

# Continuous Relation between High Frequency Component of HRV and Respiratory Frequency during Postural Change

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## Abstract

*Our aims were to use a chirp-type breathing maneuver to obtain a continuous relation between the high frequency component of HRV ( $HF_{RR}$ ) and respiratory frequency (RF), and to assess if it indicates the vagal withdrawal induced by a postural change. ECG and lung volume were registered from 30 subjects who performed, in sitting and standing, a 70-s continuous linear RF increase from 0.05 to 0.8 Hz at constant tidal volume. From the smoothed pseudo-Wigner-Ville distribution of the RR intervals and tidal volume series,  $HF_{RR}$  and RF were computed to obtain the relation. After log-transformation, correlations were  $-0.88 \pm 0.03$  in sitting and  $-0.89 \pm 0.04$  in standing. With the postural change the intercept decreased ( $p < 0.001$ ) and the slope increased ( $p < 0.009$ ), indicating a vagal withdrawal. The continuous  $HF_{RR}$ -RF relation we obtained can assess the vagal effect of the postural change independently from the RF influence, improving the interpretability of  $HF_{RR}$  as vagal index.*

## 1. Introduction

The high frequency ( $HF_{RR}$ ) component of the heart rate variability (HRV) power spectrum, synchronous with the respiration, is a satisfactory measure of the cardiac vagal outflow [1]. Changes in the magnitude and frequency of this component are result of the interplay of respiratory and non-respiratory inputs integrated by the vagal nuclei. The responsiveness of these nuclei is mainly modulated by the respiratory and baroreflex influences [2]. In consequence, if the  $HF_{RR}$  component is to be interpretable, the respiration must be controlled [3]. However, the response of the  $HF_{RR}$  component to the respiratory frequency (RF) and lung volume influences is complex. Even more, respiration affects the HRV spectral power below 0.15 Hz. The relationship between the total power of the RR intervals spectrum ( $TP_{RR}$ ) and the RF shows a characteristic nonlinear and inverse behavior, similar to that of a low-pass filter [4].

Studies that obtained the  $TP_{RR}$ -RF relationship have in common the use of breathing maneuvers of long duration (ranging from 6 to 21 min) executed with the aid of auditory control, but differ in the continuity of the maneuver, in the manner in which the RF is varied and in the method employed for the spectral estimation. Thus, Saul et al. [4] used a continuous broad-band random breathing maneuver without controlling the tidal volume and computed the transfer function between respiration and heart rate utilizing the Fast Fourier Transform for the spectral estimation; Novak et al. [5] employed a continuous slowing respiratory rate maneuver with uncontrolled tidal volume and a time-frequency distribution for the spectral analysis; Brown et al. [3] utilized a discontinuous breathing maneuver consisting of seven increasing respiratory frequencies with controlled tidal volume and used the periodogram method of Welch; and Taylor et al. [6] employed a discontinuous respiratory protocol that involved 13 decreasing respiratory frequencies and utilized the Fast Fourier Transform for the spectral analysis.

It has been repeatedly demonstrated that the spectral analysis of HRV is capable to quantify the changes in autonomic activity induced by orthostatic stress. It is well-established that the change from supine to standing position elicits a sympathetic activity increase associated to vagal withdrawal [7].

Time-frequency distributions are suitable tools that provide useful instantaneous spectral estimators of nonstationary signals. Because of its computation efficiency and excellent time and frequency resolutions, the smoothed pseudo-Wigner-Ville distribution has been extensively applied in HRV studies [8].

We hypothesized that the  $HF_{RR}$  component magnitude as a function of the widest possible range of RF could assess the non-respiratory vagal effect induced by a provocative maneuver. Therefore, the aims of the present study were to obtain a continuous relationship between the  $HF_{RR}$  component and RF from a brief chirp-patterned breathing maneuver with constant tidal volume, and to evaluate the ability of this relation to specifically indicate

the vagal withdrawal produced by the change from sitting to standing position.

## 2. Methods

**Subjects.** Thirty healthy and sedentary subjects, 18 men and 12 women, participated. Mean age, height and weight were  $23.5 \pm 1.5$  years,  $168 \pm 7$  cm and  $65.4 \pm 8.0$  kg respectively. The written informed consent of the volunteers was requested to participate.

**Protocol.** In a first visit to the laboratory the subjects were examined to assess their health status and were trained to execute the breathing maneuver correctly. In a second visit, subjects performed a 70-s continuous and linear RF increase from 0.05 to 0.8 Hz at target tidal volumes of 0.6 liters for women and 0.8 liters for men, values in proportion to their respective vital capacities. The maneuver performance was visually guided by the chirp pattern displayed by an electronic device developed by us. The breathing maneuver was carried out in both sitting and standing positions. ECG and tidal volume were recorded throughout the protocol.

**Recorded variables and signal acquisition.** ECG was detected at the thoracic bipolar derivation CM5 using a bioelectric amplifier (Biopac Systems). Tidal volume was computed by the set composed of a pneumotachometer (Hans Rudolph), a differential pressure transducer (Validyne), a carrier demodulator (Validyne) and an integrator (Validyne). ECG and tidal volume signals were digitized at a sampling frequency of 500 Hz via an acquisition and display system (Biopac Systems).

**Data processing.** Consisted of: (a) R-wave peak detection for the computation of the RR interval series; (b) cubic-spline interpolation and resampling of the RR intervals and tidal volume series at 8 Hz to attain equidistantly sampled time series; (c) detrending of the time series using the smoothness priors method [9]; (d) estimation of the smoothed pseudo-Wigner-Ville distribution of the RR intervals and respiratory series, since they were nonstationary [8]; (e) extraction of the instantaneous power in absolute units and instantaneous frequency of RR intervals and tidal volume time series from the first two-order moments of their time-frequency distributions [10] in two frequency bands.  $TP_{RR}$  was the instantaneous power of the RR interval series in the 0.05 to 0.8 Hz band and the  $HF_{RR}$  component was the instantaneous power of RR interval in the 0.15 to 0.8 Hz band. RF and  $RF_H$  were the instantaneous frequency of the tidal volume series in the 0.05 to 0.8 Hz and the 0.15 to 0.8 Hz bands respectively; (f) obtaining of the relationships between  $TP_{RR}$  and RF and between  $HF_{RR}$  and  $RF_H$  for each subject and posture. After natural logarithmic transformation, the linear regressions and correlation coefficients of the individual  $HF_{RR}$ - $RF_H$  relations were computed; (g) ensemble averaging of the

individual  $TP_{RR}$ -RF,  $\ln(HF_{RR}$ - $RF_H)$ , and RF-time relationships, for visualization purposes only.

**Statistical analysis.** According to the Shapiro-Wilk test, data were normally distributed and therefore expressed as mean  $\pm$  sd. Student's paired *t*-test was employed to compare the slopes, intercepts and correlation coefficients between sitting and standing. Statistical significance was accepted at  $p < 0.05$ .

## 3. Results

The relationship between the increasing RF and time was highly linear, with correlation coefficients very close to 1.0 (Table 1) in both positions (Fig. 1).

Table 1. Correlation coefficients, slopes and intercepts of the RF-time and  $\ln(HF_{RR}$ - $RF_H)$  relationships in the two postures. Data are mean  $\pm$  sd, N=30.

	Sitting	Standing
RF-time correlation	0.992 $\pm$ 0.006	0.994 $\pm$ 0.004
RF-time slope (mHz s <sup>-1</sup> )	10.0 $\pm$ 0.7	10.1 $\pm$ 0.6
$\ln(HF_{RR}$ - $RF_H)$ correlation	-0.88 $\pm$ 0.03	-0.89 $\pm$ 0.04
$\ln(HF_{RR}$ - $RF_H)$ intercept (ln-ms <sup>2</sup> )	7.6 $\pm$ 1.1	7.0 $\pm$ 1.0*
$\ln(HF_{RR}$ - $RF_H)$ slope (ln-ms <sup>2</sup> Hz <sup>-1</sup> )	-0.74 $\pm$ 0.58	-0.95 $\pm$ 0.60†

\*  $p < 0.001$  between sitting and standing.

†  $p < 0.009$  between sitting and standing.

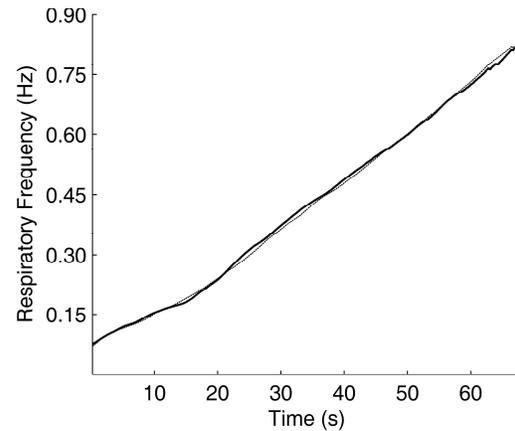


Figure 1. Linear increase of the respiratory frequency during the chirp-type breathing maneuver in both sitting (solid line) and standing (dashed line) positions. The ensemble-averaged patterns were overlapped.

Slopes and correlation coefficients of this relation did not differ significantly ( $p > 0.05$ ) between sitting and standing postures (Table 1). The comparison between the

tidal volumes of the two postures were not different ( $p>0.05$ ). These results indicated that the performance of the breathing maneuver was constant in both postures, fact that guaranteed that the respiratory influence was invariable.

The time-frequency distribution of the tidal volume series showed a linear frequency increase with constant power throughout the entire maneuver (Fig. 2A), while the distribution of the RR interval series displayed large power at low frequencies that decayed as the frequency was increased (Fig. 2B).

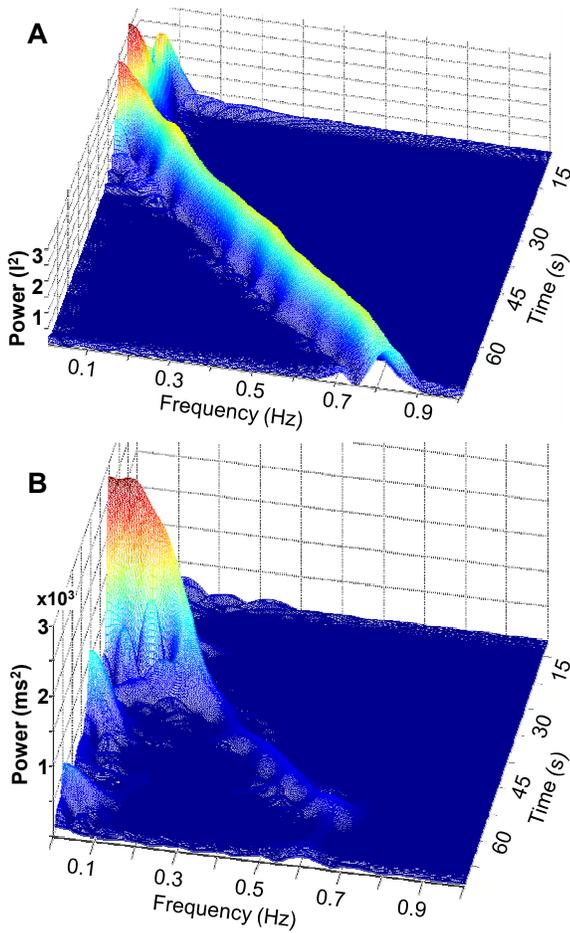


Figure 2. Typical time-frequency distributions of (A) tidal volume and (B) RR interval series during the chirp-type breathing maneuver.

In both postures the ensemble average of the individual  $TP_{RR}$ -RF relationships depicted a continuous, non linear and inverse trace, analogous to that of a low-pass filter (Fig. 3).  $TP_{RR}$  presented a small increment between 0.05 and 0.15 Hz. From this last frequency and up to 0.8 Hz the power decreased, first abruptly and then gradually (Fig. 3). While in the 0.2 to 0.8 Hz frequency

band the  $TP_{RR}$ -RF relationship corresponding to standing position was shifted downwards with respect to that of sitting, below 0.2 Hz the ensemble-averaged traces of both postures were overlaid (Fig. 3).

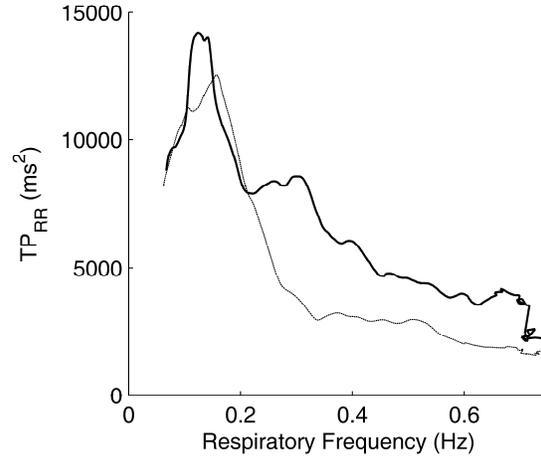


Figure 3. Ensemble average of the individual  $TP_{RR}$ -RF relationships in sitting (solid line) and standing (dashed line) postures. The relationship corresponding to standing was shifted downwards with respect to that of sitting.

Mean correlation coefficients of the individual  $\ln(HF_{RR}-RF_H)$  relationships were very high in both postures (Table 1). Similarly, the ensemble averages of the  $\ln(HF_{RR}-RF_H)$  relationships were linear, as depicted in Fig. 4. The  $\ln$ -regression intercept decreased ( $p<0.001$ ) and the slope increased ( $p<0.009$ ) with the change from sitting to standing position (Table 1 and Fig. 4).

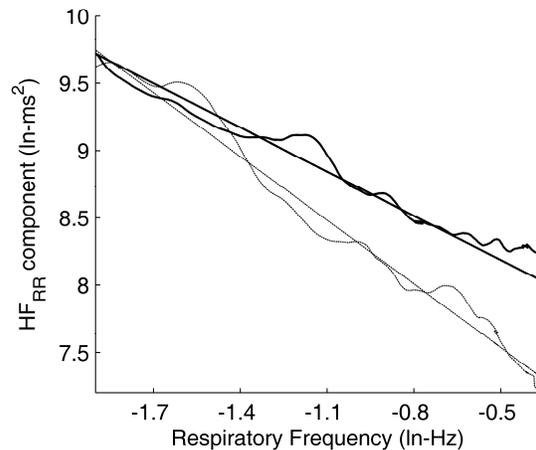


Figure 4. Log-log plot of the  $HF_{RR}$ - $RF_H$  relationships during sitting (solid line) and standing (dashed line) postures, with their respective regression lines. The regression of standing was steeper and shifted downwards with respect to that of sitting position.

#### 4. Discussion and conclusions

The main findings of this study are twofold. First, a more efficient procedure to characterize the effect of RF on the cardiac vagal outflow in healthy humans is attained. Second, by keeping the complex respiratory influence invariable throughout different maneuvers the interpretability of the  $HF_{RR}$  component changes is improved, i.e. it becomes less ambiguous.

We established a continuous  $TP_{RR}$ -RF relationship with similar shape to the one depicted by the bode plot of a low-pass filter, using a time-frequency distribution to perform the spectral estimation of the HRV and lung volume during a brief chirp-patterned breathing maneuver at constant tidal volume. Because our methodology has a very short duration, is easy to execute, is non-fatiguing, includes a wider RF range and is carried out at constant tidal volume, we consider that it is more efficient than others reported earlier [4-6].

As suggested by Brown et al. [3], the respiratory rate must be controlled to correctly interpret the  $HF_{RR}$  component changes. To do so, it is a common practice to employ paced breathing at an arbitrary frequency, thus working with a single point of the  $HF_{RR}$ - $RF_H$  relationship. In contrast, our vagal measure derived from the continuous  $\ln(HF_{RR}-RF_H)$  relationship takes into account the RF influence over a wide range, thus it is no longer necessary to perform paced breathing at specific frequencies. In addition, the chirp breathing maneuver can be carried out simultaneously with other provocative tests. The use of the  $\ln(HF_{RR}-RF_H)$  relationship to assess the cardiac vagal outflow simplifies the comparison between the effects of the maneuvers to be tested, since it is sufficient to evaluate the slope and intercept of the regression, given the strong correlation between  $\ln HF_{RR}$  and  $\ln RF_H$ . In this sense, we demonstrated the ability of the  $\ln(HF_{RR}-RF_H)$  relationship to clearly indicate the non-respiratory vagal withdrawal produced by the change from sitting to standing position.

Since our results support that the respiratory influence was invariable in both postures, we suppose that the increase in the slope and the associated decrease in the intercept of the  $\ln(HF_{RR}-RF_H)$  relationship observed in standing is exclusively due to the baroreflex-mediated cardiac vagal withdrawal induced by the arterial pressure fall resulting from the postural change.

In conclusion, our brief chirp-patterned breathing procedure at constant tidal volume allows obtaining a continuous  $TP_{RR}$ -RF relationship over a very wide RF range without fatiguing the subjects, can be superimposed to other provocative maneuvers and avoids the use of arbitrary respiratory frequencies to maintain the respiratory influence constant. The intercept decrease and the slope increase of the  $\ln(HF_{RR}-RF_H)$  relationship

clearly measure the vagal withdrawal induced by the postural change. Thus, our findings demonstrate that the vagal effect elicited by the postural change can be assessed separately from the complex RF influence; this ability improves the interpretability of the  $HF_{RR}$  component as vagal index.

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