Dynamics of Autonomic Activity during Mueller and Valsalva Maneuvers Assessed by Time-frequency Analysis of Cardiovascular Variability

Salvador Carrasco-Sosa[1], Alejandra Guillén-Mandujano[1, 2]

[1]División de Ciencias Biológicas y de la Salud, Universidad Autónoma Metropolitana-I, DF, México
[2] División de Ciencias Básicas e Ingeniería, Universidad Autónoma Metropolitana-I, DF, México

Abstract

We compared the instantaneous dynamics of spectral measures of cardiovascular variability, estimated by a time-frequency distribution (TFD), during two opposite respiratory strains, Mueller (MM) and Valsalva maneuvers (VM), and evaluated the relations among systolic pressure (SP), RR intervals (RRi) and spectral indexes. From the power spectra of RRi and SP series, estimated by TFD, the high frequency power (HF_{RR}), low to high frequency ratio and low frequency power of SP (LF_{SP}) were computed. During both maneuvers the instantaneous dynamics of their spectral indexes were similar, being the changes 50% smaller in MM ($p<0.001$). In phase II of both maneuvers the SP-HF_{RR}, RRi-HF_{RR} and LF_{SP}-SP relations showed strong correlations that support the baroreflex participation in the two maneuvers, provide a better estimate of the vagal baroreflex sensitivity, and establish the contribution of vasomotor sympathetic outflow to the SP overshoot.

1. Introduction

The opposite respiratory strains, Mueller (MM) and Valsalva (VM) maneuvers, show complex sequences of arterial pressure and heart rate changes. These responses have been widely documented for VM [1,2] but scarcely for MM [3].

We have recently established that MM produces a consistent response pattern in systolic pressure (SP) and RR intervals (RRi) time series, with characteristic points temporally coincident with those of the four classic phases of VM (unpublished observations). Only the muscle sympathetic nerve activity (MSNA) has been characterized by microneurography during both maneuvers [1,4], but the comparison between them has not been done.

Spectral analysis of cardiovascular variability (CVV) has played a major role in the study of neural control of the cardiovascular system [5]. However, this approach has not been systematically applied in the beat-to-beat characterization of the interplay between the sympathetic and vagal outflows elicited by MM and VM.

To provide new evidence about the mechanisms of cardiovascular autonomic control during MM, we compared the instantaneous dynamics of spectral measures of CVV, estimated by a time-frequency distribution (TFD), during the opposite respiratory strains MM and VM, and assessed the relationships among SP, RRi and spectral indexes in phases II and IV.

2. Methods

2.1. Subjects

Twenty four (15 male and 9 female), healthy, nonsmoking and sedentary subjects participated. Age, weight and height were 23.2±2.4 years, 64.4±10.3 kg and 165±10 cm respectively. The written informed consent of the volunteers was requested to participate. This study was approved by the ethics committee of our university.

2.2. Protocol

In a first visit to the laboratory the health status were evaluated and subjects were trained to perform the maneuvers correctly. In the second visit, subjects performed twice, in sitting position and aided by visual feedback, MM by executing an inspiratory effort to sustain a mouth pressure (MP) of -40 mmHg for 20s; and VM by an expiratory effort of +40 mmHg of MP for 20s, with a 5-min rest period between tests. During the control and recovery stages subjects breathed spontaneously.

2.3. Recorded variables and signal acquisition

ECG was detected at CM5 lead using a bioelectric amplifier (Biopac Systems). Noninvasive arterial pressure was recorded by Finapres (Ohmeda). Respiratory movements were measured by a pneumograph (Biopac Systems). MP was monitored with a pressure transducer (Validyne) connected to the distal end of a tube. All signals were digitized at a sampling rate of 500 Hz via an acquisition and display system (Biopac Systems).

2.4. Data processing

From 43 valid recordings of each maneuver, R-wave and SP maximum values were indentified to generate the tachogram and systogram respectively. The power spectra of the detrended and cubic-spline interpolated (4 Hz) RRi and SP series were estimated by the smoothed pseudo-Wigner-Villé TFD [6]. The low frequency components of RRi (LF_{RR}) and SP (LF_{SP}) in the 0.04 to 0.15 Hz band, the high frequency power of RRi (HF_{RR}) in the 0.15 to 0.4 Hz band and the LF_{RR}/HF_{RR} ratio were computed. The cardiovascular autonomic variables (CVAV) were expressed as changes from baseline and as the ratio between the two maneuvers. The characteristic points of SP that limit the phases of both VM and MM were used as reference to select segments of CVAV in early phase II (II_e), late phase II (II_L) and phase IV to form relations, and to obtain points of comparison from the spectral estimators. These procedures were carried out by a semi-automatic computational method. The ensemble averages of the CVAV, previously aligned with the onset and ending of the strain marked by MP, were computed.

2.5. Statistical analysis

According to the Shapiro-Wilk test, data were normally distributed and were expressed as mean ± sd. Differences among the characteristic points and baseline were tested by one-way ANOVA for repeated measures, with *post hoc* pairwise comparisons by the Tukey test. Student's paired *t*-test with Bonferroni correction was employed to compare the characteristic points of the same phase and the pooled means of individual records between the two maneuvers. Correlation coefficients and linear regressions were computed for the SP-lnHF_{RR}, RRi-lnHF_{RR} and LF_{SP}-SP relations of each record in both maneuvers. Statistical significance was set at $p<0.05$.

3. Results

During phases II_e and II_L of both maneuvers, with respect to control, spectral estimators changed as follows: HF_{RR} component decreased slightly and persisted reduced throughout the entire strain ($p<0.001$, Fig. 1C), LF_{RR}/HF_{RR} ratio increased during phase II_e ($p<0.001$, Fig. 1D) and tended to recover in phase II_L; LF_{SP} power rose ($p<0.001$, Fig. 1E), much more in VM than MM. Mean values of the characteristic points of the spectral indexes of MM were smaller than those of VM in phases II and IV ($p<0.01$), except for LF_{RR}/HF_{RR} ratio in the latter ($p>0.05$). During the post strain of both maneuvers and with respect to control, while HF_{RR} and LF_{SP} components were increased ($p<0.001$, Fig. 1C and E), LF_{RR}/HF_{RR} ratio returned to control values ($p>0.05$, Fig. 1D).

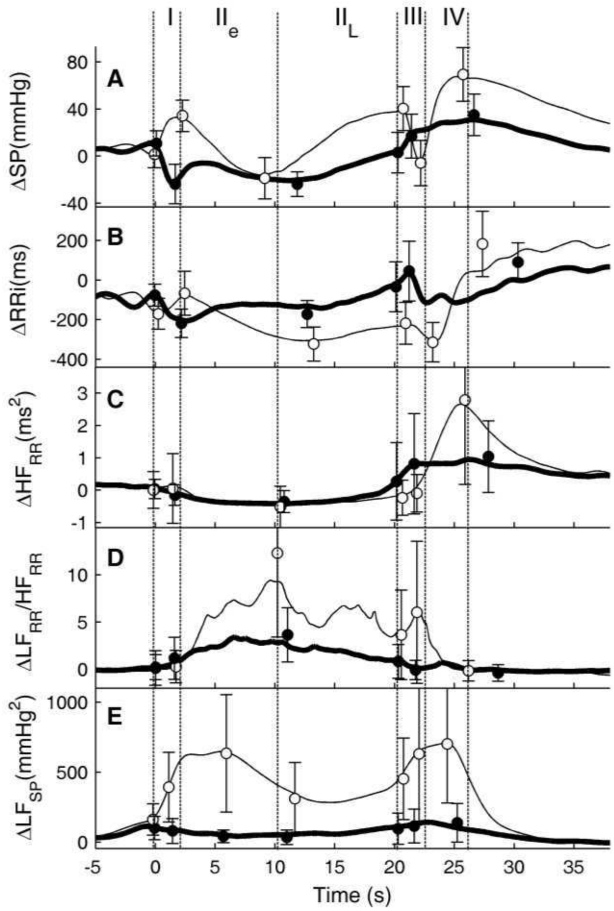

Figure 1. Ensemble averages of the dynamics of CVAV in MM (thick line) and VM (thin line), and mean values±sd of the characteristic points that mark the phases of MM (•) and VM (○).

In both strain and post strain, pooled means of the instantaneous CVAV of MM were smaller than those of VM ($p<0.001$). The MM to VM ratio ranged between 20 and 80% (Table 1).

The continuous SP-lnHF_{RR} and RRi-lnHF_{RR} relationships, plotted taking the lnHF_{RR} power as common ordinate, presented very strong correlations in phases II_e and IV of VM (Fig. 2A and B) and phase II_L of MM (Fig. 2C).

During phase II_e of MM and II_L of VM the SP-lnHF_{RR} correlations ranged from 0.56 to 0.60 ($p<0.02$) and RRi-lnHF_{RR} correlations ranged from -0.09 to 0.45 ($p>0.05$).

Table 1. Pooled data and MM/VM ratio of the CVAV during strain (S) and post strain (PS) of both maneuvers. Mean ± sd, N=43.

	Stage	MM	VM	MM/VM
SP	S	-11 ± 1	15 ± 2†	0.7 ± 0.1
(mmHg)	PS	26 ± 3	40 ± 3†	0.7 ± 0.1
RRi	S	-127 ± 11	-213 ± 10†	0.6 ± 0.1
(ms)	PS	-88 ± 14	-140 ± 13†	0.7 ± 0.1
HF_{RR}	S	-1191±1358	-1844±2018†	0.7 ± 0.8
(ms^2)	PS	8889±12795	13185±16634	0.8 ± 0.9
LF_{RR}	S	2.1 ± 1.7	5.3 ± 2.9†	0.4 ± 0.5
HF_{RR}	PS	-0.2 ± 0.7	1.0 ± 1.1	0.2 ± 0.7
LF_{SP}	S	59 ± 52	421 ± 186†	0.2 ± 0.1
($mmHg^2$)	PS	85 ± 92	327 ± 221†	0.3 ± 0.3

† p<0.001 between maneuvers

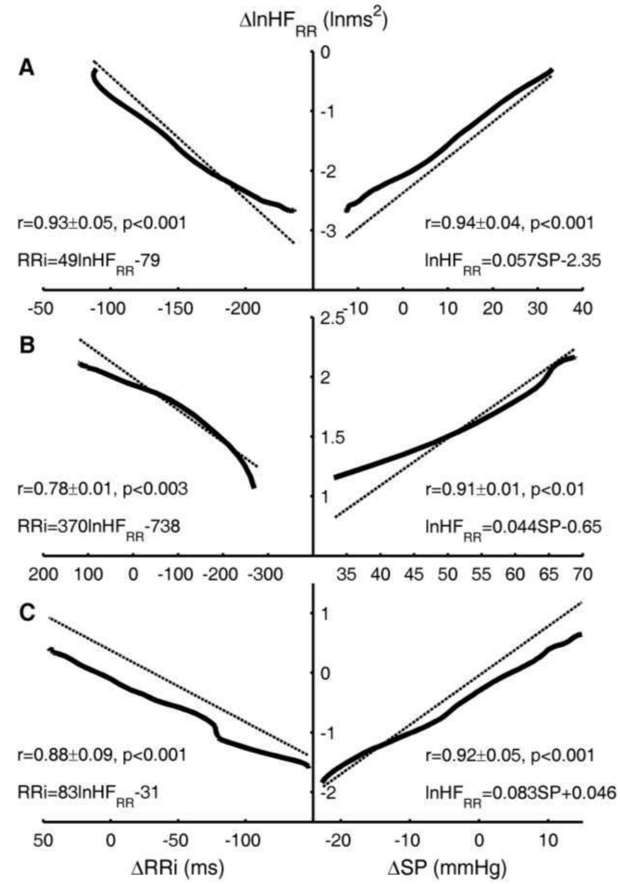

Figure 2. Ensemble averages of SP-$\ln HF_{RR}$-RR relations (thick solid line) and their respective mean regressions (thin dotted line) during phase II_e (A) and phase IV (B) of VM, and phase II_L of MM (C).

In the first part of phase II_L of VM, the SP-LF_{SP} relation was inverse (Fig. 3A). In the second part of VM and the whole phase II_L of MM, the LF_{SP}-SP relations showed positive slopes (Fig. 3B-C). All these relations presented strong correlations.

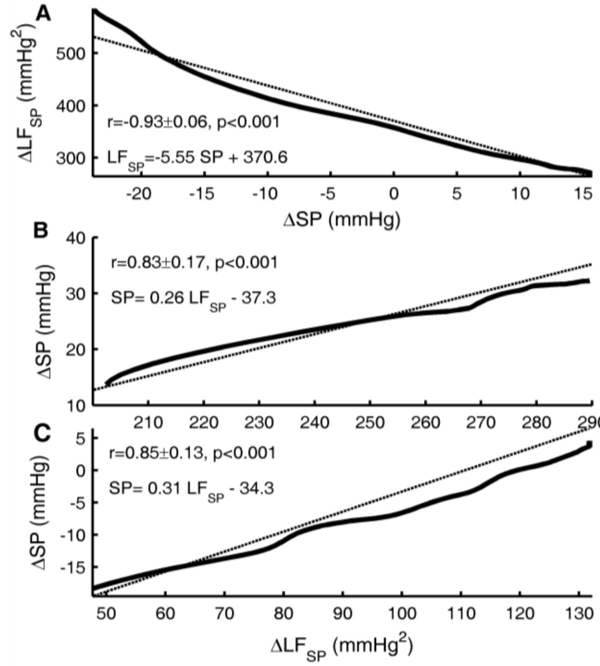

Figure 3. Ensemble averages (thick solid line) of the SP-LF_{SP} and LF_{SP}-SP relations with their respective regressions (thin dotted line) during phase II_L of both maneuvers. First part of VM (A), second part of VM (B) and MM (C).

In the post strain, the resumption of breathing did not have any important effect over the RRi. Respiratory arrhythmia was restored from the second respiration.

4. Discussion and conclusions

The spectral measures of CVV computed by a TFD during MM and VM establish that their autonomic outflow dynamics follow similar direction of change in both strain and post strain, being their amplitude 50% less in MM. The main findings of this study are: 1) during the strain, vagal activity decreases while both cardiac and vasoconstrictor sympathetic outflows increase. In the post strain, vagal and vasomotor sympathetic activities increase and cardiac sympathetic outflow decreases, being all these changes smaller in MM than in VM; 2) the strong correlations of SP-$\ln HF_{RR}$ and RRi-$\ln HF_{RR}$ relations in phase II of the two maneuvers and phase IV of VM support the important vagal baroreflex participation in MM and VM. By incorporating HF_{RR} as common ordinate these relations provide a better estimate of the vagal baroreflex sensitivity (BRS) than the SP-RRi relation alone; 3) the strong correlations between LF_{SP} and SP support the ability of this spectral component to indicate the vasomotor sympathetic outflow and its relevant contribution to the SP overshoot, greater in VM.

There is enough experimental and clinical evidence to support the good performance of the spectral estimators of CVV as markers of the autonomic outflow to the cardiovascular system. Thus, vagal activity is indicated by the HF_{RR} component, cardiac sympathetic outflow by the LF_{RR}/HF_{RR} ratio and vasomotor sympathetic modulation by LF_{SP} power [5].

Using time-varying spectral estimation techniques such as wavelets [7] and trigonometric regressive analysis [8], it has been reported that mean values of LF_{RR} and LF_{SP} increase during VM strain, while HF_{RR} power rises during the post strain. Spectral analysis of CVV by a TFD provides novel knowledge about MM, by establishing the instantaneous dynamics of vagal and both cardiac and vasoconstrictor sympathetic outflows (Fig. 1) as well as the baroreflex participation in phase II_L. This last notion challenges the main role attributed to the chemoreflex in MM [9]. In addition, our findings refine the current knowledge on VM by detailing its autonomic dynamics in an instantaneous format. In this sense, we documented the two elevations presented by the LF_{SP} component, as well as the sudden change in the sympathetic baroreflex operation mode in phase II_L (Fig. 3A-B).

In both maneuvers, sympathetic activity has been studied by microneurography. During VM strain, MSNA is prominent [10], and in MM strain MSNA is 10-fold increased [4]. The LF_{SP} power behavior we observed is consistent with these reports. This agreement confirms the ability of LF_{SP} power to indicate vasomotor sympathetic activity. Reported correlations between SP and MSNA in phases II and IV of VM are weak [1]. This situation has discouraged the attempts to use SP as a surrogate of the invasive and technically difficult MSNA. In contrast, the very strong correlations between SP, RRi, $lnHF_{RR}$ and LF_{SP} found in the present study suggest that the approach that incorporates the spectral analysis of CVV in the assessment of vagal and sympathetic BRS is appropriate, and support the use of LF_{SP} power as an adequate noninvasive substitute of MSNA.

The SP-RRi regressions obtained in phases II and IV of VM are widely used to quantify vagal BRS [11]. In the present study and based upon the very strong correlations found, we propose to incorporate HF_{RR} power as common ordinate to the usual SP-RRi relationship in order to improve the robustness of vagal BRS estimation, which now considers two gains, one afferent and other efferent.

The cardiovascular autonomic response to VM reflects the integrity of the sympathetic and vagal baroreflex [2]. Similarly, MM has the potential of being a valuable autonomic function test.

In conclusion, although MM and VM are opposite respiratory strains, both present a SP fall in phase II_e, which determines the instantaneous dynamics of their spectral indexes to be similar in the strain and post strain, being the changes 50% smaller in MM than in VM. The strong correlations of $lnHF_{RR}$ with both SP and RRi support an important baroreflex participation in both maneuvers and provide a better estimate of the vagal BRS than the SP-RRi relation alone. The strong correlations between LF_{SP} and SP indicate that the vasoconstrictor sympathetic outflow contributes in generating the SP overshoot, greater in VM than in MM.

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Address for correspondence.

Salvador Carrasco-Sosa

Depto. Ciencias de la Salud

Universidad Autónoma Metropolitana–Iztapalapa.

Av. San Rafael Atlixco # 186, C.P. 09340 D.F., México.

scas@xanum.uam.mx