Assessment of Cardiorespiratory Interactions During Spontaneous and Controlled Breathing: Linear Parametric Analysis*

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***Abstract*— In this work, we perform a linear parametric analysis of cardiorespiratory interactions in bivariate time series of heart period (HP) and respiration (RESP) measured in 19 healthy subjects during spontaneous breathing and controlled breathing at varying breathing frequency. The analysis is carried out computing measures of the total and causal interaction between HP and RESP variability in both time and frequency domains (low- and high-frequency, LF and HF). Results highlight strong cardiorespiratory interactions in the time domain and within the HF band that are not affected by the paced breathing condition. Interactions in the LF band are weaker and prevalent along the direction from HP to RESP, but result more influenced by the shift from spontaneous to controlled respiration.**

I. Introduction

The cardiac and respiratory systems operate in an oscillatory manner, providing an example of coupled biological oscillators which can be found at every level of complexity, and in almost every living system [1]–[3]. A known feature of oscillatory systems is their ability to synchronize [4], and thus it has been demonstrated that cardiac and respiratory branches are strongly coupled and exhibit plenty of different rhythms and oscillations that through interactions support life [2].

Different modes of cardiorespiratory interaction have been studied in the literature, ranging from the variation of heart rate due to respiration (i.e., the respiratory sinus arrhythmia, RSA), to the synchronization between the heart beat and the onset of inspiration (the cardio-ventilatory coupling) and to the constant phase difference between the right and the left stroke volumes over one respiratory cycle (the respiratory stroke volume synchronization) [2]. Given the importance of studying such interactions and since the physiological role of these oscillations continues to be debated, several works have been focused on the assessment of synchronization and coordination between cardiac and respiratory signals [2]–[6].

In this work, we employ an integrated framework for the linear parametric analysis of bivariate time series to evaluate cardiorespiratory interactions during spontaneous and controlled breathing conditions, evaluating total, causal and instantaneous cardiorespiratory interactions, in both time and frequency domains. In a companion paper, the analysis is performed using nonlinear model-free measures of interaction between heart period and respiration variability measured in the same experimental time series [7].

*R.P. was supported by the Italian MIUR PON R&I 2014-2020 AIM project no. AIM1851228-2. L.F. was supported by the Italian MIUR PRIN 2017 project 2017WZFTZP "Stochastic forecasting in complex systems".

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II. Materials and Methods

The analyses were carried out on an historical dataset previously employed for assessing the cardiovascular control in healthy subjects [5], [6]. Data were acquired on 19 healthy subjects (11 females, age: 27-35 years; median=31 years), during an experimental protocol consisting of an initial period of spontaneous respiration (SR), followed by controlled breathing sessions at 10 (C10), 15 (C15) and 20 (C20) breaths/min carried out in a random order. From the acquired electrocardiographic and respiratory flow signals, stationary heart period (H) and respiration (R) time series of length N=255 beats were then extracted for each breathing condition, and normalized to zero mean. Further details on signals acquisition and preprocessing can be found in [5], [6].

Each pair of H and R time series was taken as a realization of a bivariate stochastic process $\boldsymbol{Y} = [Y_1 Y_2]$, with $Y_1 = R$ and $Y_2 = H$, which was then described using a linear parametric autoregressive (AR) model as $\boldsymbol{Y}(n) = \sum_{k=1}^{p} \boldsymbol{A}(k)\boldsymbol{Y}(n-k) + \boldsymbol{U}(n)$ [8], being n the time index, k the lag of interactions, p the model order (manually fixed for each subject), $\boldsymbol{A}(k)$ the 2x2 coefficient matrices defining the time-lagged effects within and between the two processes, and $\boldsymbol{U}$ a vector of zero-mean innovation processes with 2x2 covariance matrix $\boldsymbol{\Sigma}$. The frequency-domain AR representation of the model coefficients leads to obtain the 2x2 transfer matrix as $\boldsymbol{H}(f) = [\boldsymbol{I} - \boldsymbol{A}(f)]^{-1}$ (being $\boldsymbol{I}$ the identity matrix) from which the spectral density matrix of the bivariate process is derived as $\boldsymbol{S}(f) = \boldsymbol{H}(f)\boldsymbol{\Sigma}\boldsymbol{H}^{*}(f)$ (* stands for Hermitian transpose). Starting from the power spectral density of the individual processes $S_H(f)$ and $S_R(f)$, taken as diagonal elements of $\boldsymbol{S}(f)$, we computed the spectral measure of total coupling between R and H as [9], [10]:

$$g_{H,R}(f) = ln\left(\frac{S_R(f)S_H(f)}{|\boldsymbol{S}(f)|}\right), \quad (1)$$

and the measures of spectral Granger Causality (GC) from a process to another as [10], [11]:

$$g_{R\to H}(f) = ln\,\frac{S_H(f)}{\sigma_H^2|H_{HH}(f)|^2}\,, \quad g_{H\to R}(f) = ln\,\frac{S_R(f)}{\sigma_R^2|H_{RR}(f)|^2}\,. \quad (2)$$

where σ_H^2 and σ_R^2 are the diagonal elements of $\boldsymbol{\Sigma}$ (the same applies for H_{HH}, H_{RR} w.r.t. $\boldsymbol{H}$). Given (1) and (2), it has been shown [8], [10] that the sum of the two GC terms does not yield the total coupling, so that a spectral measure of the spectral mixing between the two causal directions can be defined as:

$$g_{H\cdot R}(f) = g_{H,R}(f) - \big(g_{R\to H}(f) + g_{H\to R}(f)\big), \quad (3)$$

Each spectral measure defined in (1), (2) and (3) can be integrated along the whole frequency axis to obtain a corresponding time-domain measure $G = 2/f_s \int_0^{f_s/2} g(f)df$,

where f_s is the sampling frequency; while $G_{H,R}$ describes the total coupling between R and H, $G_{R\to H}$ and $G_{H\to R}$ are time-domain measures of GC and $G_{H\cdot R}$ is a measure of instantaneous causality [10]. Here, assuming to have fast (i.e., within-beat) interactions from R to H [12], we summed the instantaneous term to the GC from R to H, in order to obtain the time and frequency domain measures of extended causality $G_{R\to\cdot H} = G_{R\to H} + G_{H\cdot R}$, $g_{R\to\cdot H}(f) = g_{R\to H}(f) + g_{H\cdot R}(f)$. Moreover, frequency-domain measures $g(LF)$ and $g(HF)$ were obtained integrating the values (1), (2) and (3) in the Low Frequency (LF, [0.04-0.12 Hz]) and High-Frequency (HF) bands, being the latter chosen for each subject as [f_R±0.04 Hz], with f_R the respiratory peak identified in the range [0.04-0.15 Hz]. The statistical significance of the obtained results was checked with 5% significance level. Moreover, for each subject 100 surrogate time series were generated using the Iterative Amplitude Adjusted Fourier Transform (IAAFT) algorithm, setting the significance threshold to 95%.

III. Results

The time-domain measures of coupling and causality obtained as the whole-band integral of the spectral measures did not show any statistically significant variation during controlled breathing when compared with the SB condition (Fig. 1a). The same findings where obtained when the spectral measures were integrated within the HF band (Fig. 1c). In both cases, the number of subjects with significant coupling was very high, decreasing slightly along the direction from H to R.

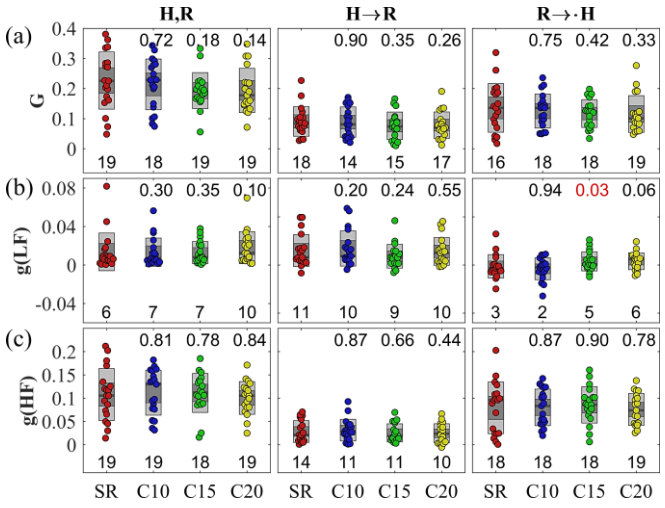

Figure 1. Boxplot distributions (95% c.i. and 1 sd) and individual values of (a) time-domain and spectral measures integrated in (b) LF and (c) HF bands, in the four breathing conditions (SR, C10, C15 and C20). Left panels, total pairwise coupling; central panels, coupling from H to R; right panels, extended coupling from R to H. Top values: *p*-values returned by the Wilcoxon non-parametric test comparing the given distribution to the reference (SR); bottom values: number of subjects (out of 19) with statistically significant coupling detected via to IAAFT surrogate analysis.

The frequency measures integrated within the LF band were statistically significant in a lower number of subjects, especially when computed from R to H (Fig. 1b). In this direction, a significant increase of the coupling was detected during C15 (p=0.03) and during C20 (p=0.06) compared to SR. Even if not significant (p=0.10), a tendency to increase during C20 was observed also for the total coupling.

IV. Discussion and Conclusion

Our results evidence that the time-domain linear measures of coupling and causality measures are not significantly altered by the paced breathing condition; this result has been evidenced as well through the use of Transfer Entropy in a companion paper focusing on nonlinear analysis [7]. Frequency-specific interactions are stronger in the RSA-related HF band, wherein they are directed mostly from R to H and do not change significantly across conditions. LF interactions are weaker, prevalent along the direction from H to R that is usually less investigated in the literature, and appear more influenced by the paced breathing maneuver along this pathway. These results confirm from the point of view of bivariate cardiorespiratory interactions previous findings on the same dataset based on measures of high-order interactions (taking also into account systolic arterial pressure) showing that paced breathing evokes significant effects within the LF band of the frequency spectrum, but not in the HF band classically studied [13].

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