

Effect of the Heart Rate Variability Representations on the Quantification of the Cardiorespiratory Interactions During Autonomic Nervous System Blockade

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Abstract

The Heart Rate Variability (HRV) is a noninvasive tool to evaluate the activity of the autonomic nervous system. To study the HRV, different mathematical representations can be used. The selection of a representation might have an effect on the evaluation of the mechanisms that modulate the Heart Rate (HR). One of these mechanisms is the Respiratory Sinus Arrhythmia (RSA), i.e. an increased HR during inhalation and a decreased HR during exhalation. A common approach to estimate the strength of the RSA is to calculate the power in the High Frequency (HF, 0.15 - 0.4 Hz) band of the spectrum of the HRV representation. However, this quantification might result in misleading RSA estimates because the respiratory rate can fall outside the HF band or it can be characterized by a narrow spectrum. For this reason, alternative methods have been proposed in the literature to quantify the RSA.

This paper studies the effect of the HRV representations on the quantification of the RSA. To this end, an experiment is used in which the sympathetic and parasympathetic branches of the autonomic nervous system are selectively blocked. Three different HRV representations are considered. Afterwards, the spectral content in the HF band of the HRV representations is calculated and the strength of the RSA is estimated using two approaches, namely orthogonal subspace projections and a time-frequency representation.

The results suggest that the selection of an HRV representation does not have a significant impact on the RSA estimates in a healthy population.

1. Introduction

The analysis of Heart Rate Variability (HRV) provides insights into the modulation of the Autonomic Nervous System (ANS) in a noninvasive way [1]. To evaluate the HRV, different mathematical tools can be used such as the

tachogram [1], the Integral Pulse Frequency Modulation (IPFM) model [2] and the point process model [3] [4]. Each of these tools generates different HRV representations.

Parameters derived from the HRV representations are useful to assess the parasympathetic and sympathetic modulations from the ANS. In the frequency domain, the power spectrum of the HRV can be used, in which the power in the High Frequency band (HF, 0.15 Hz - 0.4 Hz) is associated with pure vagal activity and the power in the Low Frequency band (LF, 0.04 Hz - 0.15 Hz) is usually linked to both sympathetic and parasympathetic modulations [1]. In addition, the HRV is modulated by the respiration. This occurs thanks to a physiological process called the Respiratory Sinus Arrhythmia (RSA) [5] which is observed as an increased HR during inhalation and a decreased HR during exhalation. Usually, the RSA is quantified as the power contained in the HF band of the HRV [6]. However, the respiratory rate might be characterized by narrow bands inside the HF or it can fall outside the HF band. For this reason, alternative methods have been proposed for the quantification of the RSA. Two of them are the subspace projections [7] and a Time-Frequency (TF) representation [8], which are evaluated in this study.

The aim of this paper is to evaluate the influence of the HRV representations on the aforementioned RSA quantifications. This evaluation is done using a dataset in which changes in autonomic regulation of the heart are pharmacologically induced with different ANS blockades (atropine or propranolol) in a healthy population.

2. Dataset

The *Pharmacological ANS blockades database (HMS-MIT-FMMS)*, recorded in the Clinical Center at the Massachusetts Institute of Technology, was used in this study. Single-lead electrocardiogram (ECG) signals and changes in the instantaneous lung volume with a two-belt chest-

abdomen inductance plethysmograph were acquired with a sampling frequency of 360 Hz from 13 healthy male volunteers (Age: 19-38 years) without any history of cardiorespiratory diseases. During the protocol, atropine (0.03 mg/kg) or propranolol (0.2 mg/kg), for parasympathetic blockade and suppression of the sympathetic activity respectively, were administered through a catheter.

The signals were first recorded with the subjects in supine position and without administering any of the drugs. Next, the volunteers were moved to standing position and, after a minimum waiting period of 5 minutes to reach hemodynamic equilibrium, the signals were recorded. Afterwards, the subjects were given one of the two drugs. 7 of them (20.29 ± 1.25 years old) received atropine and 6 (26 ± 6.5 years old) received propranolol. After 10 minutes to reach equilibrium, the signals were acquired in supine and standing positions following the same protocol described above. The recordings on each stage are referred as supine control (SUC), standing control (STC), supine atropine (SUA), standing atropine (STA), supine propranolol (SUP) and standing propranolol (STP). The volunteers were asked to breathe with an irregular respiratory rate following the indications of a recorded tone. The protocol is depicted in Figure 1 and more details can be found in [9].

3. Methods

3.1. Preprocessing

Firstly, the ECG signals were upsampled from 360 Hz to 1080 Hz using a cubic spline interpolation. Afterwards, the R-peak locations were found using the method reported in [10]. For this, the software described in [11] with the post-processing and ectopic removal options was used.

Secondly, the respiratory signals were downsampled from 360 Hz to 4 Hz after applying an antialiasing filter and next bandpass filtered between 0.01 and 1 Hz.

3.2. HRV representations

The RR-intervals are a discrete unevenly sampled time series. Hence, three mathematical descriptions of the HRV were used to generate evenly sampled HRV representations with a sampling frequency of 4 Hz:

- *The uniformly sampled tachogram*: This representation is computed by resampling the RR intervals using a cubic spline interpolation.
- *The Integral Pulse Frequency Modulation Model (IPFM)* [2]: This model assumes that the sympathetic and parasympathetic regulations on the HRV can be represented by a modulating signal that triggers a pulse when its integral reaches a certain threshold. This modulating signal was used as an HRV representation.

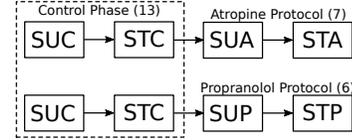


Figure 1. Recording protocol. The numbers in brackets indicate the number of subjects on each phase.

- *The Point Process model* [3]: This model characterizes the statistical properties of the pulses in the sinoatrial node as a series of discrete events in continuous time following a time-varying history-dependent inverse Gaussian probability distribution. The model order p was set as 8 and the forgetting factor to 0.98 based on the parameters reported in [3]. Δ was set to 0.25 s to obtain a HRV representation with $F_s=4$ Hz and the window for the estimation of the initial parameters was empirically set to 50 s. The HRV representation in this case is derived as the first moment of the probability of the RR-intervals.

The three representations were generated for each stage on the experimental protocol. Afterwards, they were band-pass filtered between 0.01 Hz and 1 Hz.

3.3. Normalized HF band

The normalized power in the HF band (HF_n) of the Power Spectral Density (PSD) estimation of the HRV representations was derived. This band was defined either from 0.15 Hz to 0.4 Hz, or using the extended band from 0.15 Hz to half the mean heart rate [12]. The shortest between these two was chosen. For the calculations, the PSD estimations were computed using the Welch's method and a hamming window of 40 s with 20 s overlap.

3.4. RSA quantifications

The filtered respirations and the HRV representations were used to quantify the strength of the RSA with two different approaches:

Orthogonal Subspace Projections (OSP) [7]: This method was used to decompose each HRV representation into a respiratory component (HRV_{resp}) and a residual component. The relative power of HRV_{resp} (P_{osp}) was used to quantify the dynamics of the HRV linearly related to the respiration and it was calculated as:

$$P_{osp} = (HRV_{resp}^T \cdot HRV_{resp}) / (HRV^T \cdot HRV) \quad (1)$$

Time Frequency (TF) representation [8]: Spectrograms of the respiratory signal and HRV representations based on a Cohen's class TF distribution were built. This tool analyzes changes in the frequency content of the signals over time while reducing biases in the estimates that occur with other TF representations. The coherence spectrum between the respiratory and HRV signals was also calculated

using the same TF representation. The product between the coherence spectrum and the spectrogram of the HRV representation was used to extract the spectrum of the respiratory component [8]. This spectrum was normalized by the spectrum of the HRV and then averaged to obtain a quantification of the RSA, denoted as P_{TF} .

3.5. Comparison of the methods

Two statistical tests were used for the comparisons:

- Significant differences between the estimates of the same parameter, in the same stage of the protocol using the different HRV representations. These differences were evaluated using Kruskal-Wallis and multiple comparisons tests with Bonferroni correction.

- Significant changes on the parameters between the supine and standing positions using the Friedman's tests for repeated measures.

These tests were performed with a 95% confidence interval.

4. Results and Discussion

The results are shown in figure 2 and the tests are discussed in this section.

4.1. HRV representations

The differences for the same parameter, in the same stage of the protocol and with the different HRV representations were not significant between the resampled tachogram and the modulating signal of the IPFM model. Few significant differences (marked with a \blacklozenge in Figure 2) were found when comparing with the representation based on the point process model ($p < 0.05$). This observation might be explained by the fact that the estimation of the probability distribution of the R-peaks in the point process model requires an initial number of samples. For this reason, the resulting segments are shorter, producing significantly different outcomes in some cases. This effect should be minimized in longer signals.

4.2. Supine vs. Standing position

The tests for the variation of the parameters due to the change from supine to standing position display different trends. Firstly, the reduction of the HF_n during the control stage (SUC to STC) are significant for the subjects following any of the protocols (atropine or propranolol). When a drug is administered, and despite that significant differences were not found, a decreasing trend was also observed. These results are associated with an increased sympathetic activity and/or a decreased vagal modulation in the standing position, which can be clearly observed us-

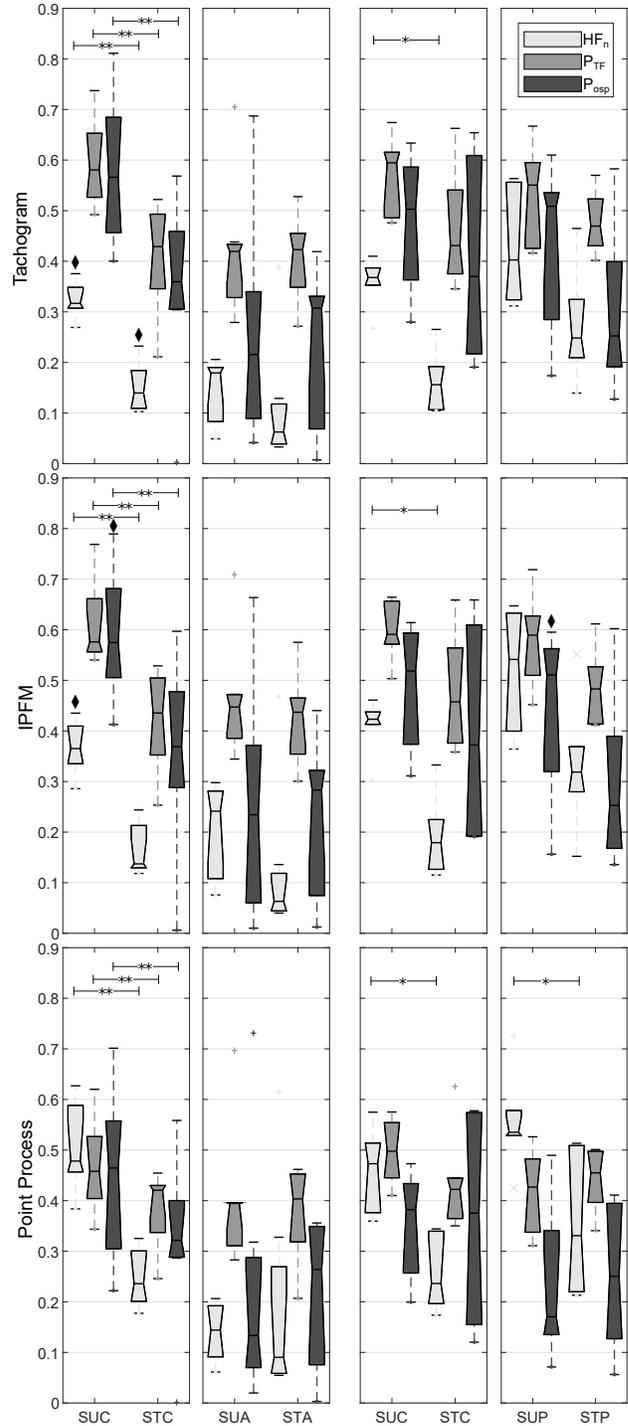


Figure 2. Boxplots for HF_n, P_{TF} and P_{osp} calculated with different HRV representations. The \blacklozenge indicate significant differences in the calculated parameters with respect to the ones calculated with the point process representation. Significant changes due to position changes from supine to standing are indicated with *.

ing any of the evaluated parameters.

Secondly, the decrease on the quantifications of the RSA in the control stage for the volunteers in the atropine protocol was significant ($p < 0.01$). Despite that the same trend was observed in the control phase of the group that received propranolol, the difference was not significant. This result might be due to the wider range of ages for the volunteers in the propranolol group. It has been shown that the strength of the RSA is dependent on changes with age [13]. Hence, the variability of the RSA strength is higher in this group and significant differences become more difficult to find.

4.3. RSA estimations

As discussed in [7] and as observed in Figure 2, the HF_n parameter tends to underestimate the respiratory modulation on the HRV because the breathing rates tend to fall below 0.15 Hz in this dataset. Hence, the respiratory information is mainly contained in the LF band and this is not captured by the HF_n parameter. In contrast, the RSA estimates evaluated in this paper do not consider a specific frequency band. On the one hand, the OSP is based on the predictability of the HRV from the respiration, and on the other hand, the TF representation is based on their spectral coherence. Therefore, these quantifications are able to better capture the RSA in conditions in which the spectrum of the respiration falls outside the HF. In general, the trends observed with the two RSA quantifications are consistent.

5. Conclusions

Despite few significant differences, the trends followed by the HF_n and the RSA estimates were very similar with the three HRV representations under investigation. These results suggest that the selection of a HRV representation is irrelevant for the analysis of the RSA in this dataset. However, these signals come from healthy volunteers, while this selection might become more important when a more irregular ECG signal occurs. Further analysis should consider datasets with a significant amount of ectopic beats or with signals recorded during exercise. In addition, the trends on the RSA quantifications were consistent when estimated with either the subspace projections or with the TF representation. This result indicates that these methods measure the respiratory modulation similarly since they are both based on the extraction of the respiratory information from the HRV representation.

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