Sensitivity and Frequency Coupling Indexes of Respiratory Sinus Arrhythmia in Response to Continuously Increasing and Decreasing Tidal Volume

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Abstract

In 40 healthy subjects we compared the effects of chirped respiratory frequency (CRF) from 0.15 to 0.5 Hz combined with continuously increasing and decreasing tidal volume (V_T) of 1.0 l on the 45-s time-courses, estimated by a time-frequency distribution, of the central frequency and power of the high frequency components of RR (CFHF_{RES}, pHF_{RES}) and of respiration (CFHF_{RES}, pHF_{RES}), from which respiratory sinus arrhythmia (RSA) sensitivity (RSA_s) by the alpha index, its coherence (RSA_{CO}), the CFHF_{RES-CFHF_{RES}} and RSA_{S-CFHF_{RES}} relations were computed. CRFV_T caused, in relation to CFR: smaller (p<0.04) slope, intercept and correlation of RSA_{S-CFHF_{RES}} relation, with accentuation of the progressive reduction of RSA_s dynamics, with smaller (p<0.03) means at 7.5, 15, 22.5 and 30 s; smaller (p<0.03) 15, 22.5 and 30 s means of RSA_{CO} dynamics; greater (p<0.02) intercept and smaller (p<0.04) slope of the CFHF_{RES-CFHF_{RES}} relation, with greater (p<0.01) means at 7.5, 15, 22.5 and 30 s of CFHF_{RES} dynamics. Our findings support that increasing-decreasing V_T provokes an important depression of the RSA_{S-CFHF_{RES}} relation and a slight elevation on CFHF_{RES-CFHF_{RES}} relation, suggesting a great reduction of the RSA gain driving mechanism and a slight enhancement of the frequency coupling one.

1. Introduction

The effect of increasing respiratory frequency (RF), applied either discontinuous or continuously, on respiratory sinus arrhythmia (RSA), indicated by the power of the high frequency component of R-R intervals (pHF_RR), has been consistently described as a nonlinear inverse relationship between RF and pHF_RR, analogous to that of a low-pass filter [1,2,3]. Most of the respiratory maneuvers used for obtaining this relation do not control the tidal volume (V_T) and, given their several minutes duration, provoke fatigue and hyperventilation in the subjects [1,2,3].

In HRV and RSA studies, the spectral analysis of the respiratory signal (RES) is not usually done. In contrast, performing the spectral estimation of RES and R-R intervals (RR) time series via a time-frequency distribution (TFD) has allowed us to obtain the relationships between the power of the high-frequency component of respiration (pHF_{RES}) and pHF_RR to compute RSA sensitivity (RSA_s) by alpha index, and between the central frequencies of pHF_{RES} (CFHF_{RES}) and of pHF_RR (CFHF_{RES}) to measure their coupling. With this method we have documented that continuously increased isometric exercise decreases RSA_s in proportion to its intensity [4] and that in response to the continuous increase of RF from 0.03 to 0.8 Hz, CFHF_{RES} only changed proportionally in the 0.18 to 0.45 Hz band [5].

How do V_T changes affect the RSA_{S-CFHF_{RES}} and CFHF_{RES-CFHF_{RES}} relationships? To document this question, we devised an easy-to-perform respiratory maneuver in which RF and V_T vary simultaneously and linearly over wide ranges in a short period of time, to minimize the subjects’ hyperventilation and fatigue. Thus, our objective was to compare, in healthy subjects, the effects provoked by the combination of continuously increasing-decreasing V_T with chirped RF (CRFV_T) to those of the same chirped RF at constant V_T (CRFV_T) on the instantaneous 45-s time-courses of CFHF_{RES}, pHF_{RES}, CFHF_{RES} and pHF_{RES}, estimated by a TFD, from which RSA_s, RSA coherence (RSA_{CO}), and the RSA_{S-CFHF_{RES}} and CFHF_{RES-CFHF_{RES}} relations were computed.

2. Methods

2.1. Subjects

Forty healthy, normotensive and sedentary subjects, 21 men and 19 women, were studied. Mean age, height and weight were 23.5±1.5 years, 168±7 cm and 65.4±8.4 kg respectively. Their written informed consent was requested to participate. This study was approved by the ethics committee of our university.
2.2. Protocol

Volunteers visited the laboratory twice. The first time, their health status and anthropometric variables were evaluated and they were trained to execute the breathing maneuvers correctly. In the second visit subjects performed, in sitting position, two breathing maneuvers in random order, with a 5-min resting period in between. Volunteers underwent: CFR, consistent in a 15-s control, followed by 30 s of continuous and linear RF increase from 0.15 to 0.5 Hz at constant VT of 1.0 l and CFRVT, linearly increasing VT from 1.0 to 2.5 l followed by linearly decreasing VT to 1.0 l simultaneously with linearly increasing RF from 0.15 to 0.5 Hz. The maneuvers execution was visually guided by displaying on a screen the target respiratory pattern for each maneuver that the subject tries to match with their RES. ECG and RES were recorded throughout the protocol.

2.3. Signal recording and acquisition

ECG was detected at the CM5 bipolar lead using a bioelectric amplifier (Biopac). RES was obtained by integrating the flow signal (Validyne) provided by a pneumotachometer (Hans Rudolph). All signals were digitized at a sampling frequency of 1.0 kHz via an acquisition and display system (Biopac).

2.4. Data processing

R-wave peaks were detected to construct the R-R time series. RR and RES were cubic-spline interpolated, resampled at 8 Hz and detrended. Auto and cross time-frequency spectra of RR and RES were estimated with the smoothed pseudo-Wigner-Ville distribution. We extracted the instantaneous RHFRR, CFHFRR, pRHFRES and CTHFRES from the first two-order moments of their TFD in the standard high-frequency band, from which we computed: RSA by alpha index (square root of the RHFRES/RES ratio), the coherence between RHFRES and pRHFRES; RSAco of the RHFRES and CFHFRES and CFHFRES; CFHFRES relations, and the difference between CTHFRES and CFHFRES (ΔCFHF). Maxima and minima of each RES cycle were detected to form the VT and RF time series for their comparison with their equivalent spectral parameters. To highlight any patterned responses of the time-courses to the respiratory maneuvers, individual indexes dynamics were ensemble averaged. For statistical purposes, indexes dynamics were segmented into 7.5-s epochs.

2.5. Statistical analysis

Data were expressed as mean±SD. Mean values of individual indexes dynamics of each 7.5 s epoch were computed. The indexes dynamics were used to compute linear regressions and correlations subject by subject. Intra-maneuver epoch mean differences were tested by ANOVA for repeated measures. Post-hoc pairwise comparisons were performed by Tukey test. Inter-maneuver differences were tested by paired t-test. Statistical significance was accepted at p<0.05.

3. Results

The correlations between RF and VT time series with C1HFRES and pRHFRES were very strong and the VT+HFRES relation presented a minimal non-significant hysteresis (Fig. 1).

![Graph](image)

Fig.1. Ensemble averages of the individual relations between: A) RF time series and C1HFRES dynamics; B) VT time series vs. pRHFRES dynamics in CRF (black thick line) and CRFVT (red thin line).

The ensemble averages of C1HFRES dynamics clearly depicted the continuous increase of RF from 0.15 to 0.5 Hz in both maneuvers, which did not show differences in any mean value (Fig. 2A). The ensemble averages of pRHFRES dynamics clearly described the continuous increase of VT from 1.0 to 2.5 l followed by its reduction in CRFVT and the constant VT of CRF, with differences in all their mean values comparisons (Fig. 2B).

The patterned responses of the spectral parameters dynamics provoked by the CRFVT maneuver, in relation to that of CRF, were: accentuation of the progressive reduction of RSA dynamics which decreased, first rapidly from the onset until the third quarter of the maneuver, and then slowly, as shown by its smaller (p<0.001) mean values at 7.5, 15, 22.5 and 30s (Fig. 2C); the time-course of RSAco did not show differences until the second half of the maneuver but then it reduced progressively as shown by its smaller (p<0.03) mean values at 15, 22.5 and 30s (Fig. 2D); elevation of the progressive increment of the C1HFRR dynamics, as shown by its greater (p<0.001) 7.5, 15, 22.5 and 30s means (Fig. 2E); depression of ΔCFHF dynamics as documented by the smaller (p<0.01) 15 and 22.5s means (Fig. 2F); reduced pRHFRR dynamics that only showed differences until the end, with smaller (p<0.01) 30s mean value. The mostly non-different pRHFRR Response contrasts with the important depression observed in the RSA dynamics (Fig. 2C).
The correlation of the RSA<sub>S</sub>–CF<sub>HF</sub>RES relation was very strong (Fig. 3). CRFV<sub>T</sub> maneuver produced a great depression of the RSA<sub>S</sub>–CF<sub>HF</sub>RES relation associated with important reductions (p<0.04) of its correlation and intercept, and to a lesser degree, of its slope (Table 1, Fig. 3).

4. Discussion

With the aim of extending the knowledge of HRV, especially the understanding of RSA, we use the TFD-based spectral estimation of the time-courses of the high frequency powers (p<sub>HF</sub>) and central frequencies (CF<sub>HF</sub>) of the RES and RR time series, to compute RSA<sub>S</sub> and RSA<sub>CO</sub>, to obtain the RSA<sub>S</sub>–CF<sub>HF</sub>RES and CF<sub>HF</sub>RR–CF<sub>HF</sub>RES relations. The changes in these relations are taken as indicators of the effects of the respiratory maneuvers. Our main findings are that CRFV<sub>T</sub> causes a marked depression
in the RSA_COHFRES relation (Fig. 3), associated with a reduction of the RSA_CO dynamics (Fig. 2D), and a slight elevation of the CFHFRR–CFHFRES relation (Fig. 4) associated with the CFHFRR dynamics increase (Fig. 2E).

One of the basic knowledge that supports the functional mechanism of RSA is the inverse and non-linear relationship between RF and pHFRR [1,2,3]. The RSA_CFHFRES relationship is similar, but with a very strong linear correlation (Fig. 3), possibly because of the continuous, linear and short RF increment that we used and because RSA_S formalizes the normalization of pHFRR by V_T in the frequency domain. Normalizing RSA amplitude by V_T via regression techniques in the time domain, improves its comparability [6].

We hypothesize that in the general mechanism of RSA, generated by the interaction of the respiratory pattern generating nuclei with the vagal nuclei [7], two dynamic interactive driving mechanisms participate: one for the frequency coupling, that allows CFHFRR to closely follow RF changes, and the other for the gain, whose instantaneous level determines, at a constant respiratory input, the amplitude of pHFRR changes. These RSA mechanisms are possibly associated to the open-close frequency and amplitude of the flow of the gate-like mechanism [8]. The functionality of the two proposed RSA mechanisms would be described by the CFHFRR–CFHFRES and RSA_S–CFHFRES relations.

pHFRES and CFHFRES can be considered surrogate variables of V_T and RF, as supported by the very strong correlation we found between them. However, the RES spectral variables allow the uniform and coherent management in the frequency domain, i.e., computing RSA_S and RSA_CO time-courses.

The strong correlations found for the RSA_S–CFHFRES and CFHFRR–CFHFRES relations (Fig. 3 and Fig. 4) justify performing the statistical comparison between the slopes and intercepts of their linear regressions to assess the effect of CRFV_T. This maneuver provokes the reduction of the slope and the increase of the intercept of the CFHFRR–CFHFRES relation, and the reduction of both in the RSA_S–CFHFRES relation, but with greater effect on their intercepts (Table 1). In a previous study we reported the depression of the intercepts of the RSA_S–CFHFRES and CFHFRR–CFHFRES relations elicited by the active orthostatic test [5]. The marked depression of the RSA_S dynamics is associated with the decrease of RSA_CO time-course (Fig. 2 C, D), effect that suggests some uncoupling in the gain driving mechanism. Additionally, while all the epoch means of the time-course of RSA_S during CRFV_T were significantly different than those of CRF (Fig. 2C), only one of pHFRR was significantly different (Fig. 2E). This finding suggests that RSA_S outperforms pHFRR as indicator. The increment elicited on the CFHFRR dynamics (Fig. 2E), and the elevation of the CFHFRR–CFHFRES relation (Fig. 4) are possibly associated to the enhancement of the frequency coupling mechanism.

To the best of our knowledge, this is the first study to report the utilization of a TFD on the RR and RES time series to obtain the RSA_S–CFHFRES and CFHFRR–CFHFRES relations, which showed that CRFV_T provokes an important depression in the first relation and a slight increase in the second one.

The strong functional relationship between RF and pHFRR [1,2,7] supports the suggestion that the spectral analysis of RES should be included as part of the spectral analysis of HRV, practice that could improve the physiological interpretation of pHFRR, now used together with pHFRES for computing RSA_S, by indicating its mobility via CFHFRES, which is driven by CFHFRES.

In conclusion, our findings support that the 1.0-2.5-1.01 increasing-decreasing V_T provokes an important depression of RSA_S–CFHFRES relation and a slight elevation of CFHFRR–CFHFRES relation. Thus, the spectral estimation of the RR and RES time series via a TFD allows assessing the time-courses of pHF and CFHF, as well as computing RSA_S, to form the RSA_S–CFHFRES and CFHFRR–CFHFRES relations, which can be used as functional indexes of the mechanisms that drive the gain and the frequency coupling of RSA.

References


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