Cardiorespiratory Synchronization: is it a Real Phenomenon?

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Abstract

In this work we present a quantitative approach to the analysis of cardiorespiratory synchronization, which is a newly discovered phenomenon. The primary aim of this study is to determine whether cardiorespiratory synchronization is a real phenomenon or a random one.

We utilized the surrogate data analysis approach. A surrogate data set was constructed from recordings of ECG and respiration obtained from 14 healthy adults. The surrogate data lacks the coupling between the heart and respiration. The real and surrogate data were subjected to a quantification algorithm in order to determine the statistical properties of synchronization in the two data sets. Synchronization was found in both the real and surrogate data. However, Synchronization was significantly less abundant in the surrogate data. In view of those results, cardiorespiratory synchronization seems to be a real phenomenon, yet it probably does not play a crucial role in cardiorespiratory interaction.

1. Introduction

Modulation of heart rate (HR) by respiration, which is the main source of heart rate variability, is long known. This phenomenon has been studied extensively, and although it is not fully understood, its physiological determinants have been unveiled. Lately, the study of phase synchronization in chaotic oscillators has led to the discovery of another aspect of cardiorespiratory interaction: synchronization between respiration and HR [1]. Cardiorespiratory synchronization (CS) was observed in young athletes in coexistence with modulation of HR by respiration. The synchronization was found using a novel visualization tool, the Synchrogram [1]. The Synchrogram enables to visually detect epochs of synchrony between two noisy signals, with any rational frequency ratio.

The qualitative analysis of cardiorespiratory interaction presented in [1,2] raises two questions: a) is cardiorespiratory synchronization a real phenomenon, implying the mutual adjustment of the subsystems, or does it occur randomly? b) what is the physiology underlying synchronization?

The two questions are related. Associating distinct physiological conditions to CS negates the hypothesis of CS being random. Indeed, preliminary results indicate that CS is associated with lower HR variability, and more specifically, with reduced values of parasympathetic activity [1-2].

In this work, we apply the approach of surrogate data analysis to the study of CS, in order to answer the first question. Surrogate data analysis is a widely used approach in the field of nonlinear dynamics, especially when trying to assess a functional relation between an attribute of a system to one of its features. The essence of surrogate analysis is the construction of a (surrogate) data set from the original data, while preserving all features of the data, except for the one whose influence is being tested. A difference in the measured attribute between the real and surrogate data then indicates that it is related to that specific feature that is absent in the surrogates. Our analysis relates the heart-respiration coupling to the synchronization between them. The surrogates were constructed by considering the interaction between respiration and heart rate taken from different subjects. Avoiding randomization of the signals themselves, as commonly done in surrogate data analysis, preserves all features of the cardiorespiratory system, except for the coupling between the two subsystems.

We applied a previously developed algorithm, which enables to quantify CS [3], to the analysis of the real and surrogate data. We then compared the statistical properties of the observed CS in both real and surrogate data.

Our results show that synchronization appears in both real and surrogate data, although significantly less in the surrogates. Cardiorespiratory synchronization should therefore enter the cadre of cardiorespiratory interactions. Unveiling its physiological determinants and relating cardiorespiratory pathologies to CS will undoubtedly increase our knowledge of this complex system.

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2. Method

2.1. Data set

The data set included the ECG and respiration recordings obtained from 14 healthy male subjects (aged 28-59). Respiration was assessed from measurements of abdominal movements (using Respitrace, by Ambulatory Monitoring). Recordings lasted 30 min, in the supine position. The 2 signals were later digitized at a sampling rate of 300 Hz (see ref [4] for details). R-waves were detected automatically from the ECG signal.

Before detecting the peaks of the respiratory signal, this signal had to be low-passed filtered, in order to reduce the noise. The asymmetrical breathing pattern compelled us to consider the first 4 harmonics of the respiration. Moreover, the asymmetrical shape of the respiration signal is highly sensitive to dispersion of the filter, since a frequency dependent group-delay would alter the signal. Such alteration of the signal results in timing error when detecting the peaks of the signal, thus introducing effective noise to the series of the times of maxima. The respiration signal was therefore low-pass filtered digitally using a Chebyshev filter with cutoff frequency f_c=1 Hz and passband ripple of 0.01 dB. The respiration signal was filtered twice: first in the usual way and then in the reversed direction. While this filtering technique is not causal, it cancels the group delay of the filter.

2.2. The synchrogram

The Synchrogram is a visualization tool, which enables the detection of synchronization epochs (SE) in bivariate data. It is most valuable in cases where one of the signals resembles a point process, i.e. almost periodic and wideband, such as the human ECG. The Synchrogram is a stroboscopic view of the phase of the respiration signal at the times of R-waves. Full description of the Synchrogram can be found in [1] and [2].

We will briefly describe the construction of the Synchrogram. The first step is computation of the phase of the respiration signal. The unwrapped phase $\phi_r(t)$ is assessed by detecting the local maxima, which represent the beginning of expiration. A 2π phase increase is then assigned to every peak (which means that the signal has completed one cycle). The discrete-time phase signal is interpolated to provide a continuous phase signal. The phase of the respiration signal is then assessed at the times of R-waves t_k. Synchronization with ratio of n:m means that respiration completes m cycles (and its phase increases by $2\pi m$) while the ECG completes n cycles (and its phase increases by $2\pi n$). The mathematical implication of the last observation is that in the case of n:m synchronization: $\phi_r(t_{k+n})=\phi_r(t_k)+2\pi m$. Therefore, define: $\psi_r(t_k)\equiv\phi_r(t_k) \bmod 2\pi m$. Plotting $\psi_r(t_k)$ versus t_k results in n horizontal lines in case of m:n synchronization (see figure 1, initially disregarding the different markers).

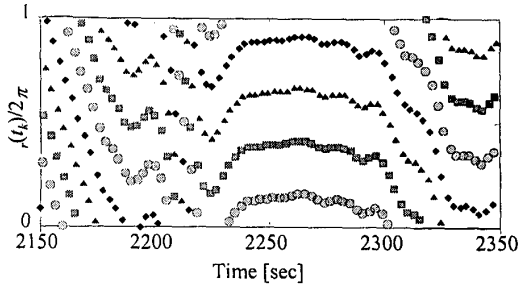

Figure 1: An example of a SE in a normal adult, as detected from the Synchrogram. The different markers represent the different subgroups.

2.3. Quantification of the synchrogram

The quantification process is based on the automation of the search for horizontal parallel straight lines in the Synchrogram. The search is performed for every couple of m and n (the ratio of the instantaneous frequencies). The quantification algorithm will be described briefly; a more detailed description can be found in [3]. The first step is choosing the m and n and constructing the Synchrogram. Next, the phases $\psi_r(t_k)$ are divided into n subgroups alternatively (see the different markers in figure 1). Note that when the Synchrogram exhibits an n lines structure, every subgroup will coincide with one of the lines.

We then use the transformation: $\psi_r(t_k)\rightarrow e^{i\psi_r(t_k)}$ in order to avoid phases discontinuities. The geometrical average of every subgroup is computed. The resulting vector has a magnitude of 1 and its phase is the average of the all group members' phases. The averaged phase is then subtracted from all group members, thus eliminating the vertical distance between the lines (figure 2).

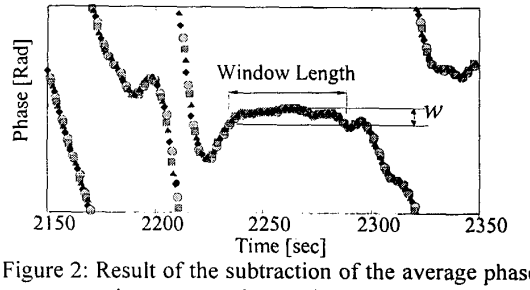

Figure 2: Result of the subtraction of the average phase from every subgroup members. The resulting line has a small vertical width during SE (t=2340÷2290) and a large one in the absence of synchronization.

The width of the resulting line, which is effectively the collection of all points after subtraction of the differences

between the lines, is a measure of the synchronization between the 2 signals. This measure, denoted by W was computed in a sliding window in order to assess the dynamical behavior of synchronization. The length of the window was set to 31 sec, hence discarding too short epochs and transients. A threshold for W was set to 0.03. The cardiorespiratory system is considered to be synchronized when W is below this threshold. A misdetected R-wave or an arrhythmia increase the value of W locally. Therefore, gaps between SEs shorter than 11 sec were discarded. The values of the parameters were set to detect epochs which were detected visually as synchronization epochs.

2.4. Construction of the surrogate data

The delicate part of surrogate data analysis is always the construction of the surrogates. The easy task of generating surrogates when analyzing simulated data becomes a difficult one when analyzing real data. In principle, the surrogates should be the respiration and heart rate of a subject, but without the coupling between them. This way of constructing surrogates is impossible when considering data acquired from a natural system, since the exact nature of the subsystems is unknown. Moreover, models for the cardiorespiratory system have been suggested but none of them has succeeded in describing both linear and nonlinear features of the system. Therefore, a different approach was adopted to deal with the problem. The surrogate HR-respiration couples were constructed by associating the respiration signal of every subject with the heart rate of all others. The 14 recordings thus yielded 182 surrogates. The main advantage of using combinations of respiration and heart rate signals is that all the features of the signals, linear as well as nonlinear, are preserved, while the coupling is eliminated. Any manipulation of the signals themselves, while enabling to generate large numbers of surrogates, would destroy some basic features of the system, thus obscuring the factors of CS.

However, two problems arise. The first is the limited number of surrogates: N^2-N surrogates, where N is the number of subjects. This should be contrasted with the conventional method of randomizing some features of the signals, thus providing large quantities of surrogate HR-respiration couples. The second problem rises from lack of full confidence that a couple of respiration and heart rate, taken from different subjects, represents a probable physiological condition. The second limitation of the method promotes the use of numerous kinds of surrogates, each preserving different feature of the system.

2.5 Measured parameters

Several parameters of the synchronization epochs were compared between the original and surrogate data. Although synchronization was expected to appear in the surrogates, SEs in the surrogates were expected to be shorter than SE in the original data. Therefore, the duration of the SEs in both the original and surrogate data was compared. Let n_{O_i} and n_{S_j} be the number of detected synchronization epochs in the i original couple and the j surrogate couple respectively. The duration of a SEs of the i original couple are denoted by $T_p^{O_i}, 0 \le p \le n_{O_i}$ and of a SE of the j surrogate couple by $T_q^{S_j}, 0 \le q \le n_{S_j}$. The relatively low number of long SEs in both data sets (figure 3), compelled us to consider also the HR-respiration couples which do not exhibit any synchronization at all. Thus, a second parameter was computed for the original and surrogate data: the total duration of SEs in every HR-respiration couple:

$$\widetilde{T}^{O_i} = \begin{cases} \sum_{p=1}^{n_{O_i}} T_p^{O_i} & n_{O_i} > 0 \\ 0 & n_{O_i} = 0 \end{cases}$$

Note that the smallest value of $\widetilde{T}^{O_i}$ is 0, and the next larger value is 31 sec. The total duration of SEs of the surrogates $\widetilde{T}^{S_j}$ was constructed similarly.

Patterns of synchronization might appear in the absence of coupling when both heart rate and respiration rate are constant. In order to check whether the detected SEs in the surrogates are caused by constant heart and respiration rates, we measured the standard deviation of the RR interval during SE in both the original and surrogate data. Constant HR together with synchronization implies constant respiration rate, therefore only the HR was examined.

2.6 Statistics

All the measured statistical quantities are not guassian distributed. Therefore, a nonparametric approach was used. The quantities were compared using the one-sided Mann-Whitney U-test [5].

3. Results

An important result of the surrogate data analysis is the existence of SEs in the surrogates. 9 SEs were found in 8 of the subjects, lasting 31-78 sec and 71 SEs were found in 51 surrogate HR-respiration couples (out of 182), lasting 31-105 sec. The percentage of HR-respiration couples, which exhibited synchronization, is considerably higher in the original data (57%) than in the surrogates (28%). However, the difference is not statistically significant.

The mean and standard deviation of the duration of the SEs in the original data was 40.2±15.3 sec, and 41.3±13.6 for the surrogate data. Clearly, there is no significant

difference.

While the distribution of the SEs' duration appears to be similar in the 2 data sets, it is clear that synchronization is more abundant in the real data. The histograms of $\widetilde{T}^{O_i}$ and $\widetilde{T}^{S_j}$ are shown in figure 3. The 2 data sets were found to be statistically different in that sense (p=0.03). Moreover, considering only the number of SEs in every couple yielded even better significance (p=0.02). The histograms are shown in figure 4.

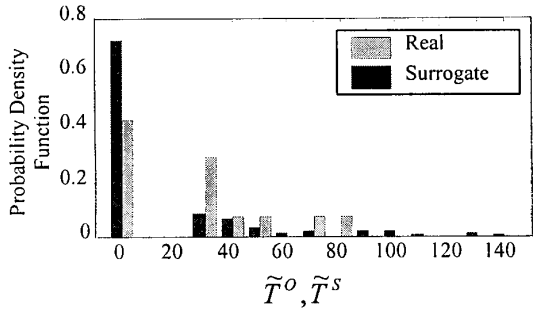

Figure 3: Histogram of the total duration of SEs in HR-respiration couples. Note that more than 70% of the surrogates did not exhibit any SE at all.

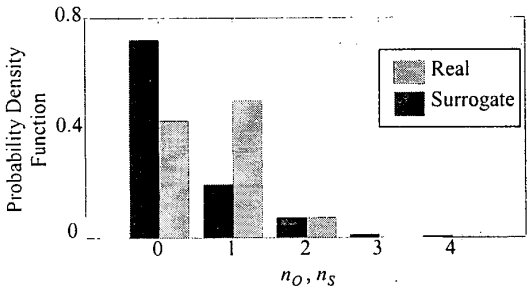

Figure 4: Histogram of the number of SEs in the HR-respiration couples.

No difference was found with respect to the variability of the RR interval during SE between the 2 data sets.

4. Discussion

The presence of synchronization in the surrogate data is intriguing. The immediate conclusion from this result is that at least some of the SEs in the real data occur randomly. However, concluding that all SEs are the result of random matching of heart rate to respiration rate might be erroneous. The more reasonable conclusion from the existence of SEs in the surrogate data is that some of the SEs in the real data occur at random, while others are the result of true synchronization. The difference in the statistical properties of the SEs between the real and surrogate data supports the last conclusion. This conclusion is also supported by the correlation between SEs and heart rate variability reported in [3].

The fact that out of the 420 min of recordings, synchronization was observed only during 5 min, indicates that it does not play a major role in cardiorespiratory interaction. In comparison, modulation of the heart rate by respiration is present, to some extent, during most of the time. The hypothesis of the secondary role of synchronization in cardiorespiratory interaction is also supported by the fact that the difference between real and random SEs is statistical in nature, rather than deterministic.

The quantification method applied to real and surrogate data is useful for verifying the existence of synchronization in bivariate data. However, it does not enable to probe into the origins of the phenomenon. Therefore, this statistical approach should be extended to larger samples and to various physiological conditions, which affect the coupling, in order to further validate the presence of real synchronization in the cardiorespiratory system and to assess its physiological importance.

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