A novel approach for the analysis of respiratory sinus arrhythmia using breath phase information

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Abstract

Respiratory Sinus Arrhythmia (RSA) refers to periodic oscillations in heart rate in synchrony with respiration. RSA is considered a healthy form of heart rate variability and is thought to facilitate pulmonary gas exchange and to reflect the level of cardiac vagal tone. As a result, the measurement and quantification of RSA provides researchers and clinicians with a useful, fast, and non-invasive methodology to investigate the relationship between the cardiovascular and respiratory systems, and to assess autonomic system function. Unfortunately, the most commonly used analysis methods do not typically take respiratory information into account, and seek to quantify and describe RSA based solely on fluctuations in heart rate. Here, we propose a simple method to assess RSA that accounts for respiratory information, and places changes in heart rate in the context of the respiratory cycle. In this way, heart rate variability associated with RSA may be separated from variability arising from other sources. We collected heart rate and respiration information from five healthy, young-adult subjects using a pulse oximeter and respiratory inductance plethysmography. Data was collected during two-minute intervals of eupneic breathing, followed by two minutes of volitionally controlled breathing at several different rates (6, 7.5, 10, and 15 breaths/minute). Each record was then analyzed by treating the respiratory cycle as an almost-sinusoidal oscillation, and associating each heartbeat with the phase of the respiratory cycle during which it occurred. The results of this analysis indicate that, in healthy individuals at rest, typically around 70% of the variability in heart rate may be explained by the location of a beat within the respiratory cycle. Importantly, here are substa Galbraith, R. F. “Trigonometric Regression.” In Encyclopedia of Biostatistics. John Wiley & Sons, Ltd, 2005. ntive differences between RSA as measured using more traditional methods which ignore respiration and the method outlined here. Furthermore, increases in respiratory rate lead to predictable changes in the phase relationship between RSA and the respiratory cycle which are easily quantified using this methodology. The method outlined here is a useful tool for the investigation of RSA and cardio-respiratory coupling that offers several advantages over more common time- and frequency-domain analysis methods.

Methods

Subjects

Data as collected from 9 healthy adults and 5 adults with obstructive sleep apnea (OSA).

Data collection

Subjects performed 2 minutes of paced breathing, using an auditory cue, in order to maintain breathing rates at approximately 6, 7.5, 10, and 15 breaths per minute. Chest wall expansion was measured using a Respitrace band, and heart rate information was collected via pulse oximetry.

Analysis

Each heart beat was associated with (1) respiratory-phase using a Hilbert Transform [1] based on the preceding 50 msec of the respiratory trace, and (2) the change in heart rate relative to the previous heartbeat, in Hz. In all cases, a phase of 0 corresponded to the beginning of inspiration. Heart rate changes (HRC) were modeled using a regression approach [2] with the sine and cosine of the respiratory phase (RP) as predictors, as in (1).

$$(1)\ HRC_i = \alpha_0 + \alpha\cos(RP_i) + \beta\sin(RP_i) + e_i$$

The resulting coefficients can be used to estimate the phase of the sinusoidal RSA component relative to the beginning of inspiration (in radians) using (2), and the peak amplitude of the RSA wave using (3). The RSA amplitude component indicates the estimated peak amplitude of the sinusoidal RSA wave in whichever units are used to measure heart rate variation.

$$(2)\ \hat{\phi}_{RSA} = \tan^{-1}(\beta, \alpha) \qquad (3)\ \hat{A}_{RSA} = (\alpha^2 + \beta^2)^{1/2}$$

Importantly, this approach allows for significance testing regarding the existence of a significant RSA component using p-values, and also allows for an estimate of the variance in heart-rate changes that can be attributed specifically to RSA, which can then be used to estimate effect sizes.

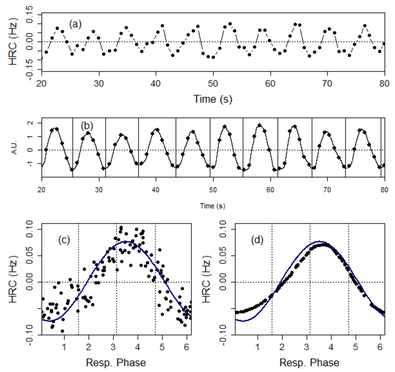


Figure 1. An outline of the processing involved in the analysis. (a) The rate change associate with each heartbeat is determined. (b) Each heartbeat is associated with a different respiratory phase along the respiratory trace. (c) The amplitude and phase of the RSA wave is found by pooling beats across cycles, rather than carrying out smoothing within-cycle first. (d) A comparison of the resulting estimated RSA phase (solid line) and a non-parametric lowess smoothed curve, indicating an excellent fit for the data.

- By finding the maximum-likelihood parameters of the sinusoidal RSA component using least-squares regression, no smoothing or interpolation is carried out on the signal (as in, for example [3,4]) resulting in fewer assumptions built into the analysis.

- This approach also specifically models the characteristics of RSA and the error component, allowing for the separation of a low RSA amplitude (see Figure 3), and low regularity in heart-rate changes (i.e., a low R^2 value in this regression framework).

Results

Figure 2. Each panel plots all heartbeats in a two-minute session based on heart-rate change (HRC) and respiratory phase. Green points indicate accelerating heartbeat, and red points indicate decelerating heart beats. The top row is an example of a healthy subject, and the bottom row a subject with OSA. Columns differ in terms of breaths per minute (BPM). The broken line indicates the best-fit sinusoidal RSA component.

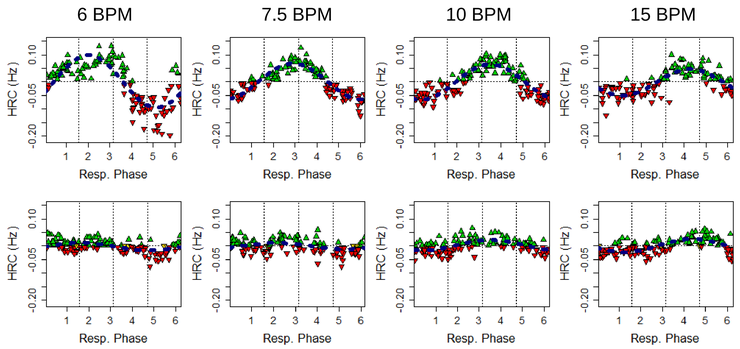


Figure 3. Comparisons of RSA wave estimates for healthy (top row) and OSA (bottom row), according the breaths per minute (BPM). Each wave indicates a different subject. Despite the diminished RSA amplitude for OSA subjects, <u>every single subject</u> in every group had a significant (p<0.05) RSA component at every breathing rate.

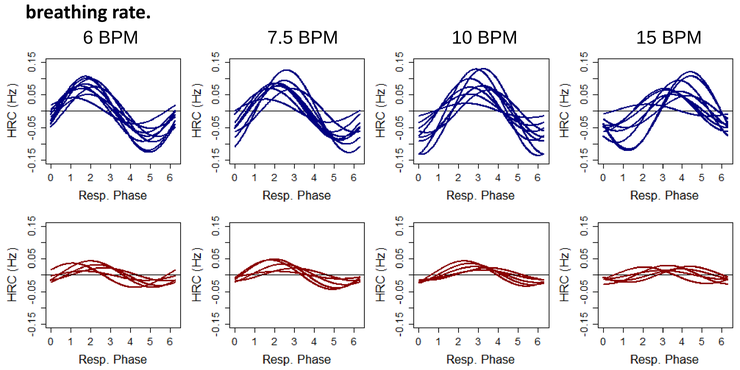
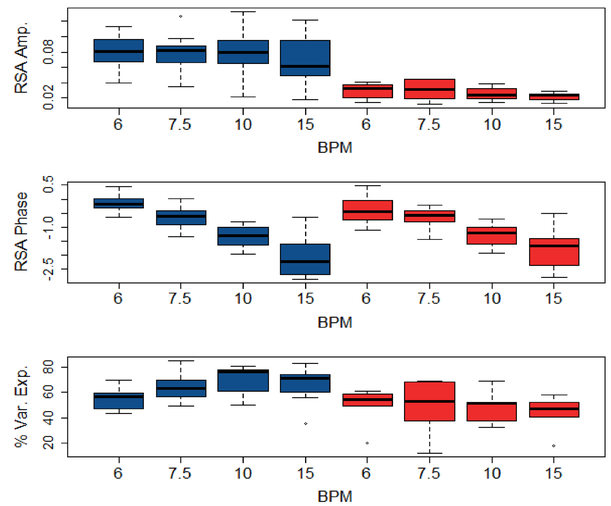


Figure 4. Boxplots show the distribution of RSA wave amplitudes (top row), RSA wave phase delay (middle row) and percent variance in heart rate variability explained by RSA (bottom row). These are divided according to breaths per minute (BPM) and subject group: Healthy subjects (blue) and OSA subjects (red).



A 2-way repeated-measures ANOVA was carried out on RSA amplitude, phase and variance explained. In each case breathing rate was a within-subjects factor and subject group was a between-subjects factor.

- There is a significant main effect (p = 0.001) for subject group on RSA amplitude, but no breathing rate main effect or interactions.

- There is a significant main effect for breathing rate on RSA phase (p<0.0001), but no subject group main effect or interactions.

- There is a significant main effect (p = 0.01) for subject group on RSA amplitude, but no breathing rate main effect or interactions.

Conclusions

The method outlined allows for significance testing of the sinusoidal RSA component within-subjects. This analysis established that every subject exhibits a statistically significant RSA component in their heart rate variability.

The estimated characteristics of the RSA wave (amplitude, phase, variance explained), were then used to test for between-group differences in RSA. Results indicate significant differences in RSA amplitude (indicating less heart rate variability) and variance explained (indicating less predictability in heart rate changes), but not in phase shift as a result of changing breathing rate.

These results strongly suggest that the mechanism governing the phase of the RSA wave relative to respiratory phase is independent of the general mechanism driving RSA amplitude and orderliness, since one appears to be intact for subjects with OSA, while the others are significantly blunted relative to healthy subjects.

References

[1] Boashash, Boualem. “Estimating and Interpreting the Instantaneous Frequency of a Signal. I. Fundamentals.” Proceedings of the IEEE 80, no. 4 (1992): 520–38.

[2] Galbraith, R. F. “Trigonometric Regression.” In Encyclopedia of Biostatistics. John Wiley & Sons, Ltd, 2005.

[3] Gilad, O. “Phase-Averaged Characterization of Respiratory Sinus Arrhythmia Pattern.” AJP: Heart and Circulatory Physiology 288, no. 2 (October 14, 2004): H504–H510. doi:10.1152/ajpheart.00366.2004.

[4] Kotani, K., K. Takamasu, Y. Jimbo, and Y. Yamamoto. “Postural-Induced Phase Shift of Respiratory Sinus Arrhythmia and Blood Pressure Variations: Insight from Respiratory-Phase Domain Analysis.” AJP: Heart and Circulatory Physiology 294, no. 3 (December 27, 2007): H1481–H1489. doi:10.1152/ajpheart.00680.2007.