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Internal Synchronization of the Main 0.1-Hz Rhythms in the Autonomic Control of the Cardiovascular System

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Abstract—Synchronization parameters of 0.1-Hz rhythms isolated from the heart rate and the oscillations of the blood volume in microcirculatory vessels were studied in 12 healthy subjects and 32 patients with acute myocardial infarction. Recordings of the electrocardiogram and the pulsogram from the distal phalanx of the index finger, as well as mechanical recording of respiration with the body in a horizontal position, were performed. In patients with myocardial infarction, the recordings were performed during the first three to five days and the third week after the infarction. Synchronization was tested by plotting phase differences and calculating the total percentage of phase synchronization. Synchronization parameters of 0.1-Hz rhythms were high in healthy subjects. In patients with acute myocardial infarction, synchronization of 0.1-Hz rhythms was considerably poorer. The data obtained suggest that the studied 0.1-Hz rhythms are two independent oscillatory processes that are synchronized in healthy subjects. However, this interaction may be disturbed in cardiovascular pathologies, e.g., myocardial infarction.

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INTRODUCTION

According to current notions on the organization of the autonomic control of the cardiovascular system, this control is characterized by a major self-sustained oscillatory process at a frequency of about 0.1 Hz (the low-frequency spectral range) [1–5]. These oscillations are believed to characterize the main properties of the central link of this control system [6–11]. The finding of periodic 0.1-Hz oscillations in heart rate variability [6, 7] and blood pressure variability [1–4, 10, 11] indicates the importance of this control mechanism for the functioning of the entire cardiovascular system. Thus, 0.1-Hz oscillations in the autonomic control of the cardiovascular system may be considered a general systemic control mechanism generated in the central division of the control system [1–11].

It is known that the main oscillatory processes [12] in the human cardiovascular system may be synchronized with one another [13–15], which agrees with current views on the functioning of complex systems [16]. However, the possibility of the mutual synchronization of 0.1-Hz cardiovascular rhythms has been poorly studied to date.

The term synchronization is usually taken to mean adjustment of the rhythms of oscillatory processes as a result of their interaction. Synchronization is expressed as the adjustment of the natural frequencies of two self-sustained oscillations f_1 and f_2 in such a way that $nf_1 \approx mf_2$, where n and m are integers. This is termed an $n : m$ frequency synchronization. However, to complete the picture of the quality of interaction between two oscillatory processes, the notion of phase synchronization is used. This means the adjustment of the phases of interacting rhythmic processes $\phi_1(t)$ and $\phi_2(t)$ at which $|n\phi_1 - m\phi_2 - C| < \text{const}$, where C is a constant. Thus, phase synchronization between two signals can be detected by calculating the phase difference:

$$\varphi^{12}_{n,m} = n\phi_1 - m\phi_2,$$

where $\varphi^{12}_{n,m}$ is the generalized phase difference, or relative phase [17]. If $|\varphi^{12}_{n,m} - C| < \text{const}$, where C is a constant, an $n : m$ phase locking takes place. In this case, the plot of the dependence of the relative phase on time contains a segment where $\varphi^{12}_{n,m}$ oscillates about a certain constant value. In noisy systems, phase locking is statistically evidenced by the presence of a distinct peak in the distribution of the cyclic relative phase [17]:

$$\Psi^{12}_{n,m} = \varphi^{12}_{n,m} \bmod 2\pi.$$

The synchronization between two oscillatory processes can be quantitatively characterized by various measures [17–19], e.g., the total synchronization percentage [20].

We studied the functional characteristics of the autonomic control of the cardiovascular system on the basis of the synchronization parameters of 0.1-Hz rhythms detected in different divisions of the cardiovascular system of healthy subjects and patients with acute myocardial infarction.

METHODS

We estimated the synchronization parameters of 0.1-Hz rhythms isolated from rhythmograms and pulsograms of 12 male volunteers aged 20–34 years without signs of heart pathology and 32 patients with coronary heart disease (21 men and 11 women aged 41–75 years) that received inpatient treatment for acute myocardial infarction at the Saratov Research Institute of Cardiology clinic. All subjects gave their informed written consent to participate in the study.

A diagnosis of acute myocardial infarction was based on the following criteria: (1) an attack of ischemic pain longer than 30 min; (2) characteristic changes in the electrocardiogram (ECG), namely, the typical ST segment elevation and, in some cases, the appearance of the pathological Q wave; and (3) an increase in the blood content of heart-specific enzymes.

All patients treated for acute myocardial infarction at the Saratov Research Institute of Cardiology clinic underwent a complete clinical examination. According to ECG data, 19 and 13 patients, respectively, had Q and non-Q myocardial infarctions. Signs of massive infarction were observed in seven patients. Patients with acute myocardial infarction were treated with β-blockers and angiotensin converting enzyme inhibitors [21, 22].

When studying 0.1-Hz rhythms, we did not divide the patients with acute myocardial infarction according to the degree of disturbance of myocardial contractile function because the dependence of heart rate variability on the severity of heart failure reported by some authors [23–25] is insignificant in the case of acute myocardial infarction [26, 27].

Since heart rate variability in acute myocardial infarction is practically age-independent [26], we did not take into account the patients' ages when estimating the parameters of 0.1-Hz oscillations in the cardiovascular system.

For each subject, we simultaneously recorded the ECG and the pulsogram from the distal phalanx of the index finger, which reflected the oscillations in the amount of blood in the microcirculatory vessels, and performed the mechanical recording of respiration with the body in a horizontal position using an EEGA-21/26 Entsefalan-131-03 (model 10) multichannel encephalograph/analyzer (NPKF Medikom-MTD, Russia) with a set of standard sensors. The duration of each record was 10 min. The signals were recorded at a frequency of 250 Hz with 12-digit resolution. While the signals were recorded, all subjects breathed freely. The mechanical recording of respiration was performed to check its spontaneity and exclude forced respiration and voluntary breath holding. In the group of patients with acute myocardial infarction, these recordings were performed during the first three to five days and during the third week after the infarction. All recordings were performed between 1 and 4 p.m.

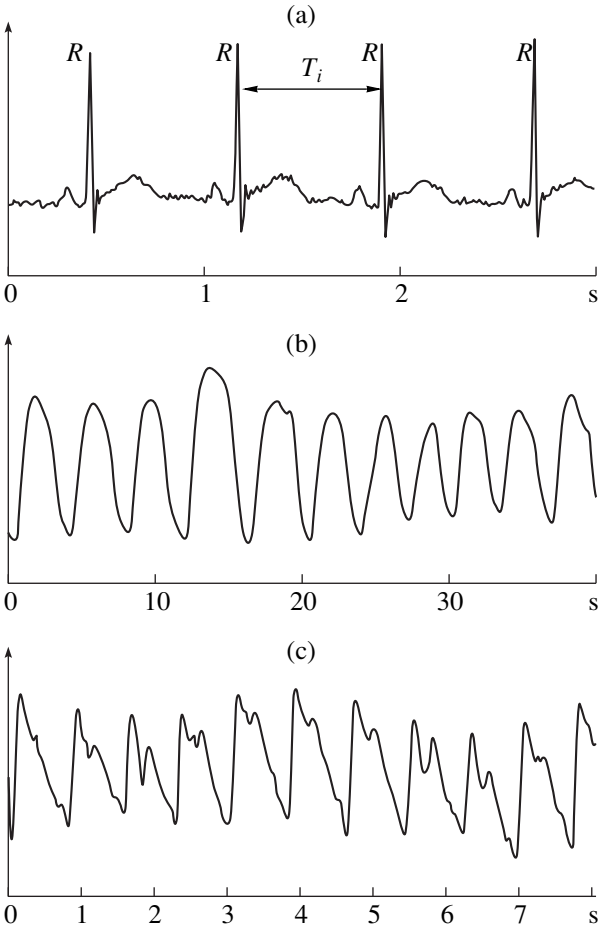

Fig. 1. Fragments of simultaneous records of (a) the ECG, (b) respiration, and (c) the pulsogram in one of the subjects. The abscissa shows time in seconds.

For subsequent analysis, we selected the records of ECG and pulsogram signals that contained no noise, extrasystoles, noticeable linear trends, or transitional processes.

Figure 1 shows fragments of typical ECG, respiration, and pulsogram signals. Information on heart rate variability was obtained by isolating the sequence of RR intervals from the ECG, i.e., by constructing a series of time intervals T_i between two subsequent R waves.

To isolate the major rhythm with a frequency of $f_v \sim$ 0.1 Hz from the series of RR intervals, we filtered the RR-interval sequence, eliminating high-frequency (HF) oscillations ($\nu > 0.15$ Hz) predominantly related to respiration, i.e., respiratory arrhythmia, and

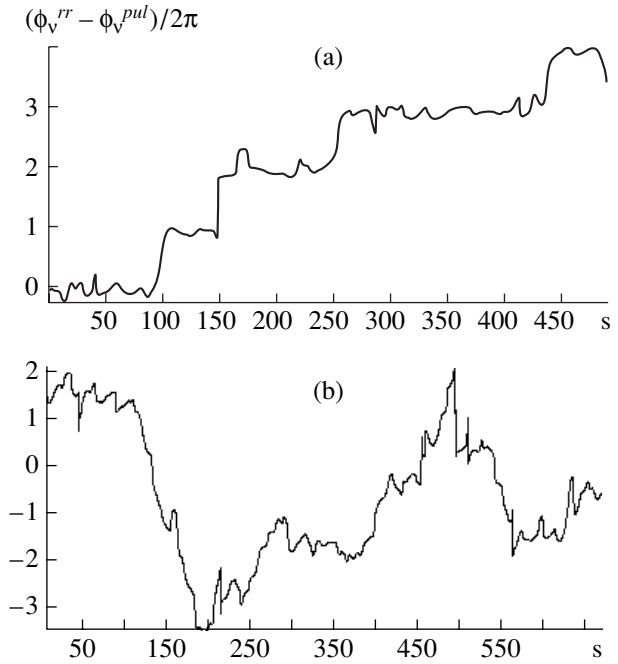

Fig. 2. The difference of the phases of the 0.1-Hz rhythms isolated from the sequences of RR intervals and the pulsogram in the groups of (a) healthy subjects and (b) patients with acute myocardial infarction. The abscissa shows time in seconds.

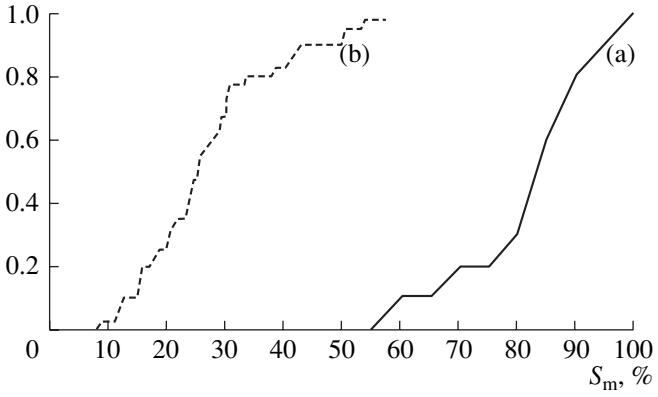

Fig. 3. Normalized distribution of the total synchronization percentage S_m in the samples of (a) healthy subjects and (b) patients with acute myocardial infarction.

ultralow-frequency (ULF) oscillations ($\nu < 0.05$ Hz). After this band filtration, we used the Gilbert transformation [28] to calculate the phase of 0.1-Hz oscillations ϕ_v^{rr} in the signal.

Similar transformations were performed in the pulsogram signal; i.e., we isolated oscillations with a frequency of about 0.1 Hz similar to those in the heart rate variability. Pulsogram records were analyzed as a periodic wave process; therefore, individual parameters of the pulsogram curve were not studied specially. The pulsogram signal was filtered in the same way as the heart rate variability signal; i.e., the HF and ULF oscillations were eliminated. Then, we calculated the phase of 0.1-Hz periodic oscillations ϕ_v^{pul} in the pulsogram with the use of the Gilbert transformation.

To check the synchronization between the rhythm with $f_v \sim 0.1$ Hz isolated from the sequence of RR intervals and the same rhythm isolated from the pulsogram, we constructed the phase difference $(\phi_v^{rr} - \phi_v^{pul})/2\pi$. The phase difference was used to calculate the total duration of all synchronization segments (the time during which the rhythms were synchronized), which was expressed in percent of the duration of the entire record (the total synchronization percentage, S_m). We determined the synchronization segments by detecting the segments of the phase difference versus time plot in which the relative phase varied about a constant value. This total rhythm synchronization percentage (S_m) was used for quantitative characterization of the synchronization between the two rhythms. The total synchronization percentage was calculated using the package Software for Calculating the Total Percentage of Phase Locking between Rhythms of the Human Cardiovascular System (Sinkhro), developed at the Saratov Research Institute of Cardiology (Computer Software Certificate no. 2005610960 dated April 20, 2005).

RESULTS

Figure 2a shows a characteristic pattern of the phase difference between the 0.1-Hz rhythms isolated from the sequence of RR intervals and the pulsogram in the group of healthy subjects. The mean total synchronization percentage S_m of these rhythms in healthy subjects was 81% (individual values varied from 58 to 100%). Figure 3a shows the normalized distribution of the total synchronization percentage S_m in the sample of healthy subjects. The entire range of its values was partitioned at a step of 1%; if the total percentage for an individual case fell within the interval $[p_{min} + (i - 1), p_{min} + i]$, where $i = 1, \ldots, (p_{max} - p_{min})$, then the distribution function was increased by 1. Thus, the distribution function was 0 at $p < p_{min}$ and 1 at $p = p_{max}$ (the function was normalized to the total number of elements in the sample, which was equal to 12).

Figure 2b shows the characteristic pattern of the phase difference between the 0.1-Hz rhythms isolated from different sources of signals in myocardial infarction patients. The mean total percentage of rhythm synchronization in this group was 27% (individual values varied from 8 to 57%). Figure 3b shows the normalized distribution of the total synchronization percentage S_m for the entire sample of patients with myocardial infarction.

Afterwards, we divided the data on myocardial infarction patients into two groups according to the time of recording. The mean total synchronization percentage

of 0.1-Hz rhythms in recordings made within three to five days after the infarction was 22% (8–50%); in the third week of the disease, S_m became 32% (17–57%). Figure 4 shows the normalized distribution of the total percentages for these records.

After that, we subdivided the group of myocardial infarction patients according to the individual patterns of the changes in the total synchronization percentage S_m in the period from the first to the third week of the disease. This synchronization parameter decreased during the period of observation in 10 patients and increased in 22 patients (Fig. 5). Note that the groups of patients that exhibited positive and negative changes in the mean total synchronization percentage were similar with respect to the main clinical characteristics.

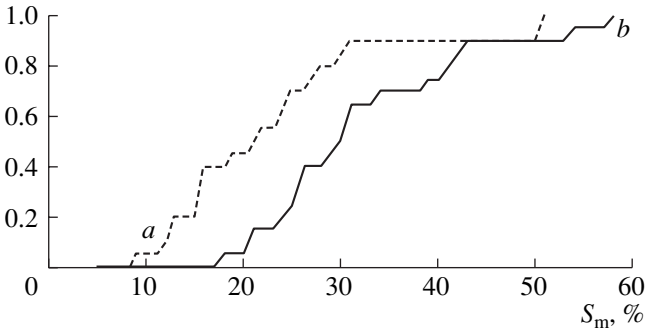

Fig. 4. Normalized distribution of the total synchronization percentage S_m in the sample of patients with acute myocardial infarction as dependent on the time of recording: (*a*) immediately after the infarction; (*b*) during the third week of the disease.

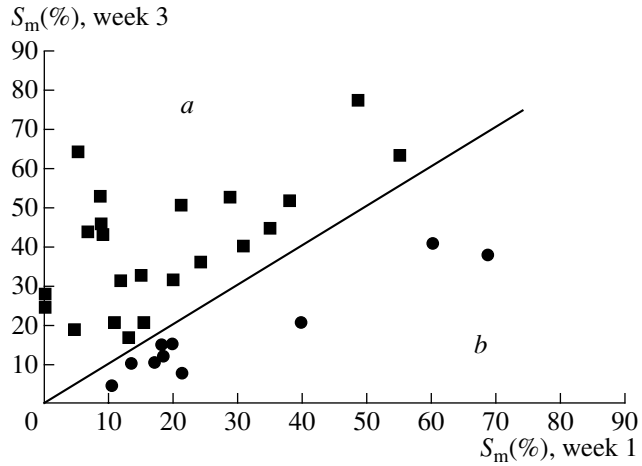

Fig. 5. Total synchronization percentage S_m in patients with acute myocardial infarction with positive and negative dynamics of this synchronization parameter in the period from the first to the third week of the disease (designated by squares and circles, respectively). The straight line arbitrarily separates sectors *a* and *b* containing the values of the total synchronization percentage S_m for the patients with positive and negative dynamics of this parameter, respectively.

DISCUSSION

The high synchronization parameters of 0.1-Hz oscillations in the human cardiac rhythm and pulsogram that have been found in this study indicate qualitative functional interaction between the mechanisms of heart rate and microcirculation control, which ensures a high adaptability of the cardiovascular system. The interaction between these two regulatory mechanisms may be accounted for by a common center controlling them; on the other hand, they may be autonomous and functionally interact with each other. The question arises of whether these 0.1-Hz periodic processes result from the activity of a single control center or they are two independent self-sustained loops that have similar oscillation frequencies and are qualitatively synchronized with each other in the normal state for optimal, efficient control of the cardiovascular system. Answering this question would add to the existing views on the autonomic control of the cardiovascular system.

The study of patients with acute myocardial infarction demonstrated that the quality of the synchronization of 0.1-Hz rhythms in the cardiovascular system is considerably deteriorated in this disease, although these periodic processes are retained in the signals studied (the heart rate and pulsogram). This finding shows that the mechanisms of 0.1-Hz self-sustained oscillations in the control of heart rate and microcirculatory blood flow may function independently of each other. This independence may be explained by the assumption that the 0.1-Hz oscillations of the heart rate and microcirculation result from the operation of different control loops, generated, presumably, in the subcortical cardiovascular center.

The results of our study suggest that the observed 0.1-Hz oscillations of the heart rate and microcirculation are two independent oscillatory processes that are strongly synchronized with each other in healthy humans. However, their interaction may be disturbed in various cardiovascular pathologies, e.g., acute myocardial infarction, where these 0.1-Hz oscillations become asynchronous. The deterioration of synchronization quality may be accounted for by both a decrease in the activity of the mechanisms determining the interaction between their respective control loops in the cardiovascular center and other factors, such as disturbances in the feedback of the oscillatory circuit or biomechanical factors. Various factors may deteriorate the quality of synchronization between oscillatory processes in biological systems; therefore, we cannot yet point to the most probable factor playing the main role in the loss of synchronization between 0.1-Hz rhythms of the cardiovascular system in acute myocardial infarction. However, it is obvious that the functional integrity of the autonomic control of the cardiovascular system as a complex biological system is disrupted in this disease.

This disruption includes destruction of functional relationships between its components controlling different divisions of the cardiovascular system, e.g., the cardiac function and regional circulation.

The data obtained demonstrate the heterogeneity of the autonomic control of the cardiovascular system. We may assume that there are at least two functionally independent control loops with a natural frequency of about 0.1 Hz: (1) the heart rate control loop and (2) the microcirculation volume control loop. The possibility of interaction between these loops indicates the existence of mechanisms ensuring their relationship. To date, it is difficult to determine at which organizational level of the cardiovascular system the given rhythmic processes interact. The location of the central components of these oscillatory mechanisms also remains an open question. Probably, the subcortical cardiovascular center, whose neurons form functional regions involved in the studied 0.1-Hz oscillatory loops, is the central component of these control loops. However, we can conclude that the mechanisms responsible for the functional synchronization of the two 0.1-Hz oscillatory mechanisms are highly sensitive to cardiovascular pathologies.

When studying the changes in the synchronization parameters in patients with acute myocardial infarction during the period from the first to the third week of the disease, we found a significant improvement in 0.1-Hz rhythm synchronization quality in the group as a whole. This finding suggests that the functional integrity of the autonomic control system may be gradually restored after various catastrophic changes in the state of the cardiovascular system, which is also an important descriptive characteristic of this control system.

Analysis of the individual patterns of the total synchronization percentage S_m in patients with acute myocardial infarction over time in the period from the first to the third week of the disease showed that the relative synchronization time was decreased in some patients (ten subjects) that received integrated treatment, which indicated further functional uncoupling of components of the circulatory system. It is conceivable that the treatment performed in the group of acute myocardial infarction patients did not ensure stabilization of or an improvement in the functional state of the cardiovascular system, which led to the further functional uncoupling of its components. The drug treatment for myocardial infarction uses some preparations affecting the autonomic control of the cardiovascular system, e.g., β-blockers and angiotensin converting enzyme inhibitors [29–31]. Therefore, we can assume that, in patients with a negative dynamics of the mean total synchronization percentage S_m, these drugs were not sufficiently effective; they may even have deteriorated the quality of 0.1-Hz rhythm synchronization because of different individual characteristics of autonomic control. Therefore, individual characteristics should be taken into account for selecting adequate treatment for acute myocardial infarction in this group of patients. The changes in 0.1-Hz synchronization quality over time, characterizing the functional interaction between the control loops of the heart rate and microcirculation volume, can be used as an individual criterion of treatment adequacy.

Thus, the new data present the possibility of an individual approach to study of the state of the autonomic control of the cardiovascular system in health and pathologies.

CONCLUSIONS

The results of this study allow us to conclude that the cardiovascular autonomic control system contains two potentially independent control loops (the heart rate control loop and the microcirculation volume control loop) with natural oscillation frequencies of about 0.1 Hz. In healthy subjects, the 0.1-Hz rhythms of these control mechanisms are mutually synchronized, which ensures optimal control over the functioning of the entire cardiovascular system and determines its adaptability. However, the mechanisms of interaction between these control loops are affected by external factors and may be disturbed in various pathologies, e.g., acute myocardial infarction. Further analysis of the synchronization parameters of the 0.1-Hz oscillations in the microcirculation volume and heart rate could make it possible to develop individual criteria for estimating the functional integrity of the cardiovascular system and parameters of its autonomic control in health and in various diseases, as well as quantitative characteristics of the effectiveness of treatment.

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