

QUANTITATIVE ANALYSIS OF SPECTRAL COHERENCE BETWEEN HEART RATE VARIABILITY AND RESPIRATORY AMPLITUDE

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RESUMEN.

El progreso reciente en ciencias multidisciplinarias ha profundizado el conocimiento sobre las interacciones cardiorrespiratorias, como la arritmia sinusal respiratoria, sin embargo, los mecanismos subyacentes continúan siendo poco claros. El objetivo fue establecer índices cuantitativos del análisis de coherencia espectral entre variabilidad de la frecuencia cardíaca (VFC) y amplitud respiratoria (AR) y probar los índices durante estímulos fisiológicos en personas sanas. Se reclutaron 11 sujetos sanos para obtener series de tiempo de VFC y AR bajo cuatro condiciones de medición: posición supina y bipedestación durante respiración espontánea y posición supina durante respiración rítmica a 0.1Hz y 0.25Hz. Los datos fueron procesados con MATLAB y se calcularon los espectros de potencia de VFC y AR y la coherencia espectral. Los índices propuestos mostraron diferencias estadísticamente significativas ($p < 0.05$) entre las cuatro condiciones probadas. Los índices propuestos permitirán comparaciones más robustas y reproducibles de las interacciones de diversas condiciones en investigación clínica y fisiológica.

Palabras Clave: Análisis de coherencia espectral, variabilidad de la frecuencia cardíaca, arritmia sinusal respiratoria.

ABSTRACT.

Recent advances in multidisciplinary sciences have deepened our understanding of cardiorespiratory interactions, such as respiratory sinus arrhythmia. However, the underlying mechanisms remain unclear. The aim was to establish quantitative indices for coherence spectral analysis between heart rate variability (HRV) and respiratory amplitude (RA) time series and to test these indices during physiological stimulus in healthy subjects. Eleven healthy subjects were recruited to obtain the HRV and RA time series under four measurement conditions: supine position during spontaneous breathing, active standing during spontaneous breathing, and supine position during rhythmic breathing at 0.1 Hz and 0.25 Hz. Data was processed using MATLAB to calculate power spectral density (PSD) and spectral coherence. The developed indices showed statistically significant differences ($p < 0.05$) between the four tested conditions. The proposed indices will enable more robust and reproducible comparisons of cardiorespiratory interactions for multiple conditions in clinical and physiological research.

Keywords: Spectral coherence analysis, heart rate variability, respiratory sinus arrhythmia.

1. INTRODUCTION

Recent advances in multidisciplinary sciences, such as bioengineering or complexity science, have strengthened the research of physiological interactions between organs and systems[1], [2]. An example of these interactions occurs between the heart and the lungs [3]. Three distinct cardiorespiratory interactions have been described: respiratory sinus arrhythmia (RSA), cardiorespiratory coupling (CC), and respiratory stroke volume synchronization (RSVS). RSA is the most studied, although the exact physiological mechanisms underlying RSA are still poorly understood. RSA is the change in heart rate variability (HRV) with respiration, accelerating during inspiration, and decelerating with expiration [4]. HRV is the oscillation in the interval between consecutive heartbeats, and it can be used to evaluate the vagal influence of the autonomic nervous system (ANS) on the heart in a non-invasive way [5]. It has been previously shown that impaired ANS function and HRV are predictors of cardiovascular and all-cause mortality [6] and are correlated with worse outcomes in settings as diverse as depression [7], anxiety [8], fetal development [9], sepsis management [10], myocardial infarction [11], hypertension [12], and stroke [13].

One technique to explore the influence of the ANS on HRV and its interaction with breathing dynamics is spectral coherence analysis (SCA) [14]. SCA estimates the interaction (coherence) between two signals across the entire frequency band, and its result is a single parameter representing the coherence value between 0 and 1. Usually, SCA in RSA studies is based on averaged coherence spectrums from all individuals in each comparison group without considering individual coherence values (i.e., the frequency of the maximum coherence), leading to a qualitative interpretation of results.

Given the intricacy of cardiorespiratory interactions, a deeper description of their frequency-domain relationship might prove helpful [3], in which quantitative indices from the SCA would allow a more reproducible comparison between conditions and study subjects when applied to cardiorespiratory interaction research. Therefore, this work aims to develop quantitative indices for SCA and to test these indices during physiological stimulus in healthy subjects.

2. METHODS

2.1 Subjects

Eleven healthy subjects were recruited by convenience sampling. The average age was 30 years old, with 55% men. The subjects underwent a clinical evaluation, and no evident pathologies were found. The research protocol was previously approved by the Institution's Research and Ethics Committees (Protocol number 12-763), and informed consent was given and signed accordingly. The protocol was performed following the principles stated in the Declaration of Helsinki.

2.2 Data acquisition and processing

Non-invasive HRV and respiratory amplitude (RA) signals were obtained with a Zephyr BioHarness 3® belt in two separate sessions for each subject, the first in the morning and the second in the afternoon. In consequence, 22 measurements were obtained. Figure 1 shows an example of the HRV signal (upper panel, indicated as RR interval) and the simultaneous RA signal (lower panel). The subjects were instructed to lie down (supine position) for at least 10 minutes, breathing spontaneously. Afterward, they were asked to stand up (Figure 1, red arrow) and remain in active standing, breathing spontaneously for 10 minutes. Then, they were asked to lie down again for another 10 minutes (Figure 1, green arrow), breathing spontaneously for 3 minutes, followed by rhythmic breathing (RB) at 0.1 Hz (5 seconds inspiration, 5 seconds expiration) for 3 minutes, and then by another 3 minutes of RB at 0.25 Hz (4 seconds

Raw signals of electrocardiogram (ECG, sampled at 250 Hz) and RA (sampled at 20 Hz) were extracted and processed with MATLAB 2023 software. Heartbeat detection on the ECG signal was performed using a previously validated program [15]. The identification of each heartbeat was visually inspected and manually corrected when necessary. Then, RR interval and RA signals were visually reviewed to extract a 3-minute segment from each protocol section. The selection process prioritized signal stability and reduction of artifacts and extrasystoles. An example of the selected segments is shown in (Figure 1). Detrending of the chosen segments using a second-order polynomial was performed. Subsequent resampling at a frequency of 3 Hz was applied to both signals (Figure 2).

2.3 Spectral coherence analysis

The total length of both resampled signals was 3 minutes (540 samples). Power Spectral Density (PSD) was calculated using Welch's periodogram (function "pwelch" in MATLAB) with a window ratio of 1/3 of the total signal, which corresponds to 180 samples, or 60 seconds. An overlap of 50% was used. A separate analysis for the high-frequency range (0.15 - 0.5 Hz) was performed due to its importance in breathing dynamics [3], [16].

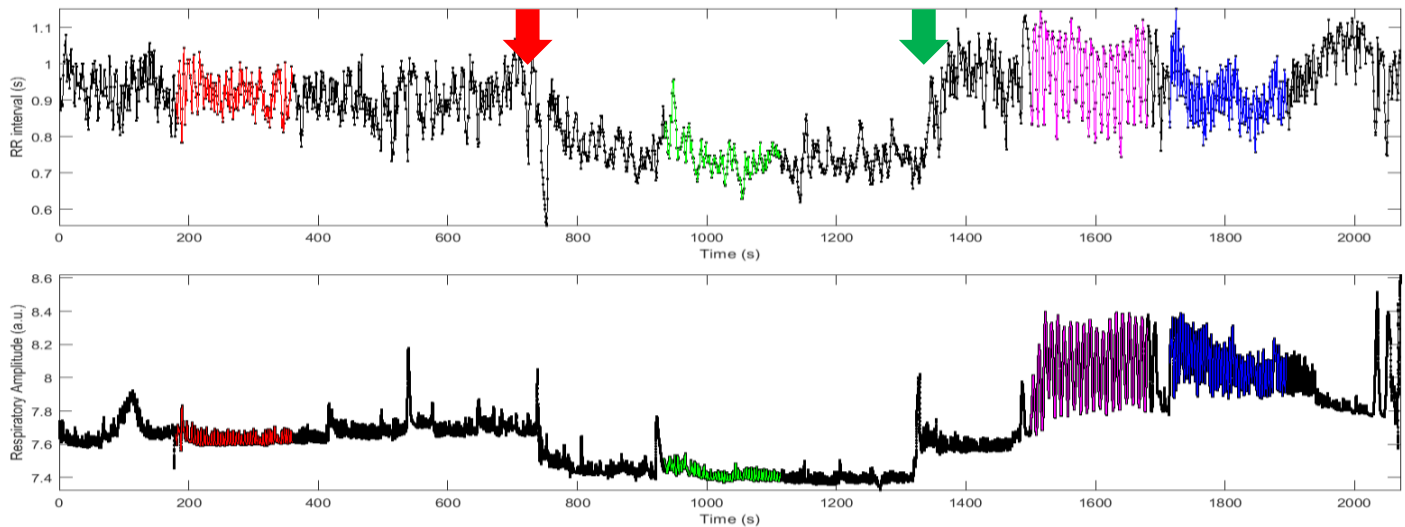


Figure 1. Time series of the RR interval (top) and the Respiratory Amplitude (bottom) signals. The segments corresponding to supine position (red), active standing (green), rhythmic breathing at 0.1 Hz (magenta), and rhythmic breathing at 0.25 Hz (blue) are highlighted in different colors. The red arrow indicates the change from supine to standing position. The green arrow indicates the return from standing to supine position.

inspiration and expiration). Subsequently, a 3-minute segment was selected from each maneuver (supine position, active standing, RB at 0.1 Hz, and RB at 0.25 Hz), as indicated with colors in the example of Figure 1.

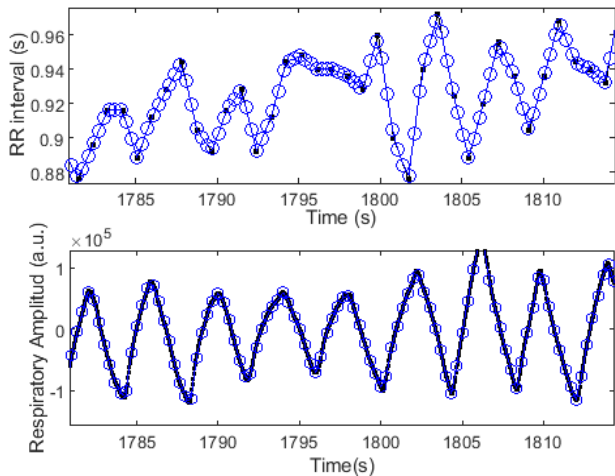


Figure 2 Resampled time series of the HRV (up) and Respiratory Amplitude Signals (down). The resampled signal (blue circles) is superimposed over the original signal (black dots). The differences in black dot density are due to the differences in the sample frequency from the source signals, 1 Hz, and 25 Hz, for RR Interval and Respiratory signals, respectively.

2.4 Quantitative indicators for spectral coherence

Figure 4 illustrates the four different indices that were measured for a quantitative description of spectral coherence analysis:

1. **N**, which refers to the number of frequencies with significant coherence values (i.e., a coherence value >0.5).
2. **Area**, area under the curve of significantly coherent frequencies.
3. **Fmax**, the frequency in Hz where the maximum significant coherence is located.
4. **Cohere max**, the maximum normalized value of coherence achieved by Fmax.

These indices were calculated for the total frequency band (0 – 0.5 Hz) and the high-frequency band (0.15 – 0.5 Hz).

2.5 Statistical analysis

A normal distribution was not assumed due to the sample size being lower than 30 and the lack of information regarding data distribution for spectral coherence in cardiorespiratory interactions. Therefore, medians and percentiles are used to describe the data. Wilcoxon's range test was applied to evaluate differences between the indicators mentioned before.

3.0 RESULTS

A total of 20 measurements were analyzed. Despite the researcher's instructions, one subject was excluded from the analysis due to the intentional slowing of breathing pace during the spontaneous breathing phases. Therefore, that measurement was excluded from the analysis.

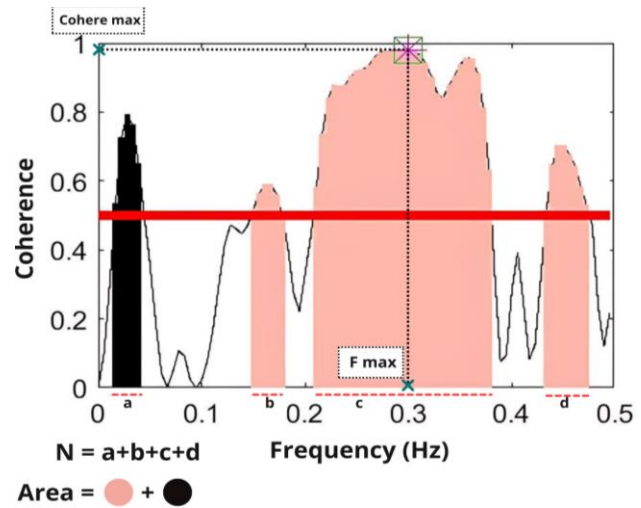


Figure 3 Spectral coherence indices. Cohere max is marked as a green cross in the Coherence axis. F max is marked as a green cross in the Frequency axis. The legend in the bottom left corner explains the composition of the "N" and "Area" indicators. The point of maximum coherence is marked with a green square, and the point of maximum coherence for high frequencies (0.15 – 0.5 Hz) is marked with a pink asterisk. In this case, both values are the same. Significant coherent frequencies are shadowed for low (black, 0 – 0.15 Hz) and high (orange, 0.15 – 0.5 Hz) frequencies. The red line marks the threshold for significant coherence at 0.5. PSD and Coherence values are normalized from 0 to 1.

Figure 4 shows an example of the analysis from one recording. The upper row shows the RR time series (blue lines) and RA time series (orange lines), the middle row shows both signals' power spectral density (PSD), and the lower row shows the corresponding spectral coherence spectrum. The four columns to each of the four different maneuvers.

During both supine position (first column) and active standing (second column), the time series of both present high signal variability, in contrast to the reduced variability during rhythmic breathing segments. During RB at 0.1 Hz (third column), there was an increased amplitude of RA and RR time series, with a smaller effect in RB at 0.25 Hz (fourth column). This is consistent with the physiological phenomenon of increased breathing amplitude and volume and reduced breathing frequency. [17]. During RB at 0.1 Hz and RB at 0.25 Hz, RR and RA signals oscillate in a coordinated, slightly out-of-phase fashion, where the RA signal can be observed to precede RR by a few seconds.

The PSD in the supine position (middle panel, first column) shows that the spontaneous breathing frequency is around 0.3Hz, where respiratory and cardiac signals increase in power and overlap. This behavior is also seen in RB at 0.1Hz and RB at 0.25Hz, where the overlapping frequency is instead the one that the subject was instructed to follow. A notable reduction in power for the rest of the frequencies is observed in both RB

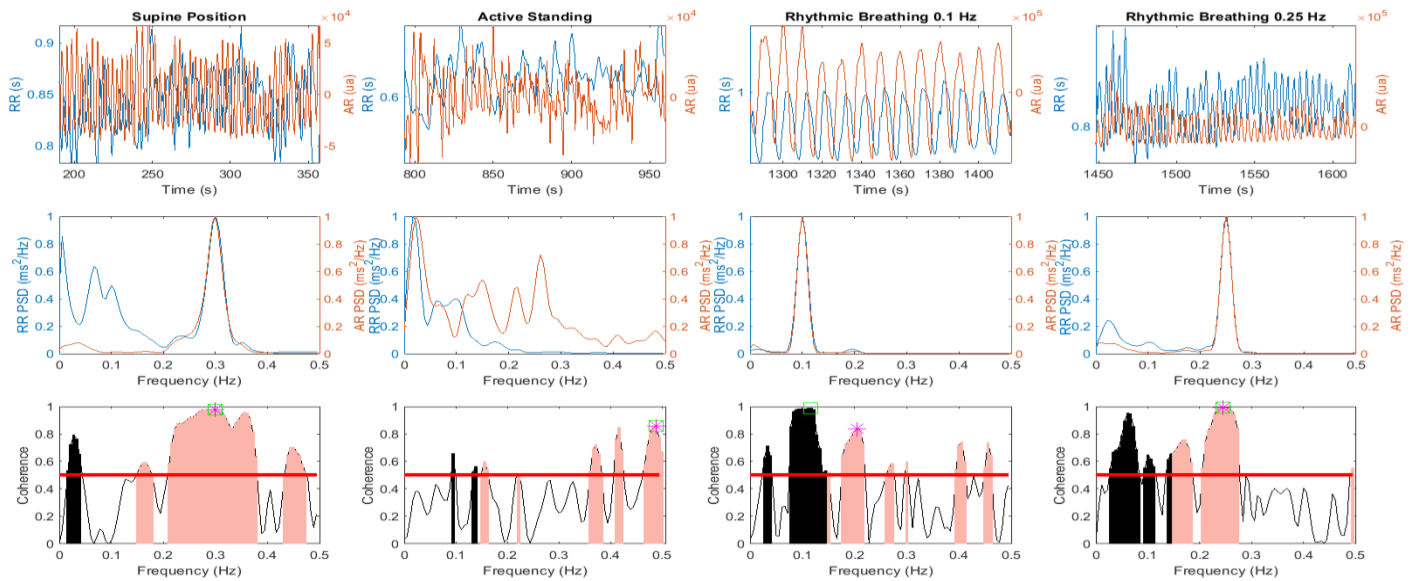


Figure 4. Superimposed time series (top), Power Spectral Density (PSD, middle), and Spectral Coherence (bottom), of RR interval (in seconds) and Respiratory amplitude (in arbitrary units), during supine position (left), active standing (center left), rhythmic breathing at 0.1Hz (center right), and rhythmic breathing at 0.25Hz (right). The RR signal is shown in blue, and the RA signal in orange. For the third row, the point of maximum coherence is marked with a green square, and the point of maximum coherence for high frequencies (0.15 – 0.5 Hz) is marked with a pink asterisk. Significant coherent frequencies are shadowed for low (black, 0 – 0.15 Hz) and high (orange, 0.15 – 0.5 Hz) frequencies. The red line marks the threshold for significant coherence at 0.5. PSD and Coherence values are normalized from 0 to 1.

segments, with a minor subharmonic at 0.2Hz for the RB at 0.1Hz maneuver.

Spectral coherence density (Figure 4, lower panel) shows that most coherent frequencies are centered around the dominant frequency shown with PSD. The supine position presents a broader range of coherent frequencies, with the point of maximum coherence around 0.3Hz. In contrast, in the RB segments, the significant coherences around the maximum coherence value are narrower and centered around the instructed breathing frequency. A relevant, coherent peak can be seen at 0.2Hz in the RB at 0.1Hz section, consistent with the subharmonic found in the PSD above.

Compared to the other conditions, active standing does not have a predominant PSD frequency where both signals overlap as strongly, which is also supported by the coherence graph, where the most coherent frequencies lie outside the normal respiratory range (0.15-0.4Hz).

When applying different stimuli that affect breathing dynamics, distinguishable patterns between them emerge at the individual level, like the ones presented previously. Figure 5 shows average coherence by condition, where the whole-group average is marked with a blue line and the individual coherence with thin gray lines. A large heterogeneity is evident between subjects. The supine position group seems to have a broad range of significant frequencies with moderate values, in contrast to the

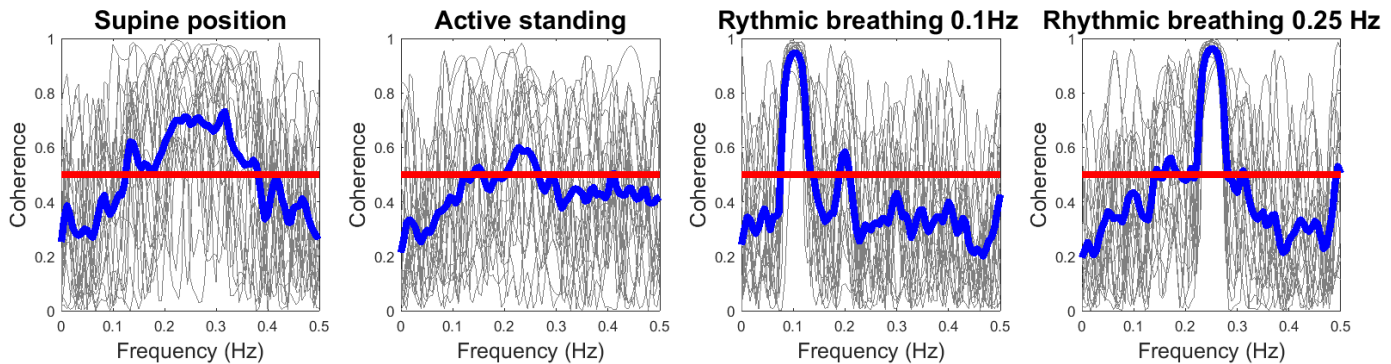


Figure 5. Average coherence by condition for all subjects. Each different coherence line in gray corresponds to a single subject. The blue line marks the group's average. Coherence values above the red line (0.5) are considered significant.

reduced amplitude and range from the active standing group. Furthermore, the influence of RB on average coherence in their respective group is evident, producing a characteristic increase in average coherence surrounding the indicated breathing frequency.

These qualitative comparisons between groups can be confirmed using the earlier quantitative indices. *Table 1* summarizes the four calculated indices. In the total frequency range (0 – 0.5 Hz), **N** and **Area** were larger during the supine position compared to the other three maneuvers. **F max** was smaller during RB at 0.1 Hz compared to all other conditions. **Cohere max** was lower in active standing compared to supine position. In the high-frequency range (0.15 – 0.5 Hz), significant differences were found between the supine position, active standing, and rhythmic breathing at 0.1 Hz for the **N**, **Area**, and **Cohere max**. No difference was found between groups for **F max** in the high-frequency range.

Table 1. Spectral coherence indicators for total and high frequencies. Data is shown as median (25th – 75th percentile).

Total frequency range (0–0.5 Hz)				
Indicator	Supine position	Active standing	RB at 0.1 Hz	RB at 0.25 Hz
N	38 (30 – 49)	36.0* (24.5 – 45.5)	35.0* (27 – 42)	35.0* (26 – 46)
Area	28.2 (20.9 – 35.6)	25.82* (15.88 – 31.43)	26.3* (19.6 – 32.4)	26.3* (19 – 33.3)
F max	0.27 (0.21 – 0.34)	0.30 (0.22 – 0.35)	0.1* (0.1 – 0.11)	0.25 (0.24 – 0.26)
Cohere max	0.968 (0.940 – 0.979)	0.901* (0.878 – 0.958)	0.962 (0.929 – 0.978)	0.973 (0.950 – 0.987)
High-frequency range (0.15 – 0.40 Hz)				
N	30.5 (25 – 37.5)	25.5* (19 – 38)	21.0* (15 – 29)	28.0 (21.5 – 37)
Area	22.3 (17.8 – 29.9)	18.1* (12.8 – 26.6)	15.0* (10 – 20.3)	20.3 (16 – 28.6)
F max	0.27 (0.22 – 0.35)	0.31 (0.25 – 0.37)	0.25 (0.20 – 0.34)	0.25 (0.24 – 0.26)
Cohere max	0.964 (0.888 – 0.979)	0.894* (0.859 – 0.956)	0.872* (0.817 – 0.929)	0.973 (0.950 – 0.987)

* Statistically significant difference when compared to supine position.

4. DISCUSSION

The main contribution of this work is to develop quantitative indices of the spectral coherence spectrum between HRV and AR time series, to assess cardiorespiratory interactions for research and clinical settings. By introducing quantitative indices, additional comparisons between studied groups or conditions are now possible, allowing more reproducible and comparable research.

Our results progressed from previous advancements [18]), where contrasting conditions use coherence values from the complete frequency spectrum by only considering frequencies whose coherence values reach a certain significance threshold, possibly resulting in less sensitivity but more specificity.

There was a significant variability in coherence values between study subjects, even within the same condition (Figure 4). Comparisons in this context benefit from using average

coherence values at the expense of losing the individual coherence behavior. Our approach seeks to find statistically meaningful relationships considering whole-group average coherence, supported by indices calculated at the individual level that reflect the different coherence profiles seen in this and future studies.

An example of the differences between groups is found in *Table 1*, which shows that significant coherence is larger in the supine position than in every other condition. This could be related to adaptability, given that a broader set of coherent frequencies allows the organism to respond to diverse physiological challenges such as the active standing position, a hemodynamic challenge, where an increase in the activity of the sympathetic element of the ANS and a reduction in the parasympathetic element are known to happen [19].

Additionally, the known decrease in parasympathetic activity and its complementary increase in sympathetic activity during active standing can be observed in this data [16]. PSD from the RR signal in active standing presents a displacement to lower frequencies during the challenge, accompanied by an RA signal that takes a broader frequency range. The changes in PSD also affect coherence values, which move away from expected respiratory frequencies (0.15 – 0.4 Hz). Consequently, the active standing condition is enough to cause changes in PSD and coherence values, even though rhythmic breathing techniques trigger a stronger physiological response.

Although meaningful differences between groups have been found in this study, further research within a clinical context will be needed to fully understand the physiological implications of the indices described here and how they are modified by disease. Furthermore, the lack of standardization to obtain the indices demands normalizing the calculated coherence values, which could hamper their suitability to compare subjects directly.

5. CONCLUSIONS

The quantitative indices for spectral coherence analysis developed in this work, even for simple maneuvers like active standing, allow more robust comparisons between study groups, which may improve the reproducibility of research in the context of cardiorespiratory interactions, encouraging additional research and clinical applications.

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