induces the minimal SA degree. This finding is relevant because only the maneuver-induced leftward shifts of cLF_RR have been reported.

There is agreement in that SA increases, via baroreflex activation, a SA increment for the adaptive adjustment of the cardiovascular response to the postural change [1]. The cLF_RR leftward shift was first documented during ST, accentuated by low-dose atropine, and was attributed to the VA reduction that this maneuver produces [2], although later it was found to be independent of respiratory frequency changes [8]. Also, the cLF_RR leftward shift provoked by tilt has been ascribed to the AP resonance loop [3]. Our findings corroborate that ST elicited a 4-mHz leftward shift of cLF_RR, whose value is consistent with those achieved by LF_HF and LF_SP, assessing the SA degree provoked by ST to a level between those of S and DE.

The cLF_RR leftward shift reported during DE was also attributed to the VA fall caused by this maneuver [4]. In our study, the maximal cLF_RR leftward shift is attained during DE (11 mHz), which, together with the minimal levels of LF_HF and RR_m, and in agreement with the 4:1 SA/VA proportion reported [9], allows to qualify the SA degree elicited by DE as the maximal among the maneuvers studied. During DE, pLF_RR decreases sharply [4]; consequently, the pLF_RR/ LF_HF ratio is also reduced and neither indicates the expected large SA increase induced by DE [7]. In contrast, when we pragmatically substituted the minimized pLF_RR with the maximized cLF_RR for computing an index of the sympathetic balance, the cLF_RR/ LF_HF ratio adequately distinguished and assessed the level of SA in DE as maximal.

Our findings corroborate the cLF_RR leftward shift in
DE reported by others, but we disagree with the notion that it is caused by the VA reduction both in this maneuver and in ST [2, 8, 4]. Instead, we attribute it to the SA increment provoked by these maneuvers. This explanation is further supported by the shift of CF LFDP, in which VA does not participate, only vasomotor SA.

After the termination of DE, SA and VA tend to return to their baseline values. In this study, CF LFRR shows a return to its baseline in accordance with the tendency presented by FHRR, RRm, and LFSP, further documenting the reversibility of the maximal CF LFRR leftward shift provoked by DE [4].

In a previous study we reported that CF LFRR, CF LFSP and CF LFDP shifted leftwards in association to the progressive increment of SA produced by continuously increasing static exercise [6]. We now extend these findings to DE, a maneuver that elicits SA increment and cardiac VA reduction via the central command, provoking important heart rate increments and HRV reductions in both low and high frequency bands [9].

Taken together, the evidence previously reported by us and others, as well as the one provided by this study, support the adequate performance of CF LF as indexes of the cardiovascular autonomic activity, although their specificity for SA or VA has not yet been convincingly demonstrated, requiring further study.

Specifically, our findings suggest that CF LFRR distinctly evaluates the SA level evoked by each maneuver, and that it varies inversely proportional to SA, properties that support the possible use of CF LFRR as a reliable SA spectral measure.

Our findings also document that the maneuvers studied, significantly CB and ST, affected CF LFSP and CF LFDP, with respect to CF LFSP, presents: greater dynamic range across the maneuvers, stronger correlations with FHRR and RRm, greater values in S, CB, ST and DER but similar values in DE. This last difference corroborates our previously reported finding that during control, in the stages prior to the maximum and during the recovery from static exercise, CF LFRR was greater than CF LFDP, but was similar at the maximal intensity of static exercise, where SA achieves its maximum [6]. This finding was roughly attributed to functional differences between the cardiac and vasomotor sympathetic branches.

Based on the modulation in the low frequency band presented by the SA, which corresponds to those of the HRV and AP variability spectra [10], a possible explanation of the larger CF LFRR and its greater range of shift than CF LFDP is that both the CF LF and the shift range of the cardiac sympathetic branch are larger than those of the vasomotor sympathetic branch. Thus, CF LFRR and CF LFDP possibly estimate the same frequency modulation properties presented by SA in its cardiac and vasomotor branches respectively.

In conclusion, the sum of our findings: 1) the progressive CF LFRR decrease from a maximum obtained in CB followed by S to a minimum in DE and its return to baseline in DER, 2) the strong correlation between CF LFRR with the robust autonomic markers FHRR and RRm and 3) that the different levels of SA elicited by the maneuvers are better discriminated by CF LFRR/FHRR than by FHRR/RRm ratio, support that CF LFRR performs adequately as a quantitative SA estimator, relevantly in DE, and that it could replace pLFRR for computing the sympathovagal balance. The striking finding that CF LFRR is greater than CF LFDP in S, CB, ST and DER although similar in DE, suggests that the cardiac SA presents greater modulating frequency than the vasomotor SA, strengthening our previously reported findings.

References


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