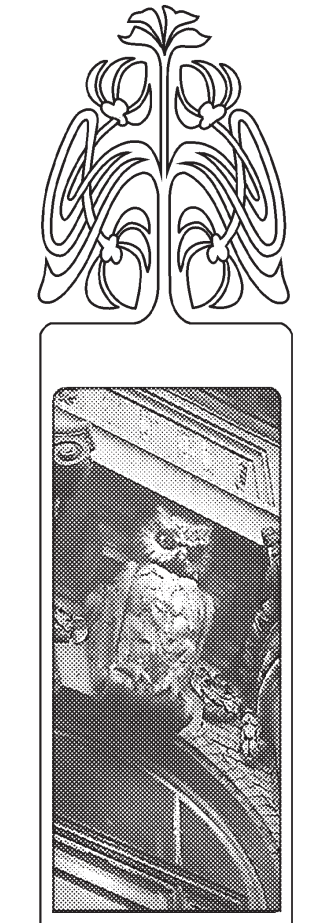

НАУЧНЫЙ ОТДЕЛ

БИОФИЗИКА И МЕДИЦИНСКАЯ ФИЗИКА

Distal Pulse Measurement Provides Statistical, but not Dynamical, Features of the Central Pulse

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Heart rate variability is recognized in medicine as an important prognostic factor. It is generally believed that the temporal characteristics of the pulse signal do not depend on the measurement point. Specifically, the distal (on the fingers) arrangement of the photoplethysmographic sensors. Using a high-precision measurement technique, we show that on the way from the heart to distally located measurement points, the value of each individual beat-to-beat time may change. It can happen since each subsequent pulse wave propagates through the vessels with a speed different from the previous one, faster or slower. We show that the magnitude of deviation from the average value seems to be mediated by systemic factors. The most likely physiological mechanisms of the detected effect include both modulations of the properties of passive elasticity of the vascular wall depending on the peak value of systolic blood pressure and neurogenic modulation of the tone of the smooth muscles of the vessels.

Keywords: heart rate variability, intervalogram, pulse wave, photoplethysmography.

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1. Introduction

Heart rate variability (HRV) is recognized in medicine as an important prognostic factor for cardiovascular risk, and it has been shown that a low value of standard deviation of RR intervals (SDNN) is associated with an increased likelihood of an adverse outcome [1]. There is a proven HRV measurement technique based on the sequence of RR-intervals (intervalograms) recorded by the ECG method [2], while the details of evaluating the results are still under discussion [3].

To date, various mobile devices that monitor heart rate and its variability are used to assess human health have become widespread. They usually use photoplethysmographic (PPG) sensors, due to their low cost and ease of use. Special studies have been conducted in order to validate the use of such sensors as an ECG replacement, including for evaluating HRV. In [4], the statistical parameters of heart rate variability obtained by various methods are compared including standard ECG, chest ECG sen-

sor of a sports heart rate monitor, and PPG method. It has been established that, statistically, heart rate parameters obtained by all three methods are close and can be considered equally representative for non-clinical applications. In [5, 6], the applicability of PPG sensors was assessed as a possible replacement in the clinical use of ECG. In [5], both the Fourier spectra of both signals and Poincare plots, which reflect poin-to-point dynamics, were compared. It is concluded that the statistical and spectral differences in the data obtained by both methods are small and not significant for clinical use. In [6], authors used autoregressive (AR) analysis, Poincare plots, cross correlation, standard deviation, arithmetic mean, skewness, kurtosis, and approximate entropy (ApEn) to derive and compare different measures from both ECG and PPG signals. The obtained results support for the idea of using PPGs instead of ECGs I in ambulatory cardiac monitoring.

Each heartbeat creates a pulse wave, the travel time of which along the vessels at a specific measurement site is called the pulse transient time (PTT). Despite the widespread use of average PTT as a marker of vascular stiffness, very few studies are devoted to assessing the clinical significance of PTT variability [7]. In [8], the contribution to the variability of PTT of the aortic valve opening time was demonstrated; this is a very rare example of a study that takes into account the complex nature of the PTT, as opposed to its generally accepted interpretation as a function of the average elasticity of the vascular wall. The spatial variability of the pulse signal on the surface of the face was demonstrated in [9]: for the promising non-contact PPG method, the pulse signal can have a complex shape, which requires the development of special techniques.

It should be noted that the variability of PTT in time has the same physiological reasons as the variability of the heart rate – this is a change in the degree of stimulation from the autonomic nervous system. Moreover, signs of chaotic dynamics were repeatedly recorded for HRV [10]. Later, it was suggested that the complex nature of the change in RR intervals can be largely explained by the influence of respiratory rhythm [11, 12]. Similar issues with respect to PTT are currently little studied. When using PPG for recording heart intervalograms, it is usually assumed that the measured sequence of time intervals at distal locations is equivalent to the sequence of RR intervals obtained by the ECG method, which is justified by the results of [4–6] and other similar studies.

In this work, we demonstrate that these sequences are indeed statistically close, but dynamically not equivalent: the PTT changes from one heart beat to another, demonstrating its own dynamics, in which both systemic and local components are distinguishable.

2. Methods

The key aspects of the measurement procedure are illustrated in Fig. 1.

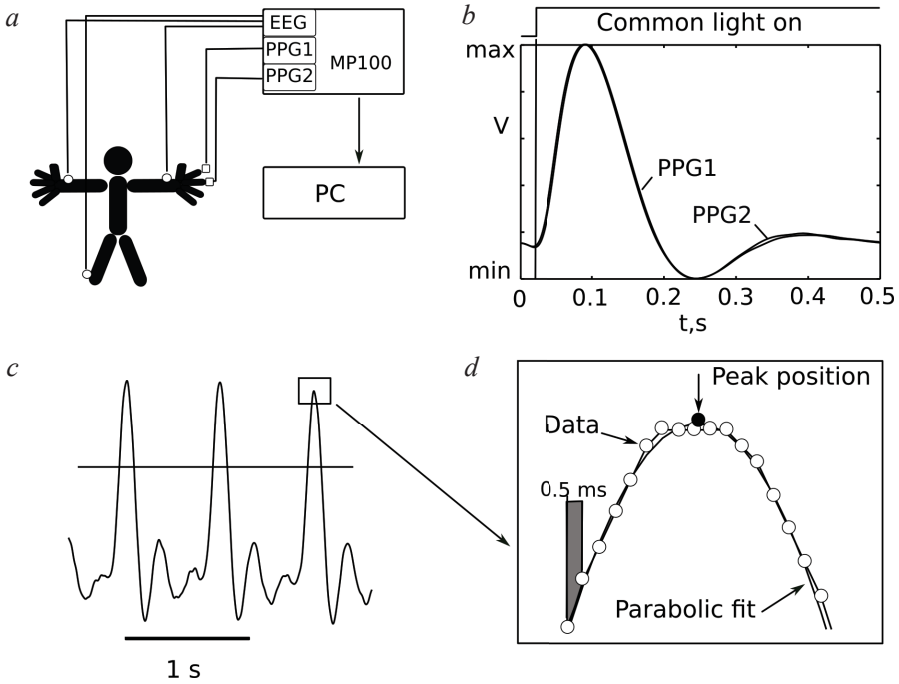

Fig. 1. Sensor connection diagram (*a*), impulse response of a pair of PPG sensors (*b*), method for preliminary search for signal peaks (*c*), algorithm for determining the peak position (*d*)

Panel (*a*) shows the arrangement of the measuring channels. To register data, we used the MP100 measuring complex (Biopac Systems, USA), with one ECG channel (lead I was used) and two PPG channels connected. Taking the PPG signals from two fingers of the same hand we presume that they could show both the coherent part of PTT variability arizing in large and middle arteris, and the contribution from local mechanisms.

The measurements were carried out on a group of 10 healthy volunteers aged 20–35 years during the rest state. In this brief report, we illustrate the obtained results with selected representative recordings, while statistics over the group of subjects will be published later. PPG sensors consisted of a factory-made electronic module (TZT, China) and a custom finger mount system, and a connection to the MP100. Since the precise and simultaneous measurement of the arrival time of the pulse wave was crucial in our study, the sensors were pre-selected to ensure the maximum identity of the parameters. Panel (*b*) of Fig. 1 shows the response of two sensors to the activation by the step-like signal from an external light source. As can be seen, a small discrepancy occurs only at $t = 0.35$ s.

In order to maximize the accuracy in determining the peak position in time, data were collected at a high sampling rate of 2000 Hz, so the time interval between subsequent points was 0.5 ms. All recorded signals were low pass filtered with a cut-off frequency of 25 Hz. At the next stage, the signal maxima were searched in the signal segments that exceed the selected threshold, see panel (*c*). The found maxima were used as initial guess data for an algorithm based on polynomial approximation. Taken together, the above-described steps have significantly improved the accuracy in determining the position of the peak. In tests of the complete system, the difference between the channels in determining the peak position did not exceed 1 ms with a typical value of less than 0.5 ms.

3. Results

When analyzing the central (by ECG signal) and distal (by PPG sensors) intervalograms, statistical and then dynamic characteristics were compared first. Fig. 2 illustrates representative results obtained from three intervalograms, where PPG1 and PPG2 signals were taken from the middle and index fingers of the left hand, respectively.

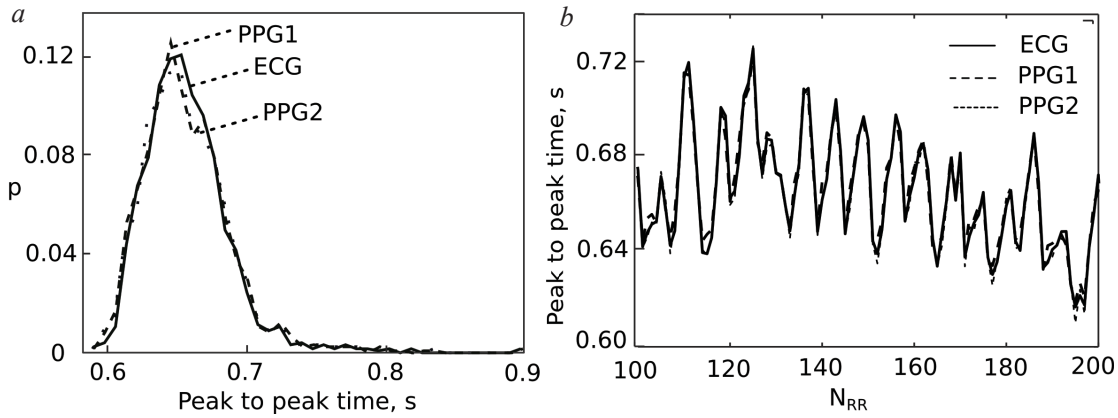

Fig. 2. Statistical characteristics of the central and distal intervalograms: (*a*) estimate of the probability density distribution curves on a set of time intervals of 0.008 s; (*b*) 100-beats fragment of all three intervalograms

Panel (*a*) displays estimates of the probability density distribution calculated using ECG and two PPG sensors, separately. As one can see, they are very close in shape, and the differences can be explained by the scattering of values between neighboring bins.

Note that the calculation of the average interval value for all three signals gives essentially the same number 0.6591s. Panel (*b*) shows a fragment of all three intervalograms in time, where oscillations at the respiratory rhythm frequency are clearly visible. Thus, the results in Fig. 2 support the conclusion made earlier in [4–6] that the characteristics of the central and distal pulses are very similar, if not completely equivalent.

Fig. 3 presents the results of a more detailed analysis of those differences that seem insignificant in Fig. 2. During this analysis, for each heart beat, a new quantity was calculated by which the RR interval changes on the way to distally located PPG sensors. Recall that the ECG signal contains times of many (specifically, 1000) consecutive RR intervals,

and the signals PPG1 and PPG2 contain the intervals between the same heartbeats, but recorded on the index and middle fingers of the left hand. Then, the pairwise subtraction of the distal and central intervalograms gives two signals:

$$dPTT_1(i) = PPG1(i) - ECG(i),$$

$$dPTT_2(i) = PPG2(i) - ECG(i),$$

which correspond to the deviation of the i-th cardiointerval when measuring it on a PPG sensor from the value of the same interval calculated from ECG peaks. This value will be positive if the pulse wave velocity (PVW, is equal to 1/PTT) has decreased during the analyzed cardiointerval, and negative in the opposite case.

Another signal calculated as

$$dPTT_{21} = PPG2(i) - PPG1(i) = dPTT_2(i) - dPTT_1(i)$$

describes the difference in the time of arrival of the pulse to the two PPG sensors.

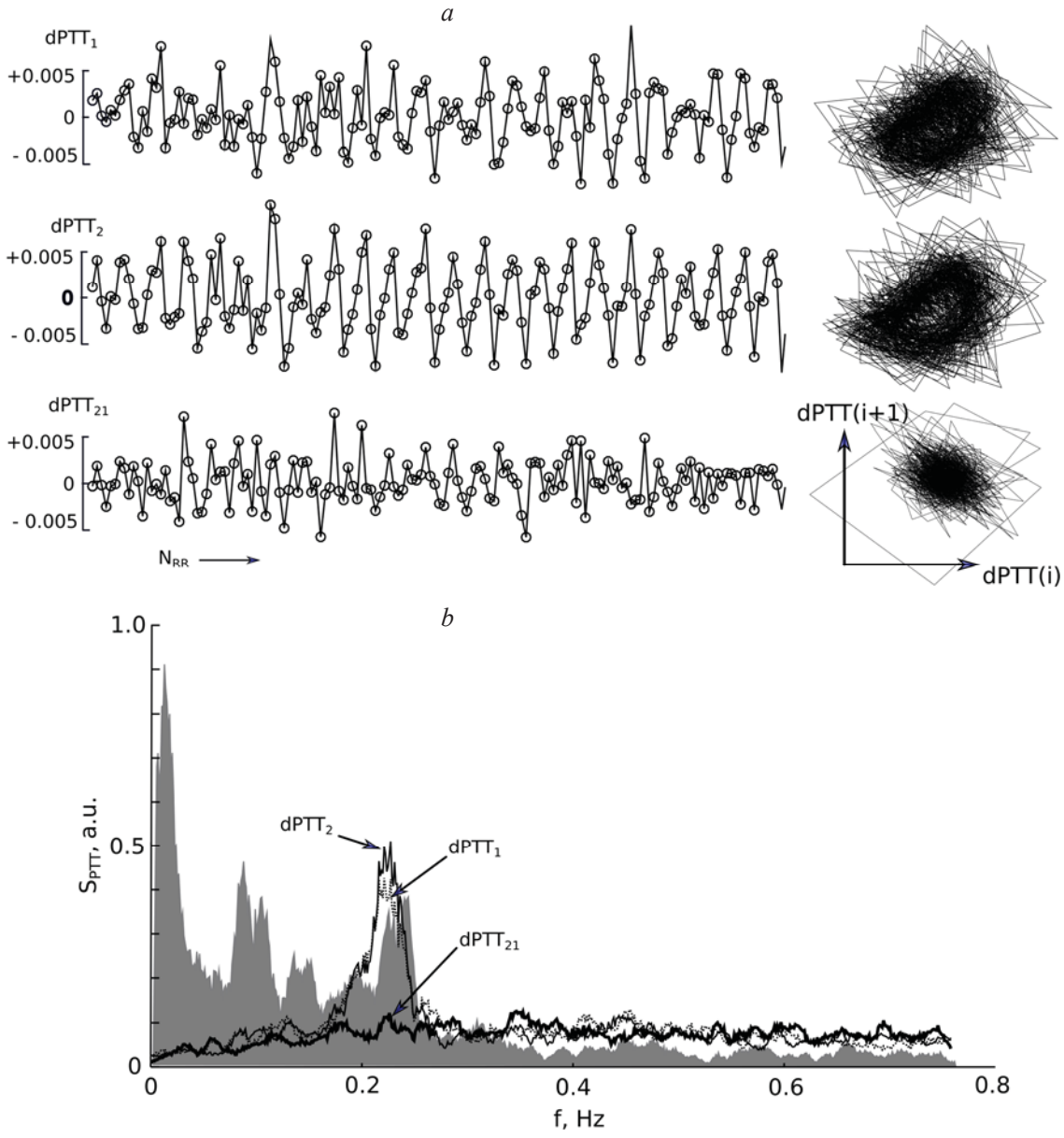

Fig. 3. Dynamics (*a*) and Fourier spectra (*b*) of the signals of the difference in the values of the cardiointervals recorded by various sensors. Each open circle corresponds to one heartbeat

From the time series (left) and recurrence map (right) in panel (*a*) of the Fig. 3, it can be seen that the PPG intervals do not follow ECG intervals, demonstrating a pronounced rhythm in this deviation, which is also visible in the recurrence map plot. The maximum value of this deviation is not the same

for different fingers. Moreover, the time difference $dPTT_{21}$ of the arrival of pulses to both sensors behaves much less regularly.

The Fourier spectra of all three signals, as well as the sequence of RR intervals, are shown in panel (*b*). The spectrum of the sequence of RR intervals is grey shaded and shown divided by 5 for better visual comparision. It has the most complex shape and demonstrates the pronounced maxima at 0.02, 0.1, 0.15, 0.25 Hz, of which the latter at 0.25 Hz corresponds to the respiratory rhythm. It is remarkable that the signals $dPTT_1$ and $dPTT_2$ show a much simpler spectrum, since the same low-frequency spectral components are subtracted when calculating these signals.

However, the peak in the 0.25 Hz region still exists and has a slightly different shape than for the ECG signal. It can be concluded that the observed rhythm dPTT signal is still the respiratory rhythm, but delivered to the PTT not from the ECG signal, but in a different way.

Note that the spectrum of the difference in the arrival times of pulses on PPG sensors, $dPTT_{21}$, does not contain any pronounced peaks, which corresponds to a random process. Thus, it can be assumed that a peak at the respiratory rhythm frequency appears on a portion of the route common to the signals PPG1 and PPG2.

4. Discussion

The results presented above show that on the way from the heart to distally located measurement points, the value of each cardiointerval changes. The obvious reason for this is that each subsequent impulse propagates through the vessels faster or slower than the previous one. That is, we showed that the PTT value, which reflects the total elastic properties of the vessels along the pulse propagation path, varies markedly from beat to beat of the heart.

A natural question arises, how reliable are the above results? According to our data, the value of the cardio interval varies on average – by 0.5% and as much as possible – by 2-3%, depending on the subject and the place of measurement. This does not look large, but an estimate of the accuracy of our measurements yields no worse than 0.15%. Thus, the discussed average values are more than three times larger than the maximum measurement error, and peak values are more than 10 times larger. The second important point is that our measurement technique is insensitive to systematic errors, such as the response time of the sensor, since we are considering changes in the PTTs, and not its magnitude. Thus, we consider the presented results are reliable. We plan to publish more representative statistics in a subsequent expanded work.

Another natural question concerns the physiological interpretation of the results. The predictive value of PTT is based on the fact that it is determined by the total elasticity of the vascular bed. This assumption, in turn, is based on the physical model of an elastic tube with a constant coefficient of elasticity (Fick`s law). However, in reality, the compliance of the vascular wall non-linearly depends on the degree of stretching, and the observed change in PTT can be caused by the variability of the blood pressure, which, in turn, depends on changes in the stroke volume of the heart.

The second important circumstance is that the R-wave of the cardiogram does not accurately reflect the moment of initiation of the pulse wave. Namely, the PTT includes a pre-ejection period (PEP), during which the pressure in the left ventricle rises until the aortic valve opens [8]. The PEP value also depends in a complex way both on the current stroke volume and on the rate of pressure drop in the diastole.

The value of PTT is significantly affected by muscle sympathetic nerve activity (MSNA). It is known that the respiratory rhythm is significantly represented in the MSNA signal [13], which mediates the neurogenic regulation of vascular tone, and which, as is known, also contains components of the respiratory rhythm [12, 14]. Finally, the respiratory rhythm is also presented in PEP [15], as a result of the action of all of the above.

As follows from the above, the very fact of the presence of the respiratory rhythm in the signal of PTT variability does not allow us to draw an unambiguous conclusion about physiological mechanisms and needs further investigations. In this regard, it is appropriate to draw attention to the fact that the spread in the arrival times of pulses for both distally located PPG sensors is random and does not show a respiratory rhythm. It suggests that the modulation of PTT by the respiratory rhythm (for any of the reasons listed above) occurs synchronously in the vascular bed, common to all fingers, and a random spread occurs due to local regulation of blood flow in the smallest vessels of each finger.

Thus, we can consider the results in the context of the general (coherent) component of the PTT variability, and the contribution of local mechanisms, which accumulates mainly in the smallest vessels. The validity of this approach is confirmed by the fact that the calculation of the correlation coefficient between dPTT1 and dPTT2 gives a value of

the order of 0.7, and between signals from the same fingers of both hands – about 0.6, which is slightly less, despite the anatomically different propagation paths in the latter case.

Last but not least, how much can the reported results be useful in biomedical applications? The authors believe that any of the hypotheses expressed above opens up its own prospects. If the passive elasticity of the vascular wall is decisive in the effect, then our results will help to build a really working blood pressure monitoring system based on PTT measurements, which is still a challenge. In the case of the predominant contribution of the active (muscle) component, a similar advance can be made in the development of methods for monitoring sympathetic activity.

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Измерение дистального импульса отражает статистические, но не динамические характеристики центрального пульса

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Вариабельность сердечного ритма признана в медицине важным прогностическим фактором. Принято считать, что временные характеристики пульсового сигнала не зависят от точки измерения, что лежит в основе широкого применения фотоплетизмографии при дистальном (на пальцах) расположении датчиков. Используя методику измерений повышенной точности, мы показываем, что на пути от сердца к дистально расположенным точкам измерения величина каждого отдельного кардиоинтервала достоверно изменяется. Это происходит, потому что каждая последующая пульсовая волна распространяется по сосудам быстрее либо медленнее предыдущей, а величина этого отклонения от среднего, по-видимому, опосредована системными факторами. Наиболее вероятные физиологические механизмы обнаруженного эффект включают как модуляцию свойств пассивной упругости сосудистой стенки в зависимости от величины пика систолического артериального давления, так и нейрогенную модуляцию тонуса гладкой мускулатуры сосудов.

Ключевые слова: вариабельность сердечного ритма, интервалограмма, пульсовая волна, фотоплетизмография.

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