Performance of Low-Frequency Power of the Maximal Amplitude of the First Derivative of Arterial Pressure Waveform as a Cardiac Sympathetic Activity Index

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Abstract

We assessed the time-frequency spectra of the maximal amplitude of arterial pulse first derivative (dP/dt_{max}) series during four maneuvers provoking different sympathetic activity levels, and examined the relations between dP/dt_{max} spectral measures and those of heart rate, systolic pressure (SP), and respiratory variabilities. Thirty healthy subjects performed 5-min maneuvers: lying, controlled breathing, standing (S) and exercise (E). Time-frequency spectra of RR intervals (RR), SP, dP/dt_{max} and respiration (Res) time series were estimated to compute their low-frequency powers (LF_{SP}, $LFdP/dt_{max}$), high-frequency powers (HF_{RR}, $HFdP/dt_{max}$, HF_{Res}), and $HFdP/dt_{max}$-HF_{Res} time-frequency coherence. While LF_{SP} and $LFdP/dt_{max}$ increased in S and E, HF_{RR} and RR level decreased. Correlations of HF_{RR} and RR level with $LFdP/dt_{max}$ were very strong and greater than with LF_{SP}. $HFdP/dt_{max}$ was maximal in E and showed significant coherences with HF_{Res}. $LFdP/dt_{max}$ and LF_{SP} correctly indicate the increasing levels of sympathetic activation in S and E. Thus, $LFdP/dt_{max}$ power can be considered a suitable noninvasive cardiac sympathetic activity-contractility index, complementary to LF_{SP}, which is associated to vasomotor sympathetic activity. $HFdP/dt_{max}$ power is originated by a mechanical respiratory effect.

1. Introduction

The first derivative of the arterial pulse is a reliable and valuable tool in assessing the cardiovascular function of healthy and ill subjects [1]. The maximal amplitude of first derivative of arterial pulse (dP/dt_{max}) has been used as a noninvasive index of the mean systolic ejection rate [2] and of cardiac contractility in various research and clinical settings such as exercise [3], pediatric [4] and critically ill patients [5].

Low-frequency (LF) power of systolic pressure (LF_{SP}) has been employed in clinical studies as a noninvasive indicator of sympathetic vasomotor activity [6]. However, it does not estimate cardiac contractility directly.

No studies have assessed the beat-to-beat variability of arterial dP/dt_{max} time series. By analyzing dP/dt_{max} series variability with a time-frequency distribution (TFD) it could be documented if its spectral measures are associated to autonomic and respiratory states. Thus, in healthy subjects, we assessed the time-frequency spectra of arterial pulse dP/dt_{max} series during four maneuvers that provoke different levels of autonomic activity, and examined the relations of its spectral measures with those of heart rate (HRV), systolic pressure (SPV), and respiratory variabilities.

2. Methods

2.1. Subjects

Thirty healthy, normotensive and sedentary subjects, 13 men and 17 women, were studied. Mean age, height and weight were 23.4±1.6 years, 164±8 cm and 61.2±13 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 cardiac autonomic activity were: lying with spontaneous breathing (L), considered the control condition; postural change from lying to standing position (S), which elicits a sympathetic activity increase; lying with controlled breathing (CB) at 0.2 Hz that increases vagal modulation, and a single bout of 100W cycling exercise (E), which provokes substantial sympathetic activation. Uniformity of the maneuvers performance was maintained as much as possible.

2.3. Signal recording and acquisition

ECG was detected at the CM5 bipolar derivation using

a bioelectric amplifier (Biopac Systems). Noninvasive arterial pressure was measured by Finapres (Ohmeda). Respirogram was obtained with a stretching pneumograph (Nihon Kohden). ECG, arterial pressure and respiration (Res) signals were digitized at a sampling rate of 1 kHz via an acquisition system (Biopac Systems).

2.4. Data processing

The first derivative of arterial pulse was obtained offline and dP/dt_{max} time series were formed with its maximal amplitudes, computed from the zero crossing to the peak value of each beat. R-wave peaks, systolic pressure (SP) and tidal volume were beat-to-beat detected to generate R-R intervals (RR), SP and Res time series. All time series were cubic-spline interpolated, resampled at 4 Hz and separated into trends and oscillations by the smoothness priors method [7] with a cutoff frequency of 0.03Hz. Series trends (levels) were evaluated by their mean values and SD. Time-frequency spectra of the oscillations of the series were estimated with the smoothed pseudo-Wigner-Ville distribution and integrated in the standard LF and high-frequency (HF) bands of HRV to compute LF_{SP}, LF power of dP/dt_{max} ($LFdP/dt_{max}$), HF of dP/dt_{max} ($HFdP/dt_{max}$), of RR (HF_{RR}), and of Res (HF_{Res}). Time-frequency coherences between $HFdP/dt_{max}$ and HF_{Res} were obtained by cross-spectral analysis. Coherences greater than 0.5 were considered significant. The dP/dt_{max} to pulse pressure (ΔP) ratio ($dP/dt_{max}/\Delta P$) was also computed [3]. Indexes dynamics were ensemble-averaged for visualization, and segmented into 50-s epochs for statistical analysis.

2.5. Statistical analysis

Due to its skewed distribution, a logarithmic transformation was applied to HF_{RR} ($lnHF_{RR}$). Data of the variables dynamics were pooled and expressed as mean±SD. Inter-maneuver differences were tested by ANOVA for repeated measures. Post-hoc pairwise comparisons were performed by the Tukey test. Individual mean values of the 50-s segments of the indexes dynamics throughout the four maneuvers were used to compute linear regressions and correlations. Statistical significance was accepted at $p<0.05$.

3. Results

In relation to L: RR level (Fig. 1A) progressively decreased in S and E ($p<0.001$), $lnHF_{RR}$ power (Fig. 1B) was maximal in CB and gradually decreased in S and E ($p<0.001$), and LF_{SP} (Fig. 1C) progressively increased in S and E ($p<0.001$). dP/dt_{max} level (Fig. 1D), its SD (Fig. 1E), and $dP/dt_{max}/\Delta P$ (Fig. 1F) rose in E ($p<0.001$), but only the latter augmented in S ($p<0.001$).

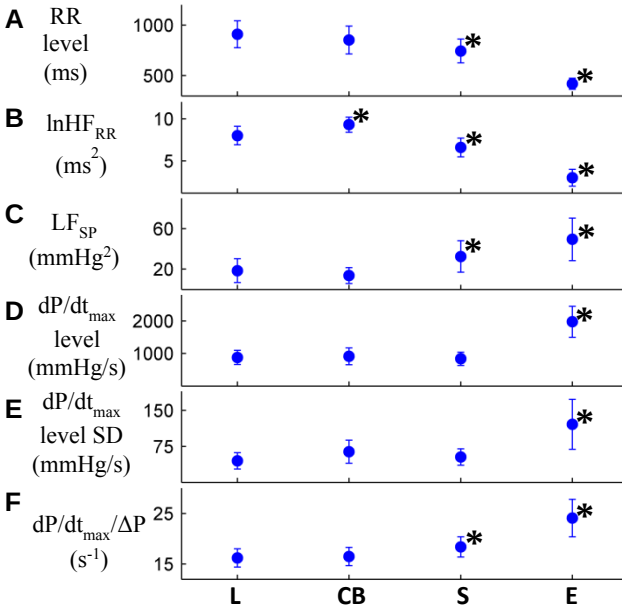

Figure 1. Mean±SD of the pooled data of the dynamics of (A) RR level, (B) $lnHF_{RR}$, (C) LF_{SP}, (D) dP/dt_{max} level, (E) SD of dP/dt_{max} level and (F) $dP/dt_{max}/\Delta P$ during the four maneuvers. *$p<0.01$ vs. L (control condition).

The TFD of dP/dt_{max} series revealed that their power was distributed in the standard HRV frequency bands (Fig. 2). In both dP/dt_{max} and SP time-frequency spectra, power in the LF band gradually rose in S and E, becoming maximal in the latter. Important fluctuations of the instantaneous power are notorious in both frequency bands during each maneuver.

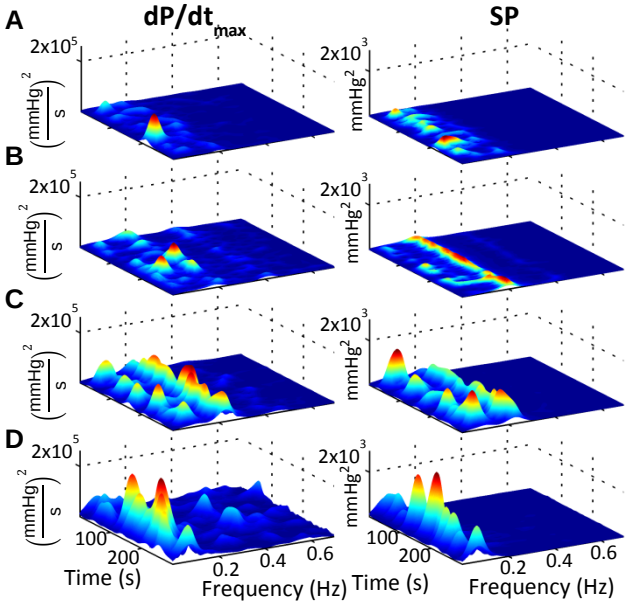

Figure 2. Representative example of time-frequency spectra of dP/dt_{max} (left column) and SP (right column) series during (A) L, (B) CB, (C) S and (D) E conditions.

Means of $LFdP/dt_{max}$ power (Fig. 3A), in relation to L, did not change in CB, but increased in S ($p<0.01$) and in E ($p<0.001$). This last change was very pronounced. Means of $HFdP/dt_{max}$ power (Fig. 3B) were greater in CB ($p<0.01$), not different in S and dramatically larger in E ($p<0.001$). The instantaneous variations presented by both components in the four supposedly stationary maneuvers are evident even in their ensemble averages (Fig. 3).

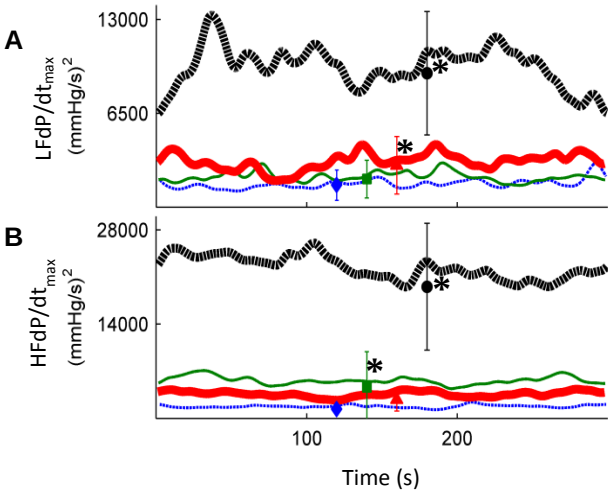

Figure 3. Ensemble averages and mean ± SD of the pooled data of the dynamics of (A) $LFdP/dt_{max}$ and (B) $HFdP/dt_{max}$ during the four maneuvers: L (thin dotted line, ♦), CB (thin solid line, ■), S (thick solid line, ▲) and E (thick dotted line, ●) *$p<0.01$ vs. L control condition.

Figure 4 depicts the ensemble averages of HF_{Res}-$HFdP/dt_{max}$ time-frequency coherences obtained during the four maneuvers. The averages of the pooled individual time-frequency coherences were greater than 0.85 in all maneuvers.

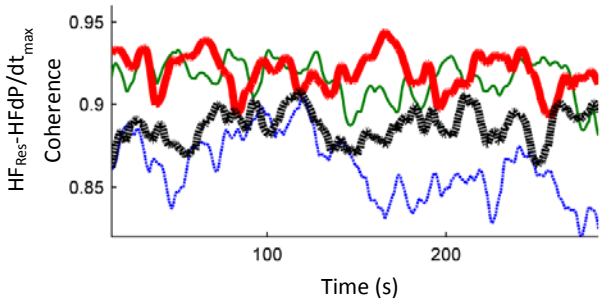

Figure 4. Ensemble averages of HF_{Res}-$HFdP/dt_{max}$ time-frequency coherences during L (thin dotted line), CB (thin solid line), S (thick solid line) and E (thick dotted line) conditions.

Mean of individual correlations of $LFdP/dt_{max}$ vs. $lnHF_{RR}$ and vs. RR level (Fig. 5A), of LF_{SP} vs. $lnHF_{RR}$ and vs. RR level (Fig. 5B), and of $LFdP/dt_{max}$ vs. LF_{SP} (Fig. 5C), ranged from 0.79 to 0.94. Intersubject dispersion of the individual regressions was large (Fig. 5).

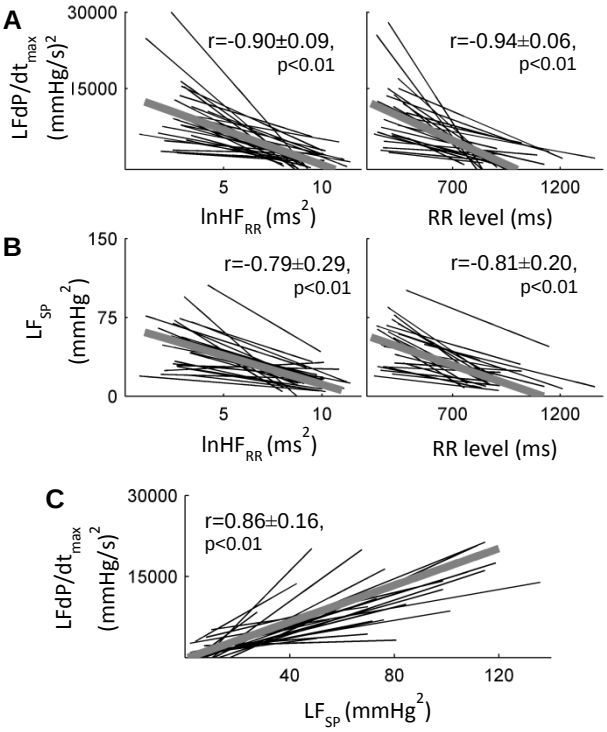

Figure 5. Individual (black lines) and mean (thick grey lines) linear regressions of: (A) $LFdP/dt_{max}$ vs. $lnHF_{RR}$, and vs RR level, (B) LF_{SP} vs $lnHF_{RR}$ vs. RR level, and (C) $LFdP/dt_{max}$ power vs LF_{SP} power.

4. Discussion

The present study establishes that, in healthy subjects, the level and spectral measures of arterial pulse dP/dt_{max} time series are related to sympathetic and mechanical respiratory activities, as supported by the following findings. With respect to L condition: 1) while LF_{SP} and $LFdP/dt_{max}$ progressively increased in S and E, $lnHF_{RR}$ and RR level gradually decreased. 2) Correlations of $lnHF_{RR}$ and RR level with $LFdP/dt_{max}$ were very strong, and were greater than those with LF_{SP}. $LFdP/dt_{max}$ was highly correlated with LF_{SP}. 3) $HFdP/dt_{max}$ was greater in E than in CB, during which $lnHF_{RR}$ was maximal. HF_{Res}-$HFdP/dt_{max}$ coherence was very high in all maneuvers.

TFD of arterial pulse dP/dt_{max} series show spectral components in the usual LF and HF bands of HRV and SPV (Fig. 2). To our knowledge, this is the first study to perform the spectral analysis of dP/dt_{max} series, establishing that, due to its strong correlations with HRV and SPV indexes, $LFdP/dt_{max}$ is an adequate index of cardiac sympathetic activity complementary to LF_{SP}, a measure that is related to vasomotor sympathetic activity, and that $HFdP/dt_{max}$ has a mechanical respiratory origin.

The use of a TFD is advantageous because it yields a better characterization of the time series variability, given that it tracks the instantaneous power over time and

avoids the problem of testing the stationarity of the signals.

Arterial pulse dP/dt_{max} values reflect the cardiac sympathetic activity and have been used as a noninvasive index of cardiac contractility in research [3] and clinical settings. From critically ill [5] and pediatric patients [4] it has been documented that arterial pulse dP/dt_{max} may be considered a suitable surrogate for left ventricular dP/dt_{max}, the most commonly used index of cardiac contractility [8]. Despite the good correlations between both indicators, they are originated by different mechanisms. While left ventricular dP/dt_{max} is produced by the maximal elevation of ventricular pressure during the isovolumic contraction phase [9], arterial dP/dt_{max} is associated to the maximal rate of aortic pressure rise during the ventricular ejection phase, which is transmitted to peripheral arteries.

Arterial pulse dP/dt_{max} levels observed in our maneuvers agree with the values reported: they decrease in S and rise in E condition [3]. An interesting finding is that both dP/dt_{max} level and its variability, evaluated by SD, are affected similarly by the maneuvers, increasing during E. When arterial dP/dt_{max} level is divided by ΔP, it also augments in S (Fig. 1F), thus correctly indicating the cardiac contractility elevation elicited by this maneuver.

Previous studies have provided evidence favoring LF_{SP} power as an indicator of vasomotor sympathetic activity, because it is tightly correlated to muscle sympathetic nerve activity [10]. In our study, the increase of sympathetic activity during S and E conditions is adequately indicated by the responses observed in the vagal measure ($lnHF_{RR}$), the sympathetic tone index (RR level) and LF_{SP} power (Fig. 1).

Arterial $LFdP/dt_{max}$ power shows very strong inverse correlations with both $lnHF_{RR}$ and RR level, and strong direct correlations with LF_{SP} power, results that suggest its ability to indicate sympathetic activity, which is only expressed in the LF band. Moreover, the correlations of $lnHF_{RR}$ and RR level with $LFdP/dt_{max}$ are greater than with LF_{SP} (Fig. 5). This fact can be explained by the more direct association of arterial $LFdP/dt_{max}$ with cardiac sympathetic activity, given that, while $dP/dt_{max}/\Delta P$ level is a marker of myocardial contractility [3], LF_{SP} is associated to vasomotor sympathetic activity [6].

If the performance of arterial $LFdP/dt_{max}$ power as an adequate cardiac sympathetic index is confirmed by further studies, complementary noninvasive markers of sympathetic activity would be made available: $LFdP/dt_{max}$ with greater association with cardiac inotropism, and LF_{SP}, more correlated to vasomotor sympathetic activity.

The high coherences of HF_{Res} with arterial $HFdP/dt_{max}$ power in all maneuvers (Fig. 4) suggest that its physiological correlate is a mechanical respiratory effect, non-neurally mediated, since this measure is maximal in E, during which there is an important reduction of HRV.

In conclusion, in healthy subjects, arterial $LFdP/dt_{max}$ power shows good performance in noninvasively tracking cardiac sympathetic activity and contractility, as supported by its strong correlation with LF_{SP} power, a suitable sympathetic index associated with the vasomotor branch, and by its very strong correlations with $lnHF_{RR}$ and RR level, greater than those obtained with LF_{SP}, which can be explained because dP/dt_{max} time series estimate cardiac contractility. The high coherences of HF_{Res} with arterial $HFdP/dt_{max}$ power document its respiratory origin, mediated by a non-neural mechanism.

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