

Causal Squared Coherence Analysis to Estimate Cardiorespiratory Coupling in Athletes

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Abstract

Cardiorespiratory coupling (CRC) accounts for the interactions between the heart period (HP) and respiration (RESP) and can be computed through the bivariate analysis of the HP and RESP time series. The study of CRC is useful to understand the chronic effects of different modalities of training on CRC regulation in athletes. Increases in CRC values have been associated with a raise of oxygen consumption. Several methods have been proposed to estimate the CRC, such as the squared coherence (K^2). However, one of the main disadvantages of this approach is its inability to impose a directionality, thus limiting its ability in elucidating physiological mechanisms involved in chronic adaptation to exercise. We propose a tool able to account for causality, namely the causal K^2 , to estimate the CRC. Analysis was performed in 42 male healthy subjects (i.e., athletes and sedentary individuals), aged between 20 to 40 years old. Causal K^2 was applied by considering the action of RESP on HP ($K^2_{RESP \rightarrow HP}$), as well as of HP on RESP ($K^2_{HP \rightarrow RESP}$). Athletes showed higher resting CRC, and this increase is attributed to the temporal direction from RESP to HP. We conclude that computing directional indexes is of value when estimating CRC, especially in athletes.

1. Introduction

The heart and respiratory system have been shown to interact in several ways and at different time scales. Respiratory sinus arrhythmia, cardiorespiratory phase locking and respiratory stroke volume synchronization are all manifestations of the so-called cardiorespiratory coupling (CRC) [1]. The characterization of the dynamic interactions between heart period (HP) and respiration (RESP) has been found to be a relevant for studying the neural circuits that govern CRC. Increases in CRC values

seem to be associated with a better gas exchange during inspiration [1], with possible effects on physical performance [2]. In fact, a decrease in CRC values has been observed in pathological conditions, as well as in a sedentary healthy population [3].

In the sports medicine, higher values of CRC have been observed in recreational athletes when compared to sedentary subjects [4]. However, the physiological mechanisms behind this phenomenon are still under investigation. Several methods have been proposed to elucidate the mechanisms underlying the interactions between the respiratory system and the heart, as well as their closed loop relationship with feedback and feedforward pathways. The non-causal squared coherence (i.e., K^2), is a linear approach which has been used to quantify CRC. However, some studies suggest that the sensitivity of this method might be limited when applied in trained individuals [4,5]. The limited power of K^2 is likely to be the effect of its inability to account for causality [6]. Indeed, a high value of K^2 can be found in presence of either a significant dependence of HP on RESP or of RESP on HP. Therefore, similar values of K^2 might be the result of very different causal patterns and this phenomenon might prevent differentiation of populations and/or experimental conditions. Therefore, causal bivariate methodologies capable of accounting for the directionality of interaction should be considered to elucidate the directed influences of RESP and HP and *vice versa*.

In this study we propose the application of traditional K^2 [7] and its causal version [8] to quantify CRC in athletes and non-athletes. Causal K^2 was computed in the temporal direction from RESP to HP and *vice versa*. Analysis was carried out in a population of male amateur cyclists and male sedentary individuals of comparable age. We hypothesize that athletes may have higher CRC values and that the causal link could elucidate the effects of training on cardiorespiratory control.

2. Methods

2.1 Squared coherence function

K^2 between HP and RESP was computed as the ratio between the squared modulus of power cross-spectral density between HP and RESP divided by the product of their respective power spectral densities via a bivariate autoregressive approach [7]. The coefficients were estimated based on traditional least squares technique and the model order was fixed at 10. K^2 was sampled in correspondence of the weighted average of the central frequencies of the components found in the HP-RESP series in the high frequency band (HF, 0.15-0.4 Hz) band [9]. The maximum value of K^2 in the HF band was indicated as the non-causal index and denoted as $K^2_{HP \leftrightarrow RESP}$. This index describes the CRC interaction without account for directionality because reversing the role between HP and RESP did not change K^2 [7].

The causal K^2 was computed to assess the strength of the directional link from HP to RESP ($K^2_{HP \rightarrow RESP}$), as well as that from RESP to HP ($K^2_{RESP \rightarrow HP}$) [8]. Causal K^2 was grounded on the identification of the bivariate autoregressive model [7] and on the explicit consideration of its inherent closed loop nature [8]. More specifically, we calculated $K^2_{RESP \rightarrow HP}$ by setting to 0 the polynomial of the closed loop model representing the arm from HP to RESP, thus virtually opening the closed loop. *Vice versa*, $K^2_{HP \rightarrow RESP}$ was computed by setting to 0 the polynomial representing the arm of the closed loop from RESP to HP. In this closed loop model, the delay from RESP to HP was set equal to 1 beat and from HP to RESP to 0 beats. $K^2_{RESP \rightarrow HP}$ and $K^2_{HP \rightarrow RESP}$ were sampled at the same frequency as $K^2_{HP \leftrightarrow RESP}$.

2.2 Surrogate data approach

One-hundred surrogate pairs were constructed via iteratively refined amplitude-adjusted Fourier transform method from the original HP and RESP series. The surrogate series preserved the power spectrum of the original series according to the number of iterations (*i.e.*, 100), while the distribution of the values is exactly the same [10]. RESP and HP surrogates were built with different seed for randomizing phases, thus being completely uncoupled. Analysis over all surrogate series adopted the same model order as the original ones (*i.e.*, 10). $K^2_{HP \rightarrow RESP}$ and $K^2_{RESP \rightarrow HP}$ were considered to be significant, and the null hypothesis of HP-RESP uncoupling was rejected, if the value assessed over the original series was higher than the 95th percentile of the surrogate distribution [11]. All K^2 indexes range from 0 to 1, where 0 indicates perfect uncorrelation, and 1 indicates full correlation.

2.3 Experimental protocol

A cross-sectional study was carried out in forty-two male healthy subjects, divided into recreational athletes' group (*i.e.*, cycling ≥ 150 minutes/week for at least six months) and sedentary subjects' group, if they did not perform any type of physical exercise or if they exercised for less than 150 min per week [12]. Subjects were eligible if they did not present abnormalities in the cardiorespiratory system.

Moreover, the study adhered to the principles of the Declaration of Helsinki for medical research involving human subjects and was approved by the ethical committee of the Federal University of São Carlos, São Carlos, Brazil (protocol number: 1.558.731 and 173/2011). Included participants provided a written informed consent to participate to the study. A MC5 lead electrocardiogram (ECG) was recorded using a bioamplifier (BioAmp FE132, ADInstruments, Australia), and a thoracic belt (Marazza, Monza, Italy) was used to acquire the respiratory movements. Signals were acquired simultaneously in supine position at rest for 15 minutes using a commercial data acquisition device (Power Lab208 8/35, ADInstruments, Australia). Signals were sampled at 1000 Hz. Subjects were instructed to breathe normally and not to talk during the experimental session.

2.4 Data analysis

The distance between two consecutive R-wave peaks was taken as n th HP, while the RESP signal was sampled at the first R-wave delimiting the onset of the n th HP. The detected series were visually inspected for misdetections and isolated ectopic beats and if necessary corrected through linear interpolation with a maximum of 5% of corrections within a single series. Mean (μ_{HP}) and variance (σ^2_{HP}) of HP series were computed, and expressed in ms and ms^2 , respectively. Additionally, respiratory frequency (RF) was measured as the frequency of the dominant rhythm in the RESP series and expressed as acts per minute (apm).

2.5 Statistical analysis

Normality of data was tested using Shapiro-Wilk test. Unpaired t-test, or Mann-Whitey test when appropriate, was performed to identify significant differences between the athletes and non-athletes for the indexes described in Table I and Table II. The percentage of subjects in the two cohorts passing the surrogate test for each K^2 index was evaluated through Fisher's exact test. A commercial software was used (Sigmaplot, Systat Software, Inc., Chicago, IL, version 11.0) to perform the statistical analysis. The $p < 0.05$ was considered as statically significant. Results are reported as mean \pm standard deviation.

TABLE 1. TRADITIONAL MARKERS IN IN ATHLETES AND NON-ATHLETES.

Index	ATHLETES	NON-ATHLETES
μ_{HP} [ms]	950 \pm 104	932 \pm 132
σ^2_{HP} [ms ²]	2812 \pm 2113	2768 \pm 1990
RF [apm]	14 \pm 3	19 \pm 3*

HP: heart period; μ_{HP} : HP mean expressed in milliseconds (ms); σ^2_{HP} : HP variance; RF: respiratory frequency expressed in acts per minute (apm). The symbol * indicates $p < 0.05$ vs athletes.

3. Results

Table I summarize the time domain results of μ_{HP} and σ^2_{HP} , as well as RF in the athletes and non-athletes, respectively. No statistically significant difference was found between groups for the time domain HP indexes. However, lower RF values was observed in the athletes when compared to non-athletes.

Values of causal and non-causal CRC indexes are shown in Table II. The higher values of $K^2_{HP \leftrightarrow RESP}$ in athletes compared to non-athletes was explained by the higher value of $K^2_{RESP \rightarrow HP}$. Conversely, $K^2_{HP \rightarrow RESP}$ was similar in the two groups. As to the percentage of subjects who passed the surrogate test, we found 100% of athletes and non-athletes exhibited significant values of $K^2_{HP \leftrightarrow RESP}$. The percentage remained high for $K^2_{RESP \rightarrow HP}$, being 80.95% for athletes and 85.71% for non-athletes, and for $K^2_{HP \rightarrow RESP}$, being 80.95% for athletes and 71.43% for non-athletes. No statistically significant difference was detected in the percentage of athletes and non-athletes passing the surrogate test regardless of considered K^2 index.

4. Discussion

The main findings of the present study can be summarized as follows: i) athletes have higher resting CRC when compared to the sedentary population ii) the high values of CRC in athletes are explained by the relevance of the pathway from RESP to HP series, while the coupling on the reverse temporal direction is weaker. Previous studies showed the potential contribution of CRC analysis to provide information related to the effects of physical exercise programs on coupling between autonomic activity directed to the heart driven and respiration in athletes [4,13]. In endurance athletes, greater CRC strength has been associated with higher oxygen supply and better integration of subsystems to deal with hypoxemic responses during intense exercise, with possible effects on physical performance [5,14]. Although

the physiological mechanisms are still under investigation, this study suggests that possible changes at respiratory level can have a causal effect on HP variability.

K^2 has previously been applied to assess CRC in cyclists and runners. However, controversial results were found [4,14]. Our results showed that non-causal K^2 was able to prove that athletes have higher CRC when compared to sedentary subjects. However, the most important disadvantage of this method is its inability of accounting for temporal directionality of influences, which makes it difficult to interpret the integration of regulatory mechanisms and to disentangle different contributions to CRC [5].

Conversely, in this study we can attribute changes of CRC to modifications of the pathway in a specific temporal direction (*i.e.*, from the respiratory system to the heart). This finding suggests that physical exercise can promote changes at the central respiratory network level affecting autonomic outflow and, in turn, acting on the sinus node. However, we stress that the strength of the causal dependence from HP to RESP is not negligible. Indeed, a significant amount of trained and non-trained subjects exhibited a sizable pathway from HP to RESP. The nature of this pathway should be more profoundly evaluated with *ad-hoc* protocol [15,16]. The present study suggests that it is independent from the training status.

We also observed lower RF values in trained individuals compared to non-athletes, which may be related with higher tidal volume. It is known that CRC is affected by the pulmonary as well as atrial stretch receptors [1]. Indeed, changes in tidal volume resulting from physical training can influence afferent response of pulmonary stretch receptors. Moreover, higher tidal volume might drive modifications of the intrathoracic pressure and venous return and act differently on the atrial stretch receptor activity [17]. The contribution to CRC due to modifications of afferent activity of pulmonary and atrial stretch receptors need to be quantified for a more profound assessment of CRC. Future studies should account for the measurement of partial pressures of oxygen, carbon

TABLE 2. K^2 AND CAUSAL K^2 INDEXES IN ATHLETES AND NON-ATHLETES GROUP.

Index	ATHLETES	NON-ATHLETES
$K^2_{HP \leftrightarrow RESP}$	0.88 \pm 0.11	0.81 \pm 0.13*
$K^2_{HP \rightarrow RESP}$	0.41 \pm 0.17	0.31 \pm 0.20
$K^2_{RESP \rightarrow HP}$	0.70 \pm 0.16	0.59 \pm 0.19*

HP: heart period; RESP: respiration; $K^2_{HP \leftrightarrow RESP}$: non causal K^2 sampled in the HF band; $K^2_{HP \rightarrow RESP}$: K^2 considering the directionality from HP to RESP; $K^2_{RESP \rightarrow HP}$: K^2 considering the directionality from RESP to HP. The symbol * indicates $p < 0.05$ vs athletes.

dioxide and tidal volume, to clarify the impact of these variables on CRC.

These results suggest the importance of establishing a causal interaction between the RESP and HP series to better understanding of cardiorespiratory regulation in athletes. The causal K^2 showed promising application in sports medicine above and beyond more traditional markers such as respiratory sinus arrhythmia [18] and more classical version of K^2 [7]. The result might be linked to the fact that these CRC indexes can be more closely associated with specific physiological mechanisms, being those computed from RESP to HP more related to the efficiency of gas exchange at pulmonary level [1], and those computed from HP to RESP more linked to cardioventilatory coupling [15].

4. Conclusion

The CRC is affected by physical exercise practice and this effect seems to have a directionality from the RESP to HP. Although the physiological mechanisms are not fully elucidated, this study stresses that physical training can promote arrangements at respiratory level with causal effects on the resting HP variability. We suggest the use of causality analysis when CRC is estimated, especially in trained individuals. Future studies should investigate the effects of different modalities of training on CRC and how the directionality is affected by different exercise protocols.

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