PROCEEDINGS OF SPIE

SPIEDigitalLibrary.org/conference-proceedings-of-spie

Study of statistical properties of the method of analysis of directional couplings based on modeling of phase dynamics

E. Borovkova, E. Dubinkina, A. Hramkov, Y. Ishbulatov, V. Skazkina, et al.

E. I. Borovkova, E. S. Dubinkina, A. N. Hramkov, Y. M. Ishbulatov, V. V. Skazkina, A. S. Karavaev, "Study of statistical properties of the method of analysis of directional couplings based on modeling of phase dynamics," Proc. SPIE 12194, Computational Biophysics and Nanobiophotonics, 121940B (29 April 2022); doi: 10.1117/12.2626038



Event: XXV Annual Conference Saratov Fall Meeting 2021; and IX Symposium on Optics and Biophotonics, 2021, Saratov, Russian Federation

Study of statistical properties of the method of analysis of directional couplings based on modeling of phase dynamics

Dubinkina E.S.*a, Borovkova E.I.a,b, Hramkov A.N.a, Ishbulatov Y.M.a,b,c, Skazkina V.V.a, Karavaev A.S.a,b,c

^aSaratov State University, Astrakhanskaya Street, 83, Saratov 410012, Russia; ^bDepartment of Innovative Cardiological Information Technology, Institute of Cardiological Research, Saratov State Medical University, B. Kazachaya Street, 112, Saratov 410012, Russia; ^cSaratov Branch of Kotelnikov Institute of Radio Engineering and Electronics of Russian Academy of Sciences, Zelyonaya Street, 38, Saratov 410019, Russia;

ABSTRACT

Known works have shown a decrease in the coherence of the process of parasympathetic control of heart rate variability and the process of respiration during healthy aging. To get an idea of the reasons for the decrease in the coherence of the processes under study, in this work we investigated the possibility of using the method for assessing the directional coupling based on modeling of phase dynamics to analyze the directional couplings between the processes of parasympathetic control of heart rate variability and the respiration process. Due to the complexity, nonstationarity and strong nonlinearity of the processes under study, an important and nontrivial task is to choose the duration of the analyzed time series of high-frequency oscillations of the RR-intervals signal and respiration in calculating the indices of directional coupling. This work shows the possibility of using the method for assessing the directional coupling with the length of the analyzed time series from 15 to 450 characteristic periods of oscillations.

Keywords: Directional Couplings, parasympathetic control of the heart rate, respiration

1. INTRODUCTION

The interaction of the human cardiovascular and respiratory systems attracts considerable attention of researchers [1-5]. It has been shown that the cardiorespiratory interaction changes in different physiological states [6-8], is important in the study of sleep [9-12], decreases in the process of healthy aging [13, 14], differs in newborn children [15].

The interaction between the cardiac and respiratory systems has traditionally been identified by respiratory sinus arrhythmia (RSA) analysis [1, 2], which explains the periodic change in heart rate during the respiratory cycle, and cardiorespiratory phase synchronization (CRPS) [3-5], which is defined as sequential occurrence of heartbeats in the same relative phases in successive respiratory cycles.

For a deeper understanding of the complex structure of communication between the cardiac and respiratory systems, researchers are trying to characterize the driver-response (causal) relationships, or directionality of coupling [16-19]. The idea of the method for assessing the direction of cardiorespiratory interaction is as follows. Instantaneous phases of oscillations are determined from the time series of signals from the CVS and respiratory systems. Then, the phase dynamics of oscillations is simulated using coupled irregular autonomous oscillators.

It is assumed that if the first system is controlled by the second system, then the evolution of the instantaneous phase of the first system also depends on the instantaneous phase of the second system. Therefore, predicting the dynamics of the instantaneous phase of the first system from its previous values can be improved by using information about the dynamics of the instantaneous phase of the second system, only if the second system controls the first system.

There were proposed several quantitative indices in works [16-19], which were used to analyze the directed cardiorespiratory interaction between the main heart rate with a characteristic frequency of about 1 Hz and respiration with a frequency of about 0.25 Hz. In these works, it was shown that in a newborn child, couplings are symmetrical.

Computational Biophysics and Nanobiophotonics, edited by Dmitry E. Postnov, Boris N. Khlebtsov, Proc. of SPIE Vol. 12194, 121940B · © 2022 SPIE · 1605-7422 · doi: 10.1117/12.2626038

During the first 6 months of a child's life, there is a tendency to a transition from a symmetrical coupling to an almost unidirectional coupling, the respiratory generator in the central nervous system becomes dominant. For adults, the coupling between the cardiovascular and respiratory systems is unidirectional, the respiratory rate affects the heart rate through stimulation of the vagus nerve and direct mechanical action on the pacemaker.

An important and open question is the study of the cardiorespiratory interaction between the process of parasympathetic control of heart rate variability and the respiration process. In work [13], we analyzed the cardiorespiratory interaction in a large group of healthy subjects from 20 to 96 years old and found that the coherence of the processes of parasympathetic control of heart rate variability and the respiration process decreases with age.

To get a further idea of the reasons for the decrease in the coherence of the processes under study, in this work we investigated the possibility of using the method for assessing the directional coupling proposed in [19] in analyzing the signals of high-frequency oscillations of the signal of RR intervals and respiration.

It is known that in order to obtain non-biased estimates of the directional coupling indices and to ensure the frequency of erroneous conclusions about the presence of the influence of systems on each other less than 0.05, it is necessary that the time series be sufficiently long and, at the same time, stationary. Therefore, the purpose of this work was to study the influence of the duration of temporary realizations on the calculated indices of the directional coupling.

2. EXPERIMENTAL DATA

We analysed data of 10 healthy subjects (3 females and 7 males) aged 19 to 21 years ($M\pm$ SD). The signals of electrocardiogram (ECG) and respiration were simultaneously recorded within 2 hours for each subject. Registration was carried out in a calm state in a horizontal position of the body approximately 2 hours after eating in the morning.

Figure 1 shows fragments of typical experimental signals. The signal of electrocardiogram was recorded in the I standard lead, the respiratory signal was recorded using a resistive sensor. Signals were recorded using a multichannel digital polyrecorder Rehacor-T (Medicom MTD, Russia) with a sampling frequency of 250Hz and a 16-bit resolution. The band pass of all recorded signals in both devices was 0.003-100 Hz.

In accordance with the recommendations [20] we extracted the time series of RR-intervals, then interpolated it and resampled at regular intervals with a frequency of 5 Hz. Figure 1(b) shows the resulting series of RR-intervals.



Figure 1. Experimental data of the subject \mathbb{N}_{2} : (a) – ECG, (b) – RR-intervals (points – nonequidistant sequence, solid line – interpolated equidistant series), (c) – respiration. ECG signal is given in millivolts, RR-intervals in seconds, respiration in mm.

3. METHODS

Figure 2 shows the Fourier power spectra obtained from the RR-intervals and respiration signals. High-frequency spectral regions of 0.14-0.5 Hz were marked in blue and red. According to a number of works [20,21], high-frequency oscillations with a frequency of 0.14-0.5 Hz in the signal of RR-intervals (Fig.2a) reflect the activity of the parasympathetic circuit of the heart rate regulation and their basic frequency coincides with the basic respiratory frequency [22] (Fig. 2b). In this work we calculate the strength of the directional coupling between the processes of RR-intervals and respiration in the HF range.



Figure 2. The Fourier power spectra obtained from the signals of: (a) – RR-intervals; (b) – respiration. High-frequency spectral regions of 0.14-0.5 Hz are marked in blue and red.

To isolate high-frequency oscillations of RR-intervals and respiration, we used a band-pass filter with a passband of 0.14-0.5 Hz. Figure 3 shows fragments of the signals of RR-intervals and respiration obtained as a result of filtering.



Figure 3. High-frequency oscillations isolated from signals of: (a) - RR-intervals; (b) - respiration.

To isolate the instantaneous phases of the signals, we used the Hilbert transform. Figure 4 shows fragments of the instantaneous phases of the RR-intervals and respiration signals.



Figure 4. The instantaneous phases of the high-frequency oscillations isolated from the signals: red line – RR-intervals; blue line – respiration.

Using the method proposed in the work [19] we calculated the directional couplings indices between the obtained time realizations of the instantaneous phases of RR-intervals and respiration at several values of the trial delay between the time series Δ . We iterated over the trial delay Δ in the range ±4 seconds (it is about one characteristic period of the investigated high-frequency oscillations) with a step of 1 second and calculated indices $G_{\text{RR}\to\text{Resp}}(\Delta)$ \bowtie $G_{\text{Resp}\to\text{RR}}(\Delta)$ for each Δ . The indices $G_{\text{Resp}\to\text{RR}}(\Delta)$ and $G_{\text{Resp}\to\text{RR}}(\Delta)$ took on values from 0 to 1. The index $G_{\text{Resp}\to\text{RR}}(\Delta)$ characterizes what fraction of the dispersion of the phase oscillations of the RR-intervals signal can be described using the values of the signal of phase oscillations of respiration. The index $G_{\text{RR}\to\text{Resp}}(\Delta)$ characterizes what fraction of the respiration signal can be described using the values of the phase oscillations of RR-intervals.

4. RESULTS

The aim of this work was to study the influence of the duration of the time series of instantaneous phases on the estimates of the indices of the directional coupling between the investigated high-frequency components of the RR-intervals and respiration signals. Therefore, for each person, the dependences $G_{\text{Resp}\to\text{RR}}(\Delta)$ and $G_{\text{RR}\to\text{Resp}}(\Delta)$ were calculated over 24 time series of duration L 1,2,3,4,5,10,15,20,25 and 30 minutes.

Figure 5 shows examples of the dependences $G_{\text{Resp}\to\text{RR}}(\Delta)$ and $G_{\text{RR}\to\text{Resp}}(\Delta)$ for subject No2, estimated by analyzing the time series of instantaneous phases with a duration L of 1, 5 and 30 minutes.



Figure 5. The example of the dependence of the directional couplings indices on the trial delay, estimated from time series of 1, 5, 30 minutes: (a) – $G_{\text{Resp}\to\text{RR}}(\Delta)$; (b) – $G_{\text{Resp}\to\text{RR}}(\Delta)$.

To reduce the dimension of the task for all the obtained dependencies, we calculated the maximum value of the strength of the directional coupling from RR-intervals to respiration $\max G_{\text{RR}\to\text{Resp}}(\Delta)$ and from respiration to RR-intervals $\max G_{\text{Resp}\to\text{RR}}(\Delta)$. Further, we used only these maximum values of the indices and for each subject, separately for each duration of the time series L, we estimated the average value of the indices of the coupling between the scatter of these values. Figure 6 shows the result of evaluating the indices $\max G_{\text{RR}\to\text{Resp}}(\Delta)$ and $\max G_{\text{Resp}\to\text{RR}}(\Delta)$ in 24 windows 5 minutes long for subject No3. For the example shown in Figure 6(b), the median (first; third quartile) of the $\max G_{\text{RR}\to\text{Resp}}(\Delta)$ index is 0.15 (0.11; 0.21). For the $\max G_{\text{Resp}\to\text{RR}}(\Delta)$ index, the median (first; third quartiles) is 0.19 (0.15; 0.22) (Fig. 6a).



Figure 6. The result of evaluating the indices of directional couplings in 24 windows 5 minutes long for subject No 3 (a) – the points show the values of the indices $G_{\text{Resp}\to\text{RR}}(\Delta)$; (b) – the points show the values of the indices $G_{\text{RR}\to\text{Resp}}(\Delta)$

Proc. of SPIE Vol. 12194 121940B-4

Figure 7 shows the result of estimating the median, the first and third quartiles of the directional coupling indices for the entire experimental sample, depending on the duration of the analyzed time series. Analysis of the data obtained from the records of all subjects shows a stable estimate of the directional coupling indices for all analyzed time series durations L. The max $G_{\text{Resp}\to\text{RR}}(\Delta)$ index varies from 0.17 to 0.26, the max $G_{\text{RR}\to\text{Resp}}(\Delta)$ index - from 0.16 to 0.21. The difference between the first and third quartiles of the max $G_{\text{Resp}\to\text{RR}}(\Delta)$ index reaches its minimum value when the length of the realization L is 120 seconds, the $G_{\text{RR}\to\text{Resp}}(\Delta)$ - when the length of the realization L is 240 seconds.



Figure 7. Numerical indices averaged over the experimental ensemble: (a) $-\max G_{\text{Resp}\rightarrow \text{RR}}(\Delta)$; (b) $-\max G_{\text{RR}\rightarrow \text{Resp}}(\Delta)$. L is the length of the time series used to estimate the indices of the coupling. Box-and-whisker diagrams show the minimum and maximum value, first, second and third quartile of indices.

5. CONCLUSION

Thus, during our studies, we have shown the possibility of using the method for assessing the directional coupling, proposed in the work [19], to analyse the directional couplings between the processes of parasympathetic regulation of heart rate variability and the respiration process. The method used shows a stable assessment of the directional link indices when analyzing time series with a duration of 15 to 450 characteristic periods of fluctuations.

This work was supported by the Grant MK-2325.2021.1.2.

REFERENCES

- Angelone, A., Coulter, N. A., "Respiratory sinus arrhythmia: A frequency dependent phenomenon," J.Appl.Physiol 19, 479–482 (1964).
- [2] Song, H. S., Lehrer, P. M., "The effects of specific respiratory rates on heart rate and heart rate variability," Appl.Psychophysiol.Biofeedback 28,13–23 (2003).
- [3] Schäfer, C., Rosenblum M. G., Kurths J., Abel H. H., "Heartbeat synchronized with ventilation," Nature 392, 239–240 (1998).
- [4] Prokhorov, M. D., Ponomarenko, V. I., Gridnev, V.I., Bodrov, M. B., Bespyatov, A. B., "Synchronization between main rhythmic processes in the human cardiovascular system," Phys. Rev. E Stat. Nonlin. Soft. Matter. Phys. 68, 041913 (2003).
- [5] Mrowka, R., Patzak, A., Rosenblum, M., "Quantitative analysis of cardiorespiratory synchronization in infants," Int. J. Bifurcat. Chaos. 10, 2479–2488 (2000).
- [6] Moelgaard, H., Soerensen, K. E., Bjerregaard, P., "Circadian variation and influence of risk factors on heart rate variability in healthy subjects," Am. J. Cardiol., 68, 777–784 (1991).

- Hu, K., "Endogenous circadian rhythm in an index of cardiac vulnerability independent of changes in behavior," Proc. Natl. Acad. Sci. USA. 101, 18223–18227 (2004).
- [8] Ivanov, P. Ch., Hu, K., Hilton, M. F., Shea, S.A., Stanley, H.E., "Endogenous circadian rhythm in human motor activity uncoupled from circadian influences on cardiac dynamics,". Proc Natl. Acad. Sci. USA. 104, 20702– 20707 (2007).
- [9] Bunde, A., "Correlated and uncorrelated regions in heart-rate fluctuations during sleep," Phys. Rev. Lett., 85, 3736–3739 (2000).
- [10]Kantelhardtm, J. W., "Breathing during REM and non-REM sleep: Correlated versus uncorrelated behavior," Physica A. 319, 447–457 (2003).
- [11]Schmitt, D. T., Stein, P. K., Ivanov, P. Ch., "Stratification pattern of static and scale-invariant dynamic measures of heartbeat fluctuations across sleep stages in young and elderly," IEEE Trans Biomed Eng 56, 1564–1573 (2009).
- [12] Schumann, A. Y., Bartsch, R. P., Penzel, T., Ivanov, P. Ch., Kantelhardt, J. W., "Aging effects on cardiac and respiratory dynamics in healthy subjects across sleep stages," Sleep 33:943–955 (2010).
- [13] Ponomarenko, V. I., Karavaev, A. S., Borovkova, E. I., Hramkov, A. N., Kiselev, A. R., Prokhorov, M. D., Penzel, T., "Decrease of coherence between the respiration and parasympathetic control of the heart rate with aging," Chaos 31(7) (2021).
- [14] Bartsch, R. P., Schumann, A. Y., Kantelhardt, J. W., Penzel, T., Ivanov, P. Ch., "Phase transitions in physiologic coupling," Proc. Natl. Acad. Sci. U. S. A. 109, 10181-10186. (2012).
- [15] Mrowka, R., Patzak, A., Rosenblum, M. "Quantitative analysis of cardiorespiratory synchronization in infants,". Int. J. Bifurcat. Chaos 10, 2479–2488 (2000).
- [16] Rosenblum, M. G., Cimponeriu, L., Bezerianos, A., Patzak, A., Mrowka, R., "Identification of coupling direction: Application to cardiorespiratory interaction,". Physical. Review. E, 65(4) (2002).
- [17] Rosenblum, M., Pikovsky, A., Kurths, J., "Phase Synchronization in Driven and Coupled Chaotic Oscillators," IEEE Trans. Circuits Syst., I: Fundam. Theory. Appl. 44, 874-881 (1997).
- [18] Müller, A., Kraemer, J. F., Penzel, T., Bonnemeier, H., Kurths, J., Wessel, N., "Causality in physiological signals," Physiological Measurement 37(5), R46–R72 (2016).
- [19] Smirnov, D. A., Bezruchko, B. P., "Estimation of interaction strength and direction from short and noisy time series," Phys. Rev. E. 68, 046209 (2003).
- [20] "Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology," Circulation 93, 1043 (1996).
- [21] Lewis, M. J., Short, A. L., Lewis, K. E., "Autonomic nervous system control of the cardiovascular and respiratory systems in asthma," Respir. Med. 100, 1688 (2006).
- [22] Porges, S. W., " Cardiac vagal tone: a physiological index of stress," Neurosci. Biobehav. Rev. 19, 225 (1995).