Respiratory-Vagal Modulatory Effects of Cold Face Test on the High Frequency Components of Systolic and Diastolic Blood Pressure Variability

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Abstract

We assessed, in 23 volunteers, the respiratory and vagal effects evoked by the cold face test (CFT) on the 180-s time-courses of high frequency powers ($_{P}HF$) and their central frequencies ($_{CF}HF$) of RR intervals ($_{P}HF_{RR}$, $_{CF}HF_{RR}$), respiration ($_{P}HF_{RES}$, $_{CF}HF_{RES}$), systolic blood pressure ($_{P}HF_{SBP}$, $_{CF}HF_{SBP}$) and diastolic blood pressure ($_{P}HF_{DBP}$, $_{CF}HF_{DBP}$), estimated by a time-frequency distribution, their gains ($_{G}HF$) in relation to $_{P}HF_{RES}$ ($_{G}HF_{RR}$, $_{G}HF_{SBP}$, $_{G}HF_{DBP}$), computed by alpha index, and their respective coherences ($_{CO}HF_{RR}$, $_{CO}HF_{SBP}$, $_{CO}HF_{DBP}$). The response patterns dynamics of $_{P}HF_{RR}$ showed similitude with $_{P}HF_{DBP}$ and those of $_{P}HF_{RES}$ with $_{P}HF_{SBP}$. $_{P}HF_{DBP}$ and $_{G}HF_{DBP}$ means were greater ($p<0.04$) than $_{P}HF_{SBP}$ and $_{G}HF_{SBP}$ means. Mean correlation of: $_{P}HF_{RR}$ and $_{G}HF_{RR}$ with $_{P}HF_{DBP}$ were greater than with $_{P}HF_{SBP}$ and $_{G}HF_{SBP}$; $_{P}HF_{RES}$ with $_{P}HF_{SBP}$ was greater than with $_{P}HF_{DBP}$. Dynamics and means of $_{CF}HF_{RR}$, $_{CF}HF_{DBP}$ and $_{CF}HF_{SBP}$ were similar to those of $_{CF}HF_{RES}$: relative to control, all decreased ($p<0.02$). Mean $_{CO}HF_{SBP}$ was greater than ($p<0.02$) mean $_{CO}HF_{DBP}$. Our findings suggest that the large vagal and slight respiratory overlapping effects induced by CFT provoked a greater modulation on $_{P}HF_{DBP}$, possibly mediated by $_{P}HF_{RR}$, than on $_{P}HF_{SBP}$, most likely associated to the mechanical respiratory influence. Moreover, the respiratory frequency drives $_{CF}HF_{SBP}$, $_{CF}HF_{RR}$ and $_{CF}HF_{DBP}$ changes.

1. Introduction

In clinical settings, the cold face test (CFT) is part of the battery of provocative maneuvers used for assessing autonomic cardiovascular function in a variety of neurocardiological diseases [1]. CFT is a safe, noninvasive, easy-to-apply maneuver that requires minimal cooperation from the patient. Its main functional property is the production of trigeminal non-baroreflex increments of both sympathetic and vagal activities, associated with blood pressure increase and heart rate reduction, respectively [1, 2].

The few reported studies addressing the genesis and functional properties of the high frequency component (HF) of systolic blood pressure ($_{P}HF_{SBP}$), and the fewer corresponding studies about HF of diastolic blood pressure ($_{P}HF_{DBP}$) share the following attributes: some agreement that they are generated by a modulatory mechanical respiratory effect; the use of stationary spectral analysis methods to compute $_{P}HF_{SBP}$; the use of dynamic exercise [3], head-up tilt [4], standing and heart failure [5] as study conditions.

Given that the authors of this study think that the available evidence does not sufficiently clarify the origin and functional properties of $_{P}HF_{SBP}$ and much less so of $_{P}HF_{DBP}$, we posit that analyzing the time-courses of the gains, coherences, and central frequencies of these components in response to a maneuver that evokes a large vagal activation such as CFT may provide new insight into this problematic issue. We hypothesize that $_{P}HF_{SBP}$ and $_{P}HF_{DBP}$ present vagal modulation mediated by HF of RR intervals ($_{P}HF_{RR}$) overlapped with the respiratory modulation. To test this supposition, we assessed and compared, in healthy volunteers, the respiratory and vagal effects evoked by CFT on the instantaneous time-courses of HF powers and central frequencies ($_{CF}HF$) of RR intervals ($_{CF}HF_{RR}$), respiration ($_{P}HF_{RES}$, $_{CF}HF_{RES}$), SBP ($_{CF}HF_{SBP}$) and DBP ($_{CF}HF_{DBP}$), estimated by a time-frequency distribution (TFD), their gains ($_{G}HF$) relative to $_{P}HF_{RES}$ ($_{G}HF_{RR}$, $_{G}HF_{SBP}$, $_{G}HF_{DBP}$), computed by alpha index, and their respective coherences ($_{CO}HF_{RR}$, $_{CO}HF_{SBP}$, $_{CO}HF_{DBP}$).

2. Methods

2.1. Subjects

Twenty-three healthy, normotensive, non-addicted, and sedentary subjects, 12 men and 11 women, were studied. Mean age, height and weight were 22.2±2.2 years, 167±8 cm and 69.1±10.4 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 in the second visit the experimental stage was carried out. Volunteers underwent 1-min control, 1-min maneuver and 2-min recovery stages. CFT maneuver was performed by applying a bag filled with iced-water at 0°C on the face, excluding the eyes, with the subject in supine position and breathing spontaneously. ECG, noninvasive arterial pressure, and respiratory (RES) signals were recorded during the three stages.

2.3. Signal recording and acquisition

ECG was detected at the CM5 bipolar lead using a bioelectric amplifier (Biopac). RES was obtained by inductive plethysmography (Inductotrace, Ambulatory Monitoring). 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 and fiducial points of ECG and arterial pressure recordings were beat-to-beat detected to generate R-R intervals (RR), SBP and DBP time series. The resulting series and RES were cubic-spline interpolated, resampled at 4 Hz and detrended by the smoothness priors method. Auto and cross time-frequency spectra of RR, SBP, DBP, and RES were estimated with the smoothed pseudo-Wigner-Ville TFD. We extracted the instantaneous ${}_{P}HF_{RR}$, ${}_{CF}HF_{RR}$, ${}_{P}HF_{SBP}$, ${}_{CF}HF_{SBP}$, ${}_{P}HF_{DBP}$, ${}_{CF}HF_{DBP}$, ${}_{P}HF_{RES}$, and ${}_{CF}HF_{RES}$ from the first two-order moments of their TFD in the standard HRV HF band (0.15-0.4 Hz), from which we computed: their ${}_{G}HF$ in relation to ${}_{P}HF_{RES}$, computed by alpha index (square root of the ${}_{P}HFx/{}_{P}HF_{RES}$ ratio), and their respective coherences by cross-time-frequency analysis. To highlight any patterned responses to CFT, individual indexes dynamics were ensemble-averaged once their mean baseline level was subtracted. Also, indexes dynamics were divided into 20-s epochs for statistical purposes.

2.5. Statistical analysis

Data are expressed as mean±SD. Differences between control and epoch values of each variable and between epoch values of the different variables were tested by ANOVA for repeated measures. Post-hoc pairwise comparisons were performed by the Tukey test. Indexes dynamics were used to compute linear regressions and correlations subject by subject. Comparisons between correlations were performed by paired t-test. Statistical significance was accepted at $p<0.05$.

3. Results

The spectral indexes response dynamics are expressed as changes from their baseline. The 20-s means of all the indexes were different from their control mean ($p<0.001$).

The ensemble averages of ${}_{P}HF_{RR}$ (Fig. 1A), ${}_{G}HF_{RR}$ (Fig. 1B) and ${}_{P}HF_{RES}$ (Fig. 1C) dynamics depicted two distinctive response patterns, the first two consisting in a large effect of increase up to a maximum followed by a reduction, and the third one of a slight sustained increase.

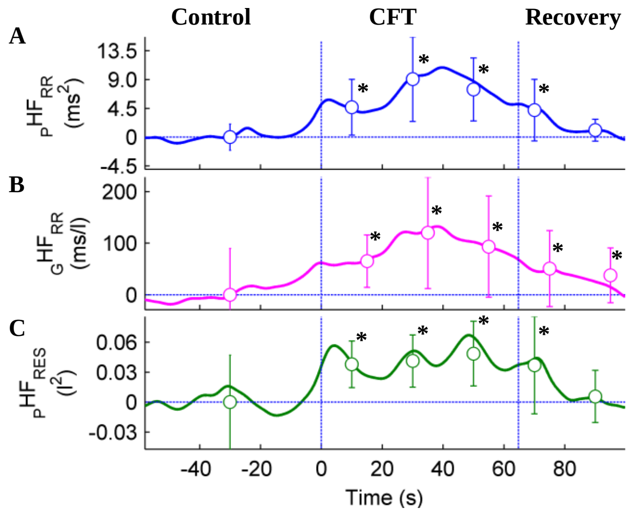

Fig. 1. Ensemble averages and epoch means±SD of the time courses of: A) ${}_{P}HF_{RR}$, B) ${}_{G}HF_{RR}$ and C) ${}_{P}HF_{RES}$. *$p<0.01$ vs. baseline.

While the ${}_{P}HF_{DBP}$ dynamics depicted a response pattern of increment until a maximum followed by a decrement (Fig. 2A), the ${}_{P}HF_{SBP}$ one showed a sustained increment (Fig. 2A), being the 20-s means of ${}_{P}HF_{DBP}$ greater than ($p<0.04$) those of ${}_{P}HF_{SBP}$. In control, ${}_{P}HF_{SBP}$ was greater than ${}_{P}HF_{DBP}$ ($p<0.001$). Similar to the trajectories shown by the power dynamics, ${}_{G}HF_{DBP}$ dynamics was of increase followed by decrease (Fig. 2B) and ${}_{G}HF_{SBP}$ dynamics was of sustained increase (Fig. 2B). The 20-s means of ${}_{G}HF_{DBP}$ were greater ($p<0.003$) than those of ${}_{G}HF_{SBP}$, but with more marked differences than those between the powers, hinted by their greater significance (0.003 vs. 0.04). Pooled means of ${}_{CO}HF_{SBP}$ and ${}_{CO}HF_{DBP}$ were 0.86±0.06 and 0.83±0.06, respectively. The ${}_{CO}HF_{SBP}$ 20-s means were greater than ($p<0.02$) those of ${}_{CO}HF_{DBP}$ (Fig. 2C).

While the mean correlation of ${}_{P}HF_{RR}$ with ${}_{P}HF_{DBP}$ dynamics (0.85±0.08) was greater ($p<0.02$) than with ${}_{P}HF_{SBP}$ (0.69±0.17), the mean correlation of ${}_{P}HF_{RES}$ with ${}_{P}HF_{SBP}$ dynamics (0.66±0.19) was greater ($p<0.04$) than with ${}_{P}HF_{DBP}$ (0.58±0.20). Similarly, the mean correlation of ${}_{G}HF_{RR}$ with ${}_{G}HF_{DBP}$ (0.78±0.18) was greater ($p<0.003$) than with ${}_{G}HF_{SBP}$ dynamics (0.56±0.24) (Fig. 3).

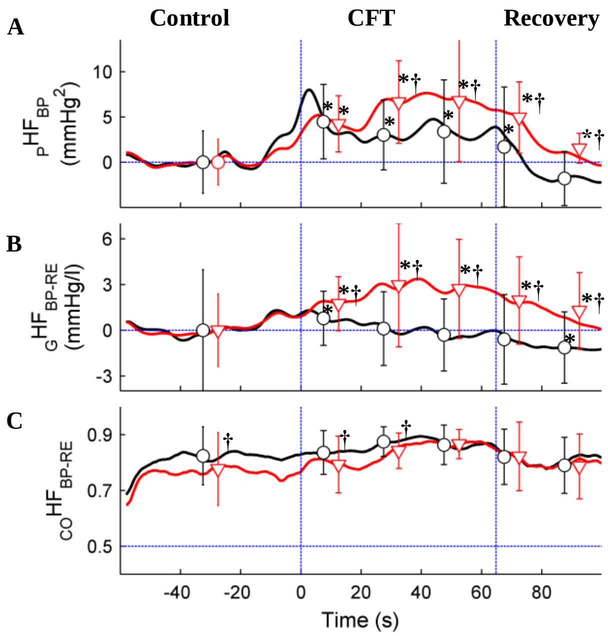

Fig. 2. Ensemble averages and means±SD of the time courses of: A) ${}_{P}HF_{SBP}$ (black) and ${}_{P}HF_{DBP}$ (red); B) ${}_{G}HF_{SBP}$ and ${}_{G}HF_{DBP}$; C) ${}_{CO}HF_{SBP}$ and ${}_{CO}HF_{DBP}$.
* p<0.01 vs. baseline; † p<0.04 vs. SBP indexes.

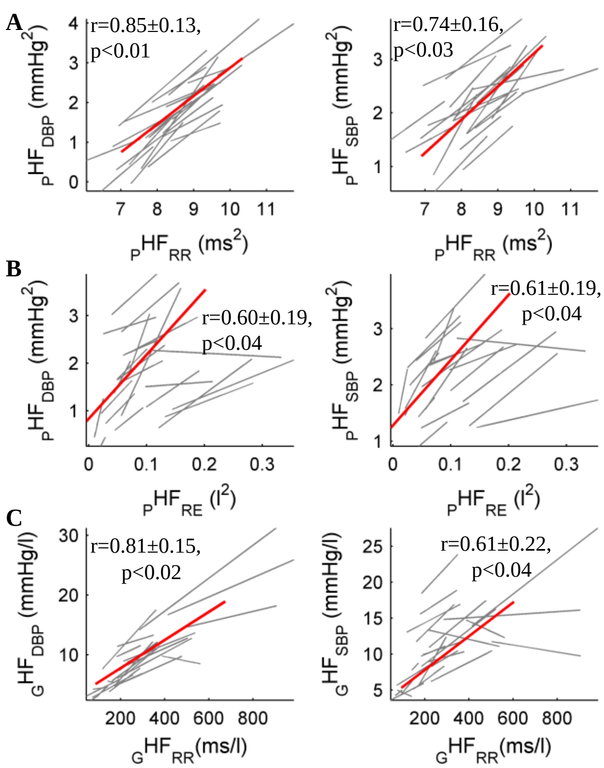

Fig. 3. Mean linear regression (red) computed from the individual regressions (grey) between: A) ${}_{P}HF_{RR}$ – ${}_{P}HF_{DBP}$ and ${}_{P}HF_{RR}$ – ${}_{P}HF_{SBP}$; B) ${}_{P}HF_{RES}$ – ${}_{P}HF_{SBP}$, ${}_{P}HF_{RES}$ – ${}_{P}HF_{DBP}$; C) ${}_{G}HF_{RR}$ – ${}_{G}HF_{DBP}$, ${}_{G}HF_{RR}$ – ${}_{G}HF_{SBP}$.

The response patterns of ${}_{CF}HF_{RES}$, ${}_{CF}HF_{RR}$, ${}_{CF}HF_{DBP}$ and ${}_{CF}HF_{SBP}$ dynamics (Fig. 4A) were similar, initial reduction that recovered progressively. The 20-s means comparison between the four ${}_{CF}HF$ did not show any significant differences. The pooled mean of ${}_{CF}HF_{RES}$ was -0.15±0.24 Hz. ${}_{CF}HF_{RES}$ dynamics presented significant mean correlations with ${}_{CF}HF_{RR}$ (0.71±0.18), ${}_{CF}HF_{SBP}$ (0.58±0.26) and ${}_{CF}HF_{DBP}$ (0.65±0.16) (Fig. 4B).

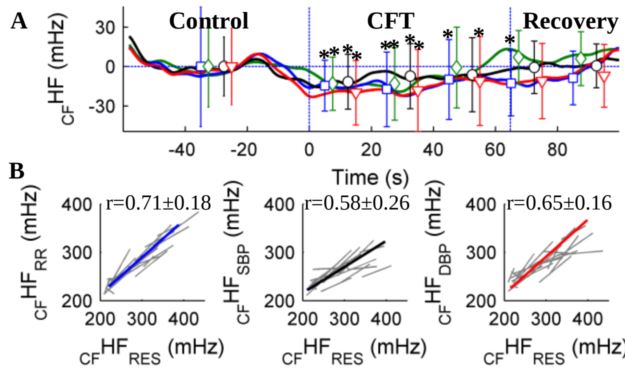

Fig. 4. A) Ensemble averages and means±SD of the time courses of: ${}_{CF}HF_{RR}$ (blue), ${}_{CF}HF_{RES}$ (green), ${}_{CF}HF_{SBP}$ (black) and ${}_{CF}HF_{DBP}$ (red). B) Individual (grey) and mean regressions between ${}_{CF}HF_{RES}$ and ${}_{CF}HF_{RR}$ (blue), ${}_{CF}HF_{SBP}$ (black) and ${}_{CF}HF_{DBP}$ (red). * p<0.01 vs. baseline.

4. Discussion

Our methodological approach for studying HRV, based on computing and analyzing the time-courses of the gains, coherences and central frequencies of its spectral components during the provocative maneuver CFT, provided new insight into the generation and functional properties of the ${}_{P}HF_{SBP}$ and ${}_{P}HF_{DBP}$ dynamics, as documented by our main findings: 1) While ${}_{P}HF_{DBP}$ and ${}_{G}HF_{DBP}$ dynamics, of larger amplitude than ${}_{P}HF_{SBP}$ and ${}_{G}HF_{SBP}$ dynamics, present greater correlation with ${}_{P}HF_{RR}$ dynamics than with ${}_{P}HF_{RES}$ dynamics, the correlation of ${}_{P}HF_{SBP}$ with ${}_{P}HF_{RES}$ is greater than with ${}_{P}HF_{RR}$; 2) ${}_{CF}HF_{SBP}$, ${}_{CF}HF_{DBP}$, and ${}_{CF}HF_{RR}$ dynamics show reductions of similar trajectory, strongly correlated with ${}_{CF}HF_{RES}$.

A relevant methodological aspect of this study is the computation of the correlations between the HF components dynamics, made possible because we obtained their instantaneous time-courses, by using a TFD.

Our findings support that CFT evokes a large vagal activity increase, effect repeatedly reported [1, 2], and a slight increment of tidal volume with reduction of respiratory frequency, novel respiratory effect about which we could not find any reports available. These effects imply that the vagal activity increment is partially independent of that induced by respiratory changes, as indicated by the ${}_{G}HF_{RR}$ increment (Fig. 1B). The contrasting magnitude of the vagal and respiratory effects creates an adequate experimental condition for studying the modulatory effect of $_{P}HF_{RR}$ on $_{P}HF_{SBP}$ and $_{P}HF_{DBP}$.

To the best of our knowledge, this is the first report that, during CFT, $_{P}HF_{SBP}$ and $_{P}HF_{DBP}$ are originated by the overlap of vagal and mechanical respiratory modulatory influences, the former greater for $_{P}HF_{DBP}$.

Since a highly influential HRV study reported evidence of the mechanical respiratory origin of $_{P}HF_{SBP}$ in 1986 [4], posterior studies, including ours, have corroborated this effect, although the reports on the subject became scarcer over time. It is possible that these studies have documented only the respiratory modulating effect on $_{P}HF_{SBP}$ because they used maneuvers and conditions that provoke patent respiratory changes, such as dynamic exercise [3], tilting [4], standing and heart failure [5]. In addition, these conditions present important vagal activity withdrawal, which makes the modulatory effect transmitted by the $_{P}HF_{RR}$ minimal. Also, they did not consider the effect on $_{P}HF_{DBP}$. It has been suggested that the respiratory modulating influence is mechanically mediated by changes in the central venous and aortic flows induced by intrathoracic volume-pressure changes [6]. However, there are studies that disagree on the respiratory origin of the $_{P}HF_{SBP}$ component, because mimicking the respiratory increment induced by exercise by a controlled breathing maneuver did not raise $_{P}HF_{SBP}$ [7]. Moreover, a study suggested, based on the greater changes of $_{P}HF_{RR}$ and $_{P}HF_{DBP}$ than those of $_{P}HF_{SBP}$ in sleep, supine, sitting and standing conditions, that $_{P}HF_{SBP}$ mirrors the vagal activity [8]. Our findings are in line with this interpretation.

Our findings suggest that $_{P}HF_{DBP}$ and $_{P}HF_{SBP}$ arise from the overlap of vagal modulatory influences exerted through $_{P}HF_{RR}$ and the mechanical respiratory modulation on stroke volume through $_{P}HF_{RES}$, and that they are exerted differentially: while the vagal modulatory influence is larger for $_{P}HF_{DBP}$, the mechanical respiratory one is clearer in $_{P}HF_{SBP}$. This functional interpretation is supported by: a) The similarity between the response patterns of $_{P}HF_{DBP}$ with that of $_{P}HF_{RR}$ and of $_{P}HF_{SBP}$ with $_{P}HF_{RES}$ (Fig. 1 and 2A); b) The 62% greater amplitude of $_{P}HF_{DBP}$ than that of $_{P}HF_{SBP}$ (Fig. 2A); c) The greater correlation of $_{P}HF_{RR}$ with $_{P}HF_{DBP}$ and of $_{P}HF_{RES}$ with $_{P}HF_{SBP}$ (Fig.3); d) The greater similarity and correlation of $_{G}HF_{RR}$ with $_{G}HF_{DBP}$ (Fig. 1 and 2C); e) The greater coherence of $_{G}HF_{SBP}$; f) The similarity between the response patterns of $_{CF}HF_{RR}$, $_{CF}HF_{SBP}$ and $_{CF}HF_{DBP}$, strongly correlated with $_{CF}HF_{RES}$ (Fig. 4).

That the indirect vagal modulation is greater in $_{P}HF_{DBP}$ than $_{P}HF_{SBP}$ is possibly because the diastolic period, given its larger duration and flexibility, is susceptible to greater modulation by $_{P}HF_{RR}$ than the quasi-constant ejection period. The normalization of $_{P}HF_{DBP}$ and $_{P}HF_{SBP}$ by $_{P}HF_{RES}$ performed by computing the gains, an index that we use pragmatically for comparison purposes, accentuates the differences between them.

In conclusion, CFT provokes a large increment of vagal activity and slight respiratory changes, increase of $_{P}HF_{RES}$ and reduction of $_{CF}HF_{RES}$, both effects with overlapping modulatory influences on the HF components, albeit with distinctive effects: on $_{P}HF_{DBP}$, a large modulatory effect, better correlated with $_{P}HF_{RR}$, possibly mediated by this measure of vagal activity, and on $_{P}HF_{SBP}$, a small modulatory increment, with better correlation and coherence with $_{P}HF_{RES}$, most likely associated to the mechanical respiratory influence on stroke volume. Moreover, the respiratory frequency drives the changes of the central frequencies of $_{P}HF_{DBP}$, $_{P}HF_{SBP}$ and $_{P}HF_{RR}$.

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