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Synchronization between the Slow Oscillations in the Human Cardiovascular System

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***Abstract*—**Synchronization between the slow oscillations of heart rate and blood pressure having in humans a basic frequency close to 0.1 Hz is investigated. A method is proposed for quantitative estimation of synchronization between these oscillating processes based on calculation of relative time of phase synchronization of oscillations. It is shown that healthy subjects exhibit in average substantially longer epochs of synchronization between the slow oscillations in heart rate and blood pressure than patients after acute myocardial infarction.

***Keywords*—**Cardiovascular system, slow oscillating processes, synchronization.

I. Introduction

INVESTIGATION of interactions between various oscillating processes governing the dynamics of a human cardiovascular system (CVS) attracts a lot of attention. The interest to this problem is motivated by the fact that peculiarities of functioning and interaction of the elements of CVS reflect its state and may contain useful information for medical diagnostics. The longest history has the investigation of interdependence between the heartbeat and respiration. Due to their interaction the heart rate increases during inspiration and decreases during expiration. This respiratory modulation of the heart rate is known as respiratory sinus arrhythmia. It has been found that the main heart rhythm and respiration can be synchronized [1]–[4].

Besides the oscillations at a frequency of respiration named high-frequency (HF) ones, the human heart rate exhibits slow or low-frequency (LF) oscillations with a basic frequency of about 0.1 Hz [5]. The HF and LF oscillations are observed also in the signals of blood pressure [5] and blood flow [6]. These oscillations are of great importance for maintaining cardiovascular homeostasis. The origin of these oscillations is still a subject of controversy. A number of research groups supports the central oscillator theory believing that 0.1-Hz oscillations of heart rate and blood pressure represent an intrinsic property of autonomous neural network [7], [8]. On another hypothesis these LF oscillations are largely an index of baroreflex gain [9].

It has been found that 0.1-Hz cardiovascular oscillations can be synchronized with the main heart rhythm and respiration [3]. Interdependence between the LF oscillations in blood pressure and heart rate has also been studied [10]. One of the most widespread tools used to investigate this interdependence is based on the analysis of power spectra and coherence between the signals. Such approach allows one to estimate in the frequency domain the strength of linear coupling between the signals. However, the cardiovascular rhythms are known to be nonlinearly mutually interacting as a result of the presence of both feedback and feedforward coupling mechanisms [11]. Moreover, the signals under consideration are usually nonstationary. Their frequencies and amplitudes can be highly variable within the time of observation. In such a situation nonlinear measures of synchronization [12] may be preferred over the coherence function.

In this paper the interaction between the oscillating processes with a frequency of about 0.1 Hz in heart rate and blood pressure is studied by using a quantitative measure based on the analysis of phase synchronization of oscillations. A degree of synchronization between the above-mentioned slow oscillations is compared in healthy subjects and patients after acute myocardial infarction.

II. Data and Methods of their Analysis

A. Description of Measurements and Data Pre-processing

In our research 17 healthy subjects (8 women) aged 20–48 years and 42 patients (14 women) aged 41–80 years after acute myocardial infarction (AMI) took part. The study was approved by the institutional ethical board and all subjects gave their written informed consent. The signals of electrocardiogram (ECG) and blood pressure on the middle finger of the subject's hand were simultaneously recorded in a supine resting condition under spontaneous breathing. All signals were sampled at 250 Hz and digitized at 16 bits for off-line analysis with a personal computer. The duration of

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each record was 10 minutes. With each subject several measurements were carried out at different days. In all, 126 records for healthy subjects and 167 records for AMI subjects were measured. For AMI patients all recordings were performed during the first three weeks after the infarction.

Extracting from the ECG signal a sequence of R-R intervals one can obtain information about the heart rate variability (HRV). To obtain equidistant time series from not equidistant sequence of R-R intervals this sequence was approximated with cubic splines and resampled with a frequency of 4 Hz.

Generally the Fourier power spectra of R-R intervals and blood pressure signal exhibit peaks at the frequencies associated with the respiratory and slow oscillations of heart rate and blood pressure, respectively. To extract the slow component of HRV associated with a process of heart rate regulation with a frequency of about 0.1 Hz the sequence of R-R intervals was filtered removing the HF oscillations (>0.15 Hz) associated predominantly with respiration, and very low frequency oscillations (<0.05 Hz). Similarly, the LF component of blood pressure signal was extracted using the same filtration with the bandpass 0.05–0.15 Hz.

B. Method of Detection of Phase Synchronization

To investigate the interaction between the oscillating processes in blood pressure and heart rate whose fundamental frequencies are close to 0.1 Hz a phase synchronization measure based on the Hilbert transform is used. The first step in quantifying phase synchronization between two signals is to determine their phases. To calculate the phase of LF oscillations of heart rate the analytic signal $\zeta(t)$ [13] is constructed for the signal $s(t)$ obtained as a result of bandpass filtration of R-R intervals. The signal $\zeta(t)$ is a complex function of time defined as

$$\zeta(t) = s(t) + i\mathcal{H}(t) = A(t)\exp\left(i\phi(t)\right), \tag{1}$$

where $A(t)$ and $\phi(t)$ are respectively the amplitude and the phase of the analytic signal, and function $\mathcal{H}(t)$ is the Hilbert transform of $s(t)$,

$$\mathcal{H}(t) = \frac{1}{\pi}\,\mathrm{P.V.}\int_{-\infty}^{+\infty}\frac{s(\tau)}{t-\tau}d\tau, \tag{2}$$

where P.V. means that the integral is taken in the sense of the Cauchy principal value. Phase $\phi(t)$ is defined from (1) as

$$\phi(t) = \arctan\left(\mathcal{H}(t)/s(t)\right). \tag{3}$$

In a similar way the phase of LF oscillations of blood pressure is calculated from the filtered signal of blood pressure.

To detect synchronization between the slow oscillations of blood pressure and heart rate the phase difference

$$\varphi = \phi_p - \phi_h \tag{4}$$

is calculated, where ϕ_p is the phase of LF oscillations of blood pressure and ϕ_h is the phase of LF oscillations of heart rate. The presence of 1:1 phase synchronization is defined by the condition $|\varphi| < \text{const}$. In this case the phase difference $\varphi(t)$ fluctuates around a constant value as in Fig. 1(a).

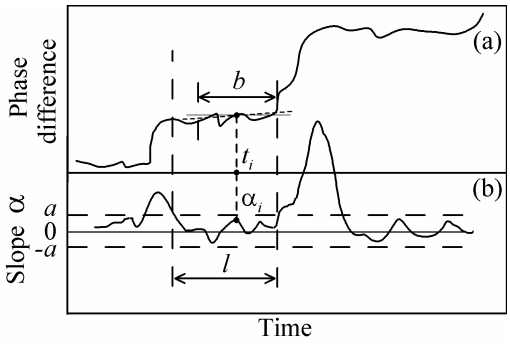

Fig. 1 Illustration of the automated procedure for detecting epochs of phase synchronization. (a) Linear approximation of normalized $\varphi(t)$ in a moving window. (b) Slope of the approximating line.

After detection of all epochs of synchronization in the plot of $\varphi(t)$ their total duration is calculated and expressed in percent of the duration of the entire record. The obtained measure S is named in our paper as the total percent of phase synchronization. The values of this measure are compared in healthy subjects and AMI patients.

For automated detection of phase synchronization epochs an algorithm is developed, which is based on a linear approximation of instantaneous phase difference $\varphi(t)$ in a moving window. A time series of $\varphi(t)$ normalized by 2π is linearly approximated in a window of width b by using the method of least squares [Fig. 1(a)]. As a result, for a time moment t_i corresponding to the middle of the window a coefficient α_i of the approximating line slope is obtained [Fig. 1(b)]. Moving the window by one point along the time series of $\varphi(t)$, one can calculate a slope α_{i+1} for a time moment t_{i+1}, and so on. In the regions of phase synchronization the relative phase $\varphi(t)$ exhibits plateaus resulting in small values of $|\alpha|$. The regions of small $|\alpha|$ values are detected as synchronization episodes if $|\alpha| \le |a|$, where a is a threshold value. A sufficiently large duration of the region of small $|\alpha|$ values is used as the second necessary condition for the detection of synchronization. The duration of this region should exceed the value l [Fig. 1(b)] to exclude short regions with a high probability of accidental coincidence of instantaneous phases of oscillations.

The method efficiency for detecting synchronization was tested depending on the choice of the parameters b, a, and l.

The total percent of phase synchronization decreases with decreasing of $|a|$ or increasing of l. The dependence of S on the parameter b is not monotonous. The choice of the method parameters was based on the following concept: the automated procedure should identify the epochs of synchronization similarly to the usually used visual detection of synchronization and ensure a statistical significance of the results. It was found that these conditions are satisfied if l is about 1–2 characteristic periods of oscillations, b is close to the characteristic period, and $|a|$ is about 0.005–0.01. In this paper the following fixed values of the parameters: $b = 13$ s, $|a| = 0.01$, and $l = 16$ s were used for the investigation of all experimental records.

C. Estimation of Statistical Significance of Results

Analyzing experimental data for which nonstationarity, noise presence, short length of time series, or closeness of basic frequencies is typical, one can detect spurious synchronization even between noncoupled oscillators and come to wrong conclusions. Therefore, it is important to estimate a statistical significance of the synchronization analysis results. In our paper a statistical significance of synchronization measure S calculation is estimated using surrogate data [14] often applied to investigation of experimental time series.

To analyze a significance of the obtained results the following procedure is exploited. At first, from each signal of blood pressure and R-R intervals filtered with the bandpass 0.05–0.15 Hz surrogate time series are generated by multiplying the Fourier transform of the original data by random phases and then transforming back to the time domain. This method of surrogate data preparation preserves periodograms of the analyzed signals but destroys couplings between them. Then, with the help of the automated procedure of phase synchronization detection a total percent of phase synchronization S_i, $i = 1,\text{K},10000$ is calculated for each i-th pair of surrogates. Over the whole ensemble of surrogates a distribution P of S_i values is plotted and the ratio of area of distribution $P(S_i)$ corresponding to $S_i \geq S$, to the entire area of distribution is defined. This ratio serves as an estimation of a significance level p for the value of S calculated from experimental data.

III. Results

The total percent of phase synchronization between the 0.1-Hz rhythms was calculated for all subjects by using the proposed method. Fig. 2 depicts the distribution functions of S values computed over all records of healthy subjects and AMI patients. It is revealed that the measure S is greater in average in healthy subjects than in AMI patients. In our experiments S took the values $34.4 \pm 16.1\%$ (mean ± standard deviation) for healthy individuals and $16.0 \pm 9.5\%$ for patients after AMI. It should be noted that the absolute values of S depend on the parameters of the automated procedure for synchronization detection. However, in a wide range of these parameters variation the value of S remains in average considerably greater in healthy subjects than in AMI patients.

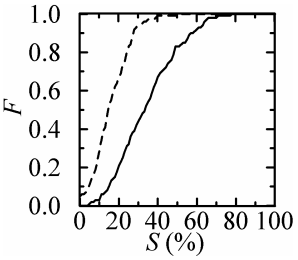

Fig. 2 Distribution functions of the total percent of phase synchronization between the cardiovascular rhythms with a frequency of about 0.1 Hz in healthy subjects (solid line) and AMI patients (dashed line) calculated over all records.

A level of statistical significance of calculated S values is presented in Fig. 3. The total percent of phase synchronization and its level of significance are shown by circles for healthy subjects and by crosses for AMI patients. The horizontal line indicates a significance level of $p = 0.05$ which is often used in practice to provide sufficiently high reliability. The results of our study show that about half of records of both healthy subjects and AMI patients exhibit S values corresponding to a 0.05-significance level conclusion that coupling between the processes is present, i.e., the conclusion of coupling presence has a confidence probability of 0.95. As can be seen from Fig. 3, a separation of circles and crosses is better in the lower part of the figure corresponding to significant S.

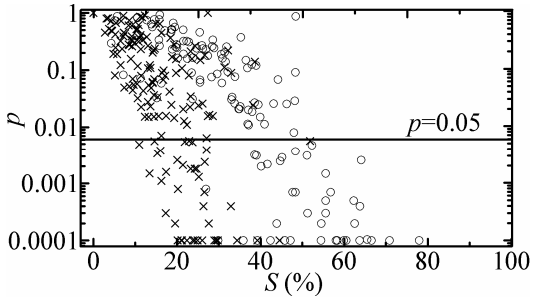

Fig. 3 Level of statistical significance of the total percent of phase synchronization for healthy subjects (circles) and AMI patients (crosses).

The distribution functions of the total percent of phase synchronization calculated only for S values significant at a 0.05 level are presented in Fig. 4(a) for both groups of subjects. S took the values $46.4 \pm 12.7\%$ for healthy subjects and $21.9 \pm 8.1\%$ for AMI patients. Fig. 4(a) is qualitatively similar to Fig. 2, but exhibits appreciably smaller region of overlapping of distribution functions. Hence, the choice of only significant S values allows one to improve separation of the considered groups of subjects.

Fig. 4(b) gives another presentation of S values corresponding to a 0.05-significance level conclusion that processes are coupled. In this figure the distributions $P(S)$ are

plotted separately for healthy individuals and AMI patients. In healthy subjects S took the values from 15% to 78% and in AMI patients from 7% to 52%. These distributions are noticeably different and have a small area of overlapping.

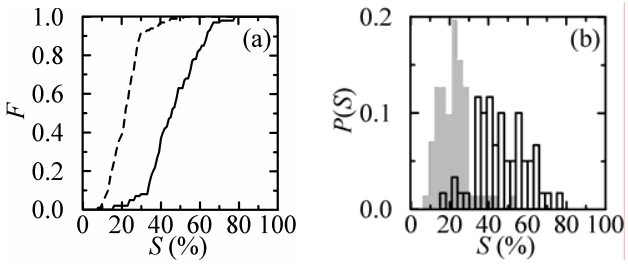

Fig. 4 (a) Distribution functions of significant S values for healthy subjects (solid line) and AMI patients (dashed line). (b) Distributions of significant S values for healthy subjects (white color) and AMI patients (gray color).

To investigate the changes in interaction between the slow cardiovascular rhythms during rehabilitation after the AMI the supplementary measurements for the same patients but after 6 months after AMI were conducted. Only several subjects took part in this investigation and only 4 of them showed the values of the total percent of phase synchronization significant at a 0.05 level both during the first 3 weeks after AMI and after 6 months after AMI. Three of these subjects showed a pronounced increase of S in 1.5 times in average in comparison with their own S values during the first 3 weeks after AMI. One subject showed a small decrease of S in 1.1 times. However, these S values were less in average in comparison with average S values in healthy subjects.

Since the slow oscillating processes in CVS exhibit complex nonlinear interactions and the frequencies and amplitudes of these processes can be variable within the experiment, the considered phase synchronization measure based on the analysis of instantaneous phase difference seems to be more suitable for investigation of synchronization than usually used coherence function. For the signals under examination a situation is typical where their frequencies are varied while the frequency ratio remains stable. In this case the sensitivity of phase synchronization analysis may be higher than that of coherence. In our study the values of the total percent of phase synchronization were significant more often than the values of coherence function.

IV. Conclusion

Interaction is studied between the oscillating processes with a frequency of about 0.1 Hz observed in the human heart rate and blood pressure. The method for quantitative estimation of synchronization between these processes is proposed based on calculation of the total percent of phase synchronization of oscillations. The method of automated detection of phase synchronization epochs is developed. This method is based on a linear approximation of instantaneous phase difference of analyzed signals in a moving window. A statistical significance of the calculated synchronization measure is analyzed using surrogate data.

The presence of synchronization between the 0.1-Hz oscillations in heart rate and blood pressure is detected. It is found that healthy subjects show in average substantially longer epochs of synchronization between the LF cardiovascular rhythms than patients after AMI. Optimal adjustment between the slow cardiovascular rhythms resulting in their comparatively high synchronization ensures a high adaptability of the CVS that is necessary for global healthy behavior of the organism. However, this synchronization may be deteriorated at AMI leading to a disruption of natural functional couplings within the system of the CVS autonomic regulation. Thus, the analysis of synchronization between the LF oscillations in heart rate and blood pressure seems to be promising for studying a degree of disruption of autonomic regulation of the CVS and for controlling the efficiency of medical treatment and rehabilitation.

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