Chaos

Decrease of coherence between the respiration and parasympathetic control of the heart rate with aging

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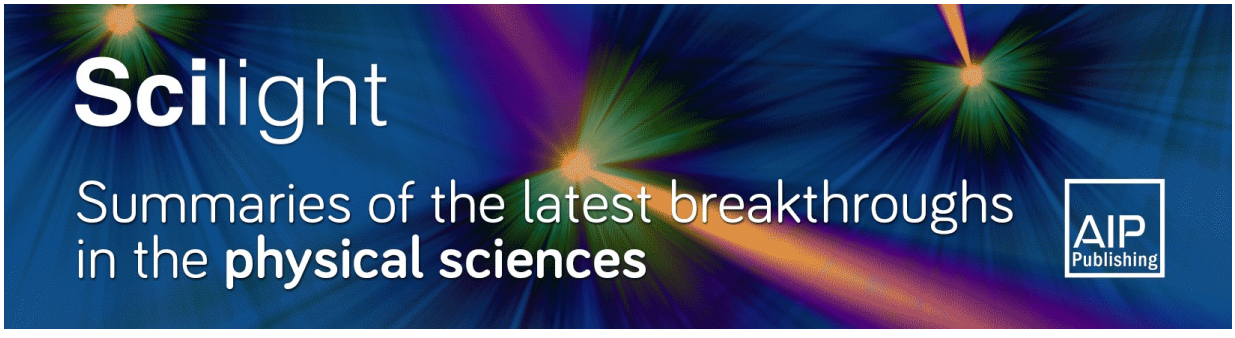

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ABSTRACT

The study of coordinated behavior between different systems of the human body provides useful information on the functioning of the body. The peculiarities of interaction and coordinated dynamics of the heart rate and respiration are of particular interest. We investigated the coherence of the processes of respiration and autonomic control of the heart rate for people of different ages in the awake state, in sleep with rapid eye movement, and in deep sleep. Our analysis revealed a monotonic decrease in the coherence of these processes with increasing age. This can be explained by age-related changes in the system of autonomic control of circulation. For all age groups, we found a qualitatively similar dynamics of the coherence between the studied processes during a transition from the awake state to sleep.

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The aging process is accompanied by physiological changes in various organs and systems of the body, in particular, the circulatory and respiratory systems. For the timely detection of pathological changes, it is necessary to develop methods for noninvasive control of their severity. In this paper, we study the signals of the cardiovascular system and respiration in subjects of different age groups without cardiovascular and respiratory pathologies in the awake state and in different stages of sleep. We have shown that the analysis of the coherence of the amplitudes and phases of the signals makes it possible to quantitatively characterize age-related changes in the cardiorespiratory interaction. A decrease in the coherence of the studied processes with increasing age is revealed, both in the awake state and in different stages of sleep. This indicates deterioration with age in the coordination of the respiratory and cardiovascular systems. It has been shown in our study that for all age groups, the coherence of respiration and the process of parasympathetic control of the heart rate is minimal in sleep with rapid eye movement and is maximal in deep sleep. Thus, a quantitative assessment of the degree of coherence of the processes under study is a promising tool for solving problems of the automated classification of different stages of sleep in polysomnography studies.

INTRODUCTION

Nonlinear, including chaotic, oscillations are typical for the work of various body systems.[1–3] In particular, the complex dynamics of the cardiovascular system and respiration attracts much attention for researchers.[4–12] Vadim Anishchenko and co-workers made a significant contribution to research in this area.[13,14] In Ref. 15, he

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studied the complex nonlinear dynamics of the blood pressure signal. In Ref. 16, he has shown a possibility of reconstructing the phase portrait from a human electrocardiogram and from the signal of an isolated heart of a frog. In Ref. 17, a method was proposed for constructing a model of interbeat intervals in the form of a discrete map. Using this model, the synchronization between the processes that regulate the heart rate was investigated.[18]

The complex dynamics of the cardiovascular system is explained by both chaotic self-oscillations of its subsystems[19–21] and their interactions.[22] Such complex collective dynamics ensures the normal functioning of the body,[23,24] while the deterioration of the coordinated behavior of the body's subsystems and the simplification of their dynamics may indicate the problems in health.[1,25–29] One of the most important interactions within the human body is the interaction between the cardiovascular and respiratory systems.[30,31] This interaction results in the frequency modulation of the heart rate, known as respiratory sinus arrhythmia (RSA).[32,33] A number of studies have shown that the rhythms of the cardiovascular system can be synchronized with the respiration.[14,31,34–40] It has been shown that the degree of synchronization of the main heart rhythm and respiration as well as the direction of their coupling are different in different sleep stages[41] and depend on the age of subjects.[31,42–44]

In contrast to the papers referenced above, studying the synchronization of respiration with the main heart rate, we have shown the presence of synchronization between the respiration and oscillations of heart rate variability (HRV) in the low-frequency (LF) range ($0.04 - 0.15$ Hz) and the high-frequency (HF) range ($0.15 - 0.5$ Hz).[40,45,46] The frequency components of HRV in the LF-range reflect the control of blood circulation from the sympathetic nervous system.[47] The main HRV frequency in the HF-range corresponds to the frequency of spontaneous respiration in healthy subjects,[48] and the power of HF-oscillations in HRV is associated with the parasympathetic control of the heart rate.[49,50] In active experiments, the synchronization between the respiration and infra-slow oscillations of brain potentials,[51] which are associated with the autonomic control of blood circulation, was also investigated.[52]

In this paper, we test a hypothesis that the degree of coherence of respiration and parasympathetic control of the heart rate in the HF-range may change during a transition from the awake state to different sleep stages and also correlate with physiological changes caused by aging. For testing this hypothesis, we analyze the coherence between the signal of spontaneous respiration and HF-oscillations in HRV in healthy subjects without cardiovascular, respiratory, and neurological pathologies.

EXPERIMENTAL DATA AND METHODS OF THEIR ANALYSIS

Subjects

Our study included 96 healthy subjects (59 females and 37 males), who were divided into four groups depending on age. The first group included 36 subjects aged $20 - 34$ years, the second group included 23 subjects aged $35 - 49$ years, the third group included 17 subjects aged $50 - 64$ years, and the fourth group consisted of 20 subjects in ages 65 and older. The data were recorded at the sleep laboratories within the European Union project SIESTA.[53] All eight sleep laboratories followed the same recording protocol in terms of recorded signals and leads. The study was approved by the local institutional review boards of the sleep centers involved. All study participants provided written informed consent. Exclusion criteria subjects for the healthy group were obstructive apnea and hypopnea, other reported sleep disorders, and identified pathologies of the respiratory, cardiovascular, and neural system.

Data preprocessing

The signals of electrocardiogram (ECG) and respiration were simultaneously recorded within 8 h at night for each subject. The ECG and respiratory signals were sampled at 200 and 20 Hz, respectively. The epochs of wakefulness, rapid eye movement (REM) sleep, and deep sleep (DS) including the stages of S2 and S3 sleep in accordance with the classification[54] were detected. We analyzed the first 5-min segments of the detected epochs without artifacts in ECG and respiratory signals.

Extracting from the ECG signal a sequence of RR-intervals, i.e., a series of time intervals between the two successive R peaks, we obtained information about the HRV.[50] To obtain an equidistant time series from a not equidistant sequence of RR-intervals, we approximated it with cubic splines and resampled with a frequency of 20 Hz.

Methods

For convenience, let us denote the sequence of RR-intervals and the respiratory signal as $x(t)$ and $y(t)$, respectively. For each subject, we estimated in awake state and in different sleep stages the cross-spectrum $R_{xy}(f)$ of the signals $x(t)$ and $y(t)$ in a 60-s window moving along the time series with a shift of 20 s,

$$R_{xy}(f) = \left\langle F_x(f) F_y^*(f) \right\rangle, \tag{1}$$

where $F_x(f)$ and $F_y(f)$ are the Fourier transform of the signals $x(t)$ and $y(t)$, respectively; the asterisk denotes complex conjugation; f is the frequency; and angular brackets denote average over 12 time windows.

Then, we calculated the coherence function $C(f)$[55,56] between the signals $x(t)$ and $y(t)$,

$$C(f) = \frac{|R_{xy}(f)|}{\sqrt{R_{xx}(f) R_{yy}(f)}}, \tag{2}$$

where $R_{xx}(f)$ and $R_{yy}(f)$ are the power spectra of the signals $x(t)$ and $y(t)$, respectively, calculated and averaged in the same way as the cross-spectrum $R_{xy}(f)$. The coherence function (2) takes values in the range from 0 (if the frequency components are not coherent) to 1 (if the phases and frequencies of the Fourier harmonics of the analyzed signals at a given frequency are coherent). For each pair of signals $x(t)$ and $y(t)$, we calculated the maximum value of the coherence function $C_{\max} = \max(C(f))$ in the HF-range.

Then, we filtered the signals $x(t)$ (sequence of RR-intervals) and $y(t)$ (respiratory signal) using a rectangular digital filter with the bandpass of 0.15–0.50 Hz and denoted the filtered signals as $s_x(t)$ and $s_y(t)$, respectively. Furthermore, for $s_x(t)$, we constructed the analytic signal $\zeta_x(t)$,[57,58] which is a complex function of time

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defined as

$$\zeta_x(t) = s_x(t) + i\tilde{s}_x(t) = A_x(t)e^{i\varphi_x(t)}, \quad (3)$$

where $A_x(t)$ and $\varphi_x(t)$ are, respectively, the amplitude and the phase of the analytic signal and function $\tilde{s}_x(t)$ is the Hilbert transform of $s_x(t)$,[58]

$$\tilde{s}_x(t) = \pi^{-1}\mathrm{PV}\int_{-\infty}^{+\infty}\frac{s_x(\tau)}{t-\tau}d\tau, \quad (4)$$

where PV means that the integral is taken in the sense of the Cauchy principal value. We constructed the analytic signal $\zeta_y(t)$ for the filtered signal $s_y(t)$ in the same way.

The instantaneous phase $\varphi_x(t)$ of the signal $s_x(t)$ was determined from Eq. (3) as $\varphi_x(t) = \arctan(\tilde{s}_x(t)/s_x(t))$. The instantaneous phase $\varphi_y(t)$ of the signal $s_y(t)$ was defined in the same way. We detected the epochs of coherence between the instantaneous phases of HF-oscillations in RR-intervals and respiration analyzing the following phase difference: $\Delta\varphi(t) = \varphi_x(t) - \varphi_y(t)$. The epochs of coherence of the instantaneous phases $\varphi_x(t)$ and $\varphi_y(t)$ correspond to the areas in which the phase difference $\Delta\varphi(t)$ fluctuates around a constant value and the condition $|\Delta\varphi(t)| < \text{const}$ is fulfilled.[59]

For detecting the epochs of phase coherence between the studied signals, we used the algorithm[45] based on a linear approximation of an instantaneous phase difference in a moving window, which has shown its effectiveness for physiological signals.[60] The algorithm for searching of phase coherence epochs is as follows. The time series of $\Delta\varphi(t)$ is linearly approximated in a window of width b by using the method of least squares. As a result, for a time moment t_i corresponding to the middle of the window, we obtain a coefficient α_i of the approximating line slope. Moving the window by one point along the time series of $\Delta\varphi(t)$, we calculate a slope α_{i+1} for a time moment t_{i+1} and so on. The epochs of phase coherence, in which the relative phase $\Delta\varphi(t)$ exhibits plateaus, correspond to areas of small $|\alpha| \le |k|$ values, where k is a threshold value. The duration of these epochs should exceed the value l to exclude short regions with a high probability of accidental coincidence of instantaneous phases of oscillations. Following recommendations given in Ref. 45, the values of b and l were chosen close to a characteristic period of oscillations ($b = 4$ s and $l = 4$ s) and $|k| = 0.01$.

Specific phase coherence (*SPC*) was calculated as the total duration of all coherent epochs divided by the duration of the entire record. The *SPC* measure is equal to 1 in the presence of coherence throughout the entire record and equal to 0 in the absence of epochs of coherence. We calculated *SPC* and $C_{\max}$ for each subject in the awake state and in different sleep stages.

Estimation of statistical significance of results

To test the statistical significance of *SPC* and $C_{\max}$, we compared their values with the values obtained from the surrogate data. From each original signal $s_x(t)$ and $s_y(t)$, we generated $M = 100$ surrogate time series by setting a uniform random distribution of the initial phases of the harmonics in the signal expansion in a Fourier series.[61] This method of preparing surrogate data preserves the periodograms of the analyzed signals but destroys coherence between their phases. Then, for each ith pair of surrogates, we calculated SPC^i and $C^i_{\max}$, $i = 1, \ldots, M$. For the ensembles of surrogate data, we plotted their distributions. Finally, we defined the 95th percentile of such distributions, which corresponds to the level of statistical significance $p < 0.05$.

To test the significance of differences in the estimates of mean values for different groups, we used the Kruskal–Wallis test and the Mann–Whitney U-test.[62,63]

RESULTS

Figure 1 shows short fragments of typical experimental signals for a healthy elderly subject (71 years old) in the awake state. The sequence of RR-intervals is presented in Fig. 1(a), and the signal of respiration is presented in Fig. 1(b). Figure 1(c) shows the time series of the signals $s_x(t)$ and $s_y(t)$ obtained by bandpass filtering of the signals $x(t)$ and $y(t)$, respectively, in the 0.15–0.50 Hz band. It can be seen in Fig. 1(c) that the signals $s_x(t)$ and $s_y(t)$ oscillate in anti-phase and demonstrate phase coherence. The phase portraits of oscillations are depicted in Fig. 1(d). Figure 1(d) shows that for the considered signals, it is possible to set the center of rotation of the radius vectors on the phase plane. This fact indicates that the instantaneous phases are defined correctly.

Figures 2(a) and 2(b) show the differences $\Delta\varphi(t)$ between the instantaneous phases of the signals $s_x(t)$ and $s_y(t)$ for a healthy young subject of 22 years old [Fig. 2(a)] and the same healthy elderly subject as in Fig. 1 [Fig. 2(b)] in the awake state, REM sleep, and deep sleep. The plots of all phase differences show long epochs, in which $\Delta\varphi(t)$ is almost constant that corresponds to high coherence between the phases of the analyzed signals. These horizontal plateaus alternate with the intervals of the rapid variation of $\Delta\varphi(t)$, which correspond to the incoherent behavior of phases. In REM sleep and in the awake state, the phase difference $\Delta\varphi(t)$ increases greater than in DS.

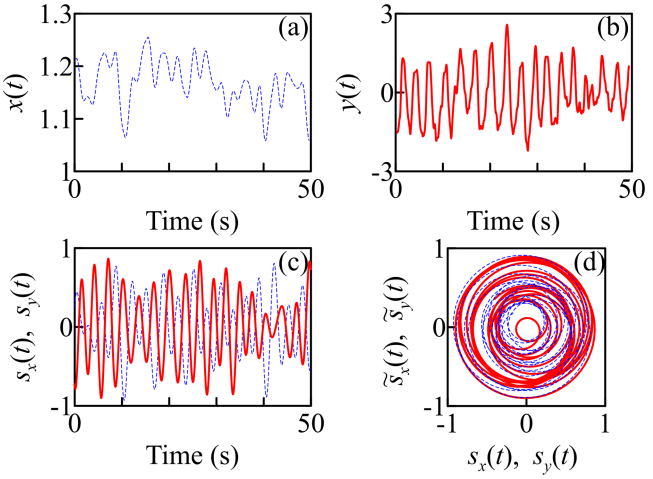

FIG. 1. Fragments of a sequence of RR-intervals (a) and respiratory signal (b) for one of the elderly subjects in the awake state. (c) Filtered signals $x(t)$ and $y(t)$. (d) Phase portraits of oscillations.

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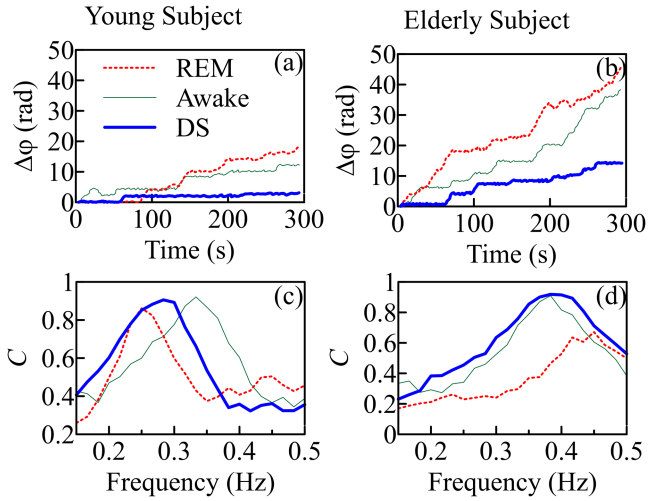

FIG. 2. Phase differences $\Delta\phi(t)$ for a selected young (a) and a selected elderly subject (b) during the awake state, REM sleep, and DS. Coherence functions $C(f)$ of RR-intervals and respiration for a young subject (c) and an elderly subject (d). REM sleep is shown by a red dotted line, the awake state is shown by a thin green line, and DS is shown by a thick blue line.

In the young subject, $\Delta\varphi(t)$ increases more slowly than in the elderly subject.

The coherence functions of RR-intervals and the signal of respiration are presented in Fig. 2 for a healthy young subject [Fig. 2(c)] and a healthy elderly subject [Fig. 2(d)] in the awake state and in different sleep stages. The coherence functions exhibit pronounced peaks in the frequency range of 0.15–0.50 Hz, indicating the coherence of signals. A decrease in the coherence is observed for the elderly subject in the REM sleep stage.

For each subject in the awake state, REM sleep, and DS, we calculated the *SPC* and C_{max} measures for the studied signals. For all age groups, we found that the degree of coherence of respiration and the process of parasympathetic control of the heart rate is different in the considered states (Fig. 3). The *SPC* and C_{max} took the values 0.80 ± 0.02 and 0.87 ± 0.01, respectively, in REM sleep; the values 0.87 ± 0.01 and 0.91 ± 0.01, respectively, in the awake state; and the values 0.91 ± 0.02 and 0.94 ± 0.01, respectively, in DS. The measures are presented as mean $\pm$ standard error.

The significance of the difference of *SPC* and C_{max} measures during the awake state, REM sleep, and DS is confirmed by the Kruskal–Wallis test for three groups [$H(2.0) = 40.86$, $p < 0.0001$ for *SPC* and $H(2.0) = 62.25$, $p < 0.0001$ for C_{max}]. These results show the sensitivity of both measures of coherence to physiological changes caused by the influence of the higher level neural centers on the systems regulating the processes of heartbeat and respiration.

Figure 4 demonstrates a monotonic decrease in the coherence of respiration and the process of parasympathetic control of the heart rate with increasing age. To construct this figure, we used all records without dividing them into states of wakefulness and sleep. When comparing the youngest and oldest groups, the difference in the coherence of the studied processes in these groups is about 6% for the *SPC* measure (the Mann–Whitney *U*-test $p = 0.0009$) and about 7% for the C_{max} measure (the Mann–Whitney *U*-test $p < 0.0001$).

The results of the analysis of the coherence of the studied processes in the awake state and in different sleep stages are presented in Fig. 5 separately for each age group. Figure 5 shows the similar dynamics of *SPC* and C_{max} measures for all age groups. As well as in Fig. 3, the coherence of respiration and the process of parasympathetic control of the heart rate is minimal in REM sleep and is maximal in DS. In the awake state, the coherence is higher than in REM sleep and lower than during DS. With aging, the difference between the coherence measures in the awake state and in different sleep stages becomes more noticeable, especially for the *SPC* measure. The most pronounced difference of *SPC* and C_{max} measures is observed between REM sleep and DS in subjects over 50 years of age.

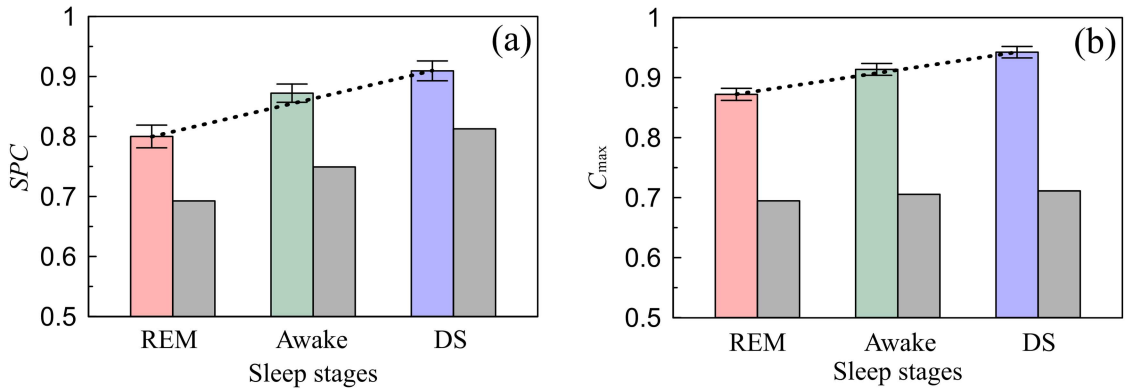

FIG. 3. Coherence of respiration and HF-oscillations in RR-intervals in the awake state, REM sleep, and DS. (a) *SPC* measure. (b) C_{max} measure. Left columns show the measures averaged over the ensemble of experimental data, and the right (gray) columns show the values of the 95th percentile of the measures calculated for surrogate data. Error bars indicate a standard error.

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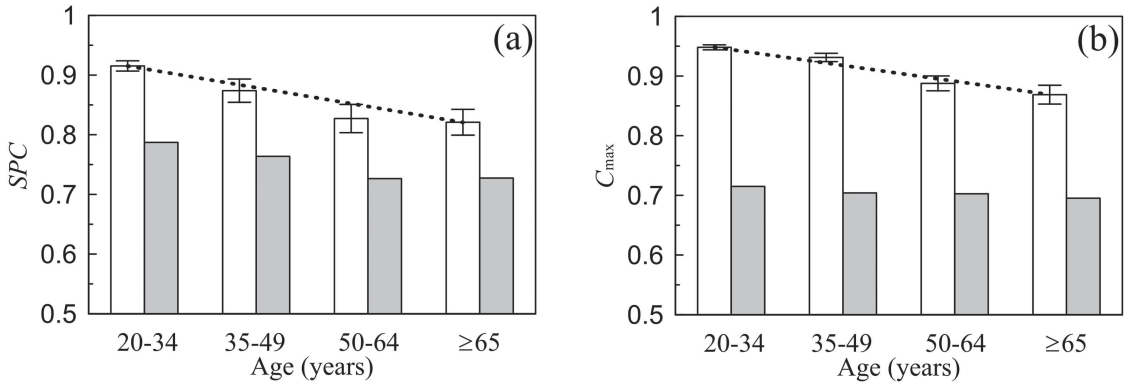

FIG. 4. Coherence of respiration and HF-oscillations in RR-intervals depending on the age of the subjects. (a) *SPC* measure. (b) C_{max} measure. White columns show the measures averaged over the ensemble of experimental data, and the gray columns show the values of the 95th percentile of the measures calculated for surrogate data. Error bars indicate a standard error.

DISCUSSION

It is known that breathing significantly affects the dynamics of the heart rate.[64] Parasympathetic fibers innervate airway smooth muscle, providing the dominant control of smooth muscle tone and, therefore, the airway caliber, as well as the airway glands and microvasculature in the respiratory tract.[49] In this case, feedback loops from the pulmonary stretch receptors and arterial baroreceptors act through the nucleus tractus solitarii on the Bötzinger complex located in the pontomedullary region of the pons, which provides regulation of the cardiovagal parasympathetic outflow by the respiratory pattern generator.[65] Such a complex ring dynamical system provides flexible regulation of the respiration process in healthy subjects. Its activity is manifested in the HF-range of HRV at the frequency of respiration. This phenomenon had been described in physiology as RSA. Therefore, the coherence between the respiration and parasympathetic control of the heart rate measures the "amount" of coherent RSA. The modulation of the activity of the nerve fibers of the parasympathetic branch of the autonomic nervous system caused by physiological processes in the body and age-related pathological changes is reflected in the change in the coherence of respiration and HF-oscillations in HRV.

It is known that in healthy subjects, the state of REM sleep is typically associated with an increase in the sympathetic activity and often with a low parasympathetic activity. During DS, the sympathetic activity is the lowest and the parasympathetic activity may increase up to very high values, exceeding the activity during the awake state.[66,67] As shown in our study, these effects are confirmed by a decrease in the coherence of respiration and the process of parasympathetic control of the heart rate in REM sleep and an increase in the coherence of these processes in DS with respect to the coherence in the awake state (Fig. 3). Moreover, this result holds true for different age groups (Fig. 5). The Kruskal–Wallis test confirms the statistical significance of the differences between the age groups.

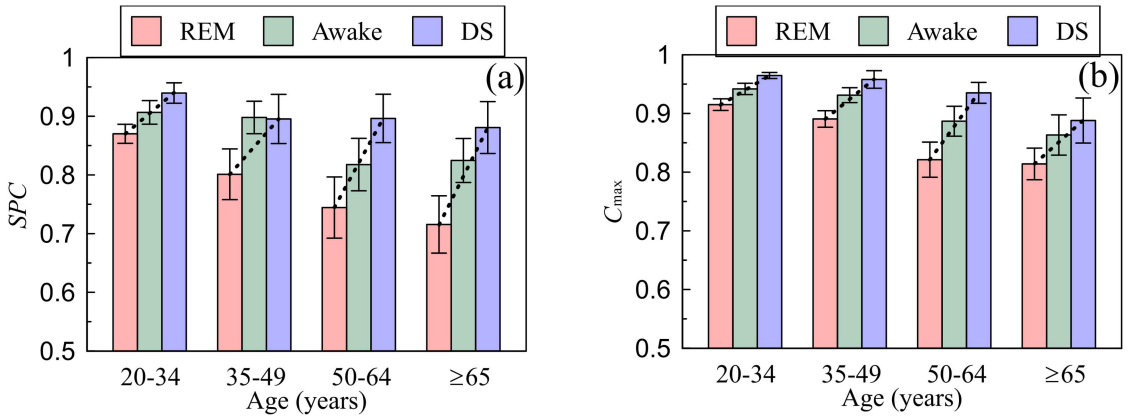

FIG. 5. Coherence of respiration and HF-oscillations in RR-intervals in the awake state, REM sleep, and DS depending on the age of the subjects. (a) *SPC* measure. (b) C_{max} measure. Error bars indicate a standard error.

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Age-related changes are accompanied by aging of the lung tissue, the lung compliance, and some changes of the chest and thoracic spine as well, which change the breathing process and its dynamics.[68,69] Age-related changes are observed in a decrease in sympathetic and parasympathetic responses[70] that leads to a decrease in the power of HRV in the LF and HF ranges.[71,72] Apparently, this is the reason for the revealed decrease in the coherence of respiration and parasympathetic control of the heart rate (Fig. 4). In a future study, it would be useful to add a test of paced breathing while awake in order to check these changes under standardized conditions in addition.

The obtained results are generally consistent with other studies[73] and provide useful additional tools for assessing the characteristics of the cardiorespiratory interaction in various physiological states of a subject. The considered coherence measures are promising as additional information for classification of sleep stages in physiological studies without recording an electroencephalogram.[74]

CONCLUSION

Aging is an irreversible process accompanied by changes in all organs and systems of the body, including the cardiovascular,[75] respiratory,[68] and autonomic nervous[70,71] systems. However, the severity of the consequences of such changes can be reduced in the case of their timely diagnostics. In this paper, linear and nonlinear measures of coherence are used to quantify age-related changes in the cardiorespiratory interaction. A decrease with age in the coherence of respiration and the process of parasympathetic regulation of the heart rate is shown, which is caused by changes in the functioning of autonomic control of the cardiovascular and respiratory systems. This can be interpreted that coherent RSA decreases with increasing age. We have also shown that the coherence measures differ in the awake sate and in different stages of sleep for all age groups. Thus, the considered coherence measures may be useful for the development of methods for classifying sleep stages in polysomnography studies.

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DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

[1] L. Glass and M. C. Mackey, *From Clocks to Chaos: The Rhythms of Life* (Princeton University Press, Princeton, NJ, 1988).
[2] K. V. Sudakov, Integr. Physiol. Behav. Sci. **32**, 392 (1997).
[3] A. C. Soong and C. I. Stuart, Biol. Cybern. **62**, 55 (1989).
[4] V. K. Yeragani, R. K. Radhakrishna, M. Tancer, and T. Uhde, Neuropsychobiology **46**, 111 (2002).
[5] M. Barahona and C. S. Poon, Nature **381**, 215 (1996).
[6] A. L. Goldberger, Lancet **347**, 1312 (1996).
[7] F. Lombardi, Circulation **101**, 8 (2000).
[8] T. A. Denton, G. A. Diamond, R. H. Helfant, S. Khan, and H. Karagueuzian, Am. Heart J. **120**, 1419 (1990).
[9] D. J. Christini and L. Glass, Chaos **12**, 732 (2002).
[10] L. Glass, A. L. Goldberger, M. Courtemanche, and A. Shrier, Proc. R. Soc. London, Ser. A **413**, 9 (1987).
[11] D. T. Kaplan and M. Talajic, Chaos **1**, 251 (1991).
[12] E. Mosekilde, Y. Maistrenko, and D. Postnov, *Chaotic Synchronization: Applications to Living Systems* (World Scientific Series on Nonlinear Science, London, 2002).
[13] V. S. Anishchenko, V. V. Astakhov, A. B. Neiman, T. E. Vadivasova, and L. Schimansky-Geier, *Nonlinear Dynamics of Chaotic and Stochastic Systems: Tutorial and Modern Development* (Springer, Heidelberg, 2007).
[14] N. B. Janson, A. G. Balanov, V. S. Anishchenko, and P. V. E. McClintock, Phys. Rev. Lett. **86**, 1749 (2001).
[15] A. N. Pavlov, D. V. Dumsky, A. R. Ziganshin, O. A. Klimova, and V. S. Anishchenko, Proc. SPIE **5330**, 66 (2004).
[16] N. B. Janson, A. N. Pavlov, and V. S. Anishchenko, *Global Reconstruction: Application to Biological Data and Secure Communication* (Nova Science Publishers, New York, 2003).
[17] N. B. Janson, A. G. Balanov, V. S. Anishchenko, and P. V. E. McClintock, Physiol. Meas. **22**, 565 (2001).
[18] N. B. Janson, A. G. Balanov, V. S. Anishchenko, and P. V. E. McClintock, Phys. Rev. E **65**, 036212 (2002).
[19] P. Bittihn, S. Berg, U. Parlitz, and S. Luther, Chaos **27**, 093931 (2017).
[20] T. Krogh-Madsen, L. K. Taylor, A. D. Skriver, P. Schaffer, and M. R. Guevara, Chaos **27**, 093929 (2017).
[21] A. S. Karavaev, Y. M. Ishbulatov, V. I. Ponomarenko, B. P. Bezruchko, A. R. Kiselev, and M. D. Prokhorov, Chaos **29**, 121101 (2019).
[22] M. R. Guevara, L. Glass, and A. Shrier, Science **214**, 1350 (1981).
[23] R. Pool, Science **243**, 604 (1989).
[24] P. C. Ivanov, L. A. N. Amaral, A. L. Goldberger, S. Havlin, M. G. Rosenblum, Z. R. Struzik, and H. E. Stanley, Nature **399**, 461 (1999).
[25] V. I. Ponomarenko, M. D. Prokhorov, A. S. Karavaev, A. R. Kiselev, V. I. Gridnev, and B. P. Bezruchko, Eur. Phys. J.: Spec. Top. **222**, 2687 (2013).
[26] N. M. De Souza, L. C. M. Vanderlei, and D. M. Garner, Complexity **20**, 84 (2015).
[27] A. R. Kiselev, V. I. Gridnev, M. D. Prokhorov, A. S. Karavaev, O. M. Posnenkova, V. I. Ponomarenko, B. P. Bezruchko, and V. A. Shvartz, Ann. Noninvasive Electrocardiol. **17**, 204 (2012).
[28] A. R. Kiselev, A. S. Karavaev, V. I. Gridnev, M. D. Prokhorov, V. I. Ponomarenko, E. I. Borovkova, V. A. Shvartz, Y. M. Ishbulatov, O. M. Posnenkova, and B. P. Bezruchko, Russ. Open Med. J. **5**, e0101 (2016).
[29] H. Krause, J. F. Kraemer, T. Penzel, J. Kurths, and N. Wessel, Chaos **27**, 093933 (2017).
[30] N. Wessel, M. Riedl, and J. Kurths, Chaos **19**, 028508 (2009).
[31] Y. Shiogai, A. Stefanovska, and P. V. E. McClintock, Phys. Rep. **488**, 51 (2010).
[32] J. A. Hirsch and B. Bishop, Am. J. Physiol.: Heart Circ. Physiol. **241**, H620 (1981).
[33] M. D. Prokhorov, A. S. Karavaev, Y. M. Ishbulatov, V. I. Ponomarenko, A. R. Kiselev, and J. Kurths, Phys. Rev. E **103**, 042404 (2021).
[34] C. Schäfer, M. G. Rosenblum, J. Kurths, and H.-H. Abel, Nature **392**, 239 (1998).
[35] M. G. Rosenblum, J. Kurths, A. Pikovsky, C. Schäfer, P. Tass, and H.-H. Abel, IEEE Eng. Med. Biol. Mag. **17**, 46 (1998).
[36] H. Seidel and H. Herzel, IEEE Eng. Med. Biol. Mag. **17**, 54 (1998).
[37] C. Schäfer, M. G. Rosenblum, H.-H. Abel, and J. Kurths, Phys. Rev. E **60**, 857 (1999).
[38] M. Bračič-Lotrič and A. Stefanovska, Phys. A **283**, 451 (2000).
[39] S. Rzeczinski, N. B. Janson, A. G. Balanov, and P. V. E. McClintock, Phys. Rev. E **66**, 051909 (2002).
[40] V. I. Ponomarenko, M. D. Prokhorov, A. B. Bespyatov, M. B. Bodrov, and V. I. Gridnev, Chaos, Solitons Fractals **23**, 1429 (2005).
[41] R. Mrowka, L. Cimponeriu, A. Patzak, and M. G. Rosenblum, Am. J. Physiol. Regul. Comp. Integr. Physiol. **285**, R1395 (2003).

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[42]R. Mrowka, A. Patzak, and M. G. Rosenblum, Int. J. Bifurcation Chaos **10**, 2479 (2000).
[43]M. G. Rosenblum, L. Cimponeriu, A. Bezerianos, A. Patzak, and R. Mrowka, Phys. Rev. E **65**, 041909 (2002).
[44]R. P. Bartsch, A. Y. Schumann, J. W. Kantelhardt, T. Penzel, and P. C. Ivanov, Proc. Natl. Acad. Sci. U.S.A. **109**, 10181 (2012).
[45]A. S. Karavaev, M. D. Prokhorov, V. I. Ponomarenko, A. R. Kiselev, V. I. Gridnev, E. I. Ruban, and B. P. Bezruchko, Chaos **19**, 033112 (2009).
[46]M. D. Prokhorov, V. I. Ponomarenko, V. I. Gridnev, M. B. Bodrov, and A. B. Bespyatov, Phys. Rev. E **68**, 041913 (2003).
[47]C. D. Wagner and P. B. Persson, Cardiovasc. Res. **40**, 257 (1998).
[48]S. W. Porges, Neurosci. Biobehav. Rev. **19**, 225 (1995).
[49]M. J. Lewis, A. L. Short, and K. E. Lewis, Respir. Med. **100**, 1688 (2006).
[50]Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology. Circulation **93**, 1043 (1996).
[51]A. S. Karavaev, A. R. Kiselev, A. E. Runnova, M. O. Zhuravlev, E. I. Borovkova, M. D. Prokhorov, V. I. Ponomarenko, S. V. Pchelintseva, T. Y. Efremova, A. A. Koronovskii, and A. E. Hramov, Chaos **28**, 081102 (2018).
[52]N. A. Aladjalova, Nature **179**, 957 (1957).
[53]G. Klösch, B. Kemp, T. Penzel, A. Schlögl, P. Rappelsberger, E. Trenker, G. Gruber, J. Zeitlhofer, B. Saletu, W. M. Herrmann, S. L. Himanen, D. Kunz, M. J. Barbanoj, J. Röschke, A. Värri, and G. Dorffner, IEEE Eng. Med. Biol. Mag. **20**, 51 (2001).
[54]A. Rechtschaffen and A. Kales, *A Manual of Standardized Terminology, Techniques and Scoring System of Sleep Stages in Human Subjects* (UCLA Brain Information Service/Brain Research Institute, Los Angeles, 1968).
[55]R. Quian Quiroga, A. Kraskov, T. Kreuz, and P. Grassberger, Phys. Rev. E **65**, 041903 (2002).
[56]L. B. White and B. Boashash, IEEE Trans. Inf. Theory **36**, 830 (1990).
[57]A. S. Pikovsky, M. G. Rosenblum, G. V. Osipov, and J. Kurths, Phys. D **104**, 219 (1997).
[58]D. Gabor, J. Inst. Electr. Eng., Part III **93**, 429 (1946).
[59]A. Pikovsky, M. Rosenblum, and J. Kurths, *Synchronization: A Universal Concept in Nonlinear Sciences* (Cambridge University Press, Cambridge, 2001).
[60]A. S. Karavaev, V. V. Skazkina, Y. M. Ishbulatov, and E. I. Borovkova, Cybern. Phys. **8**, 128 (2019).
[61]T. Schreiber and A. Schmitz, Phys. Rev. Lett. **77**, 635 (1996).
[62]W. H. Kruskal and W. A. Wallis, J. Am. Stat. Assoc. **47**, 583 (1952).
[63]H. B. Mann and D. R. Whitney, Ann. Math. Stat. **18**, 50 (1947).
[64]T. E. Brown, L. A. Beightol, J. Koh, and D. L. Eckberg, J. Appl. Physiol. **75**, 2310 (1993).
[65]P. G. Guyenet, Compr. Physiol. **4**, 1511 (2014).
[66]A. M. van Roon, L. J. M. Mulder, M. Althaus, and G. Mulder, Psychophysiology **41**, 961 (2004).
[67]D. Zemaityte, G. Varoneckas, and E. Sokolov, Psychophysiology **21**, 279 (1984).
[68]G. Sharma and J. Goodwin, Clin. Interv. Aging **1**, 253 (2006).
[69]J. E. Elliott, C. B. Mantilla, C. M. Pabelick, A. C. Roden, and G. C. Sieck, Am. J. Physiol. Lung Cell Mol. Physiol. **311**, L167 (2016).
[70]R. Parashar, M. Amir, A. Pakhare, P. Rathi, and L. Chaudhary, J. Clin. Diagn. Res. **10**, 11 (2016).
[71]A. Natarajan, A. Pantelopoulos, H. Emir-Farinas, and P. Natarajan, Lancet Digit Health **2**, e650 (2020).
[72]G. Brandenberger, A. U. Viola, J. Ehrhart, A. Charloux, B. Geny, F. Piquard, and C. Simon, J. Sleep Res. **12**, 173 (2003).
[73]A. U. Viola, E. Tobaldini, S. L. Chellappa, K. R. Casali, A. Porta, and N. Montano, PLoS One **6**, e19002 (2011).
[74]P. Mayer, A. H. Babiloni, G. Beetz, S. Marshansky, Z. Kaddaha, P. H. Rompré, V. Jobin, and G. J. Lavigne, Nat. Sci. Sleep **12**, 443 (2020).
[75]P. Pietri and C. Stefanadis, J. Am. Coll. Cardiol. **77**, 189 (2021).

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