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Assessment of Heart Autonomic Control on the Basis of Spectral Analysis of Heart Rate Variability

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Abstract—An orthostatic test with frequency-controlled breathing (with a respiration period of 10 s) or spontaneous breathing was used to analyze frequency estimates of the heart rate variability (HRV) in the low-frequency (LF) and high-frequency (HF) ranges in young men and women. It was demonstrated that the spectral components of HRV bear no signs of sex differentiation, suggesting a uniform structural organization of the system of autonomic nervous control of the heart (SANCH) in humans. The LF component of the HRV spectrum is a marker of the functional state of the SANCH; it should be studied under conditions of controlled breathing at a frequency of 0.1 Hz. The HF and LF components of the HRV characterize the state of the SANCH at a given moment and do not reflect directly its adaptation reserve. The HF component of the HRV is interesting as a parameter that may be used for estimating the changes in the adaptation reserve of heart autonomic control. It is preferable to analyze this component in the absence of external disturbances in the LF range of the spectrum.

The effect of the autonomic nervous system (ANS) on the rhythmic activity of the heart is usually referred to as a modulating one and is mediated by reciprocal interactions between the sympathetic and the parasympathetic divisions of the ANS. This mechanism of heart rate (HR) control determines the variability of the RR interval of the electrocardiogram (ECG) [1, 2], which can be efficiently studied via estimating the frequency spectrum of HR variability (HRV) [3]. However, the reciprocal interactions between ANS components are insufficient to account for the nonlinear changes in cardiac rhythm. The nonlinear component of HRV is determined by a delay in the feedback loop of the system of autonomic nervous control of the heart (SANCH) and is related to the specificity of the activity of regulatory nervous centers [4].

The model of heart control based on the baroreflex (De Boer's model) [5–9] explains the generation of the low-frequency (LF) component of the HRV spectrum and is important for studying the nonlinear characteristics of the SANCH. The stable spectral component at about 0.1 Hz (the LF range) characterizes the properties of the central link of the SANCH [10–13], such as the feedback effect in the control system, which complements the model suggested by De Boer and colleagues [11, 14, 15].

External random disturbances ("noise") [16] at the input of the SANCH have been found to generate the HRV spectrum at its output [17]; in other words, the method of controlled external disturbances is important for studying the internal characteristics of this system. The use of controlled breathing may be regarded as the introduction of a periodic component into the exogenous noise [18, 19]. According to De Boer's model, the frequency of the controlled respiratory disturbance may be selected when the presence of endogenous oscillations of the system at a frequency of about 0.1 Hz makes it possible to use the resonance response in the LF range [20] to controlled breathing with a period of 10 s, i.e., a frequency of 0.1 Hz [21]. In this case, the resonance effect is determined by the physical coincidence of the frequencies of two harmonic oscillatory processes: the external respiratory disturbance and the internal oscillations of the system.

It is known that, when a subject changes position from lying to standing, part of the circulating blood moves to lower regions of the body and the venous return decreases. In this case, the central volume of blood decreases by 20% and the minute volume, by 1.0–2.7 l/min [22]. An increase in the tone of the sympathetic nervous system against this background causes an increase in HR and total vascular resistance. The change in venous return with the use of the orthostatic functional test makes it possible to study the adaptive responses of the circulatory system that are accompanied by changes in the degree of HRV as a result of changes in the inner functional state of the SANCH.

We studied the changes in the characteristics of the SANCH with the use of De Boer's model during orthostatic tests in young healthy men and women.

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METHODS

The frequency characteristics of the HRV spectrum in the LF and high-frequency (HF) ranges [23] were estimated in 124 healthy volunteers (74 men and 50 women) aged 20 ± 1 years without signs of cardiac pathology.

The orthostatic test with controlled breathing consisted of the following stages: (1) a horizontal position and spontaneous breathing; (2) a horizontal position and controlled breathing with a period of 10 s; (3) a vertical position and spontaneous breathing; and (4) a vertical position and controlled breathing with a period of 10 s.

Each stage of the functional test lasted for 3 min, during which time rhythmograms were recorded. The stages of rhythmogram recording alternated with 2- to 3-min breaks to avoid effects of transitional processes on the results. The controlled breathing rate was set by a 0.5-s impulse sound signal. At the moment of the signal, the subject took a breath. There were no other requirements for the respiration rhythm. The subjects themselves chose the relative durations of the inhalation and exhalation phases and the depth of breathing most comfortable for them. The only additional recommendation that the volunteers received before the test was that the depth and the time structure of the respiration cycle had to be similar to those characteristic of spontaneous rather than forced respiration. Each stage of controlled breathing lasted for 3 min, after which arterial blood pressure (BP) was measured according to Korotkoff.

Frequency estimates of HRV were obtained by the parametric method, according to which the spectrum of the RR time series of the ECG was constructed on the basis of a self-regression 14th-order model. This method is an alternative to the classic Fourier transform of time series [24, 25]. The software for spectrum analysis was developed at the Saratov Institute of Cardiology (Ministry of Health Certificate no. 044). The program allows the spectral power to be calculated with a step of at least 0.01 Hz in the range from 0.01 to 0.5 Hz. For spectral analysis, we selected 3-min rhythmograms without noise, extrasystoles, a marked linear trend, or transitional processes.

In addition to the absolute powers of the components of the HRV spectrum, power increments of these components were calculated as follows: $\Delta var2\text{–}1 = (var2 - var1)/var1$. The changes in mean values for RR intervals were calculated similarly. Along with the above numeration of the test stages, we used the following designations for presenting the results obtained: *LF*, the LF component of the HRV spectrum; *HF*, the HF component of the HRV spectrum; *RR*, mean RR interval; *LF*2–1, the power increment of the LF component at the second stage of the test relative to the first stage; etc.

The Statistica 6.0 software package was used for statistical calculations based on the spectral power parameters in three ranges: HF (0.15–0.4 Hz), LF (0.04–0.15 Hz), and very LF (VLF; <0.04 Hz) [23]. All data were tested for the fit to the normal distribution in order to choose between parametric and nonparametric methods of their subsequent analysis. The data are presented in the form of quartiles (*Me* (25%, 75%)) for samples. First-type errors (α) no higher than 5% were taken to be acceptable.

The Shapiro–Wilk *W* test [26] was used to check the null hypothesis on the fit of the observed parameter distributions to the normal distribution. We found that the parameters of the HRV spectrum were not distributed normally; therefore, the subsequent calculations were performed using nonparametric methods. We used Wilcoxon's *Z* test for pairwise comparisons [27, 28] to compare the variables. Correlations were estimated by Spearman's rank-order correlation coefficients (*R*).

RESULTS

The analysis of the results of the orthostatic functional test showed a significant increase in the power of the LF component of the HRV spectrum around 0.1 Hz in response to controlled breathing compared to that recorded when the subjects breathed spontaneously (table). When the subjects were in a horizontal position, the power of the 0.1-Hz component was increased by a factor of 2.5; when the subjects were in a vertical position, the increase was by a factor of about 1.5 (table).

Initially (at stage 1 of the orthostatic test), the powers of the LF and HF components of the HRV spectrum did not differ significantly from each other (table). At the subsequent stages of the test, they were significantly different ($P < 0.0001$). The power of the HF component was decreased by a factor of 2–3 after the subjects assumed a vertical position under the conditions of both spontaneous ($Z(HF1\ \&\ HF3) = 6.401$, $P < 0.0001$) and controlled breathing ($Z(HF2\ \&\ HF4) = 7.065$, $P < 0.0001$). The response to controlled breathing was stronger in the horizontal than in the vertical position (table) ($Z(LF4\ \&\ LF2) = 2.48$, $P = 0.013$). The increments of the LF and HF powers for subjects in a horizontal position significantly differed from each other ($Z(LF2\text{–}1\ \&\ HF2\text{–}1) = 3.653$, $P = 0.0002$) (table), whereas the difference between them for subjects in a vertical position was nonsignificant ($Z(LF4\text{–}3\ \&\ HF4\text{–}3) = 0.482$, $P = 0.63$). The analysis of the changes in the HRV spectrum upon a change in position from horizontal to vertical under conditions of spontaneous breathing did not show any significant direction of the changes in the LF component ($Me(LF3\text{–}1) = 0.038$). The difference between the absolute powers of the LF component for the horizontal and vertical positions was nonsignificant ($Z(LF1\ \&\ LF3) = 1.1$, $P = 0.271$), whereas the changes in the power of the HF component were substantial ($Me(HF3\text{–}1) = -0.6$; $Z(HF3\ \&\ HF1) = 6.401$, $P < 0.0001$) (table). A similar analysis of the vectors of orthostatic changes in HRV spectral components under the conditions of controlled breathing with

Absolute spectral powers of the HRV spectrum components and their changes during the orthostatic test with controlled breathing

Parameter	Stage of the test			
	1	2	3	4
LF, m^2	916.5 (667; 153.5)	2367.5 (1349; 3354)	1014 (706; 1554)	1481 (895; 2230)
HF, m^2	873.5 (518.5; 1552.5)	1416 (520.5; 2076)	335.5 (183; 590)	415 (241; 786)
RR, s	0.817 (0.725; 0.877)	0.827 (0.744; 0.897)	0.658 (0.598; 0.729)	0.643 (0.58; 0.716)
BP_s, mm Hg	115 (110; 120)	–	110 (107.5; 120)	–
BP_d, mm Hg	75 (70; 80)	–	75 (70; 80)	–

	2–1	4–3	3–1	4–2	3–2
Δ*LF*	1.161 (0.191; 3.247)	0.476 (–0.206; 1.708)	0.038 (–0.359; 1.186)	–0.292 (–0.669; 0.552)	–
Δ*HF*	0.314 (–0.273; 1.907)	0.498 (–0.407; 1.573)	–0.6 (–0.827; –0.138)	–0.648 (–0.839; –0.181)	–
Δ*RR*	0.006 (–0.091; 0.131)	–0.033 (–0.162; 0.113)	–	–	–0.165 (–0.285; –0.05)

Notes: BP_s and BP_d, systolic and diastolic blood pressures, respectively; *LF* and *HF*, the LF and HF components of the HRV spectrum, respectively; *RR*, mean RR interval; 1, the first stage of the orthostatic test (a horizontal position + spontaneous breathing); 2, the second stage (a horizontal position + controlled breathing with a period of 10 s); 3, the third stage (a vertical position + spontaneous breathing); 4, the fourth stage (a vertical position + controlled breathing with a period of 10 s); 2–1, the increment of the parameter at the second stage of the test relative to the first stage, etc.

a period of 10 s also demonstrated greater changes in the HF range ($Me(HF4–2) = –0.648$; $Z(HF4 \& HF2) = 6.496$, $P < 0.0001$) compared to those in the LF range ($Me(LF4–2) = –0.292$; $Z(LF4 \& LF2) = 2.48$, $P = 0.013$) (table). Note that, in contrast to the changes in the LF component ($Z(LF2–1 \& LF4–3) = 2.888$, $P = 0.004$), the HF power increments in response to controlled breathing in the horizontal and the vertical positions did not differ significantly from each other ($Z(HF2–1 \& HF4–3) = 0.158$, $P = 0.874$). The comparison between the increments in the powers of spectral components in response to the orthostatic test under conditions of spontaneous and controlled breathing showed significant differences in the LF range ($Z(LF3–1 \& LF4–2) = 2.255$, $P = 0.024$) but not in the HF range of the HRV spectrum ($Z(HF3–1 \& HF4–2) = 0.208$, $P = 0.835$).

The change of position from horizontal to vertical was accompanied by an increase in the HR and a decrease in the total HRV, with changes in BP being insignificant (table). Note that the HR and BP remained unchanged during the functional tests when the subject's body position was not changed.

Correlation analysis of the data obtained did not show significant relationships between the absolute values of HRV spectral powers of the same range at different stages of the test ($R(LF? \& LF?) < 0.17$, $P > 0.05$; $R(HF? \& HF?) < 0.18$, $P > 0.05$). In contrast, the powers of the LF and HF components correlated with each other at different stages of the orthostatic test ($R(LF1 \& HF1) = 0.69$, $P < 0.0001$; $R(LF2 \& HF2) = 0.43$, $P = 0.0002$; $R(LF3 \& HF3) = 0.71$, $P < 0.0001$; $R(LF4 \& HF4) = 0.66$, $P < 0.0001$). Note that the coefficients of correlation of the LF and HF components of HRV under the conditions of spontaneous breathing (*LF*1 and *HF*1, *LF*3 and *HF*3) were higher than those under the conditions of controlled breathing (*LF*2 and *HF*2, *LF*4 and *HF*4). Analyzing the relationships between power increments for different components of the HRV spectrum, we found a significant correlation between the changes in the LF and HF components in response to controlled breathing, which was stronger for the vertical than for the horizontal position ($R(LF4–3 \& HF4–3) = 0.61$, $P < 0.0001$, and ($R(LF2–1 \& HF2–1) = 0.47$, $P < 0.0001$, respectively). The orthostatic test under the conditions of spontaneous breathing caused strongly correlated changes in the powers of the LF and HF components of the HRV spectrum ($R(LF3–1 \& HF3–1) = 0.77$, $P < 0.0001$). Under the conditions of controlled breathing with a period of 10 s, this correlation was moderate (almost 1.5-fold lower than in the case of spontaneous breathing) ($R(LF4–2 \& HF4–2) = 0.52$, $P < 0.0001$).

Analysis of the correlations of mean RR intervals of the ECG showed that the higher the initial HR (the inverse of the RR interval), the lower its subsequent increment during the functional test ($R(RR1 \& RR2–1) = –0.76$, $P < 0.0001$). We found moderate but significant correlations between the absolute values of mean RR intervals and the powers of the LF and HF components ($R(RR1 \& LF1) = 0.4$, $P = 0.0002$; $R(RR1 \& HF1) = 0.57$, $P < 0.0001$; $R(RR2 \& LF2) = 0.44$, $P = 0.0002$; $R(RR2 \& HF2) = 0.43$, $P = 0.0003$), which became stronger after the subjects changed position from hori-

zontal to vertical ($R(RR3 \& LF3) = 0.57$, $P < 0.0001$; $R(RR3 \& HF3) = 0.47$, $P < 0.0001$; $R(RR4 \& LF4) = 0.73$, $P < 0.0001$; $R(RR4 \& HF4) = 0.55$, $P < 0.0001$). There was also a moderate correlation between HR and the increments in the LF and HF powers ($R(RR2 \& LF2–1) = 0.36$, $P = 0.0006$; $R(RR4 \& LF4–3) = 0.53$, $P < 0.0001$; $R(RR2 \& HF2–1) = 0.33$, $P = 0.002$; $R(RR4 \& HF4–3) = 0.37$, $P < 0.0001$). We did not find a significant correlation between the HRV components and a subsequent increase in HR during the orthostatic test under the conditions of controlled breathing ($R(LF2 \& RR3–2) = –0.2$, $P = 0.06$; $R(HF2 \& RR3–2) = –0.19$, $P = 0.06$); in the case of spontaneous breathing, weak, nonsignificant correlations were observed ($R(LF1 \& RR3–2) = –0.12$, $P = 0.27$; $R(HF1 \& RR3–2) = –0.007$, $P = 0.95$). The correlations of the orthostatic changes in the LF and HF components of the spectrum with the corresponding HR increments were weak in the case of controlled breathing and moderate in the case of spontaneous breathing ($R(LF4–2 \& RR3–2) = 0.28$, $P = 0.009$; $R(HF4–2 \& RR3–2) = 0.26$, $P = 0.012$; $R(LF3–1 \& RR3–2) = 0.38$, $P = 0.0003$; $R(HF3–1 \& RR3–2) = 0.34$, $P = 0.001$).

No sex-related difference in the test results was observed.

DISCUSSION

The resonance nature of the 0.1-Hz component of the HRV spectrum. The considerable increase in the power of the 0.1-Hz component in response to controlled periodic breathing with a frequency of 0.1 Hz relative to the power of this component under the conditions of spontaneous breathing indicates an increased sensitivity of the HRV spectrum to external disturbances at a frequency of about 0.1 Hz, which agrees with the assumption that the 0.1-Hz component of the HRV is essentially resonant. According to the theory of the SANCH organization, the resonance characteristic of the LF range of the HRV spectrum results from endogenous oscillations within the system at a frequency of about 0.1 Hz; therefore, we can estimate the changes in the internal nonlinear characteristics of autonomic control by the strength of the resonance response to external, controllable respiratory disturbances at a frequency of 0.1 Hz [29]. In this case, the changes in the internal characteristics of the system will be expressed as changes in the strength of the resonance response of the HRV spectrum.

Only when the subjects were in a horizontal position did the response of the LF component to periodic breathing differ from the increment in the HF range; however, irrespective of the subject's position, the LF component was characterized by significantly higher absolute spectral powers. Therefore, we may assume that the activity of the 0.1-Hz oscillations of the system was higher when the subjects were in a horizontal position, as evident from the considerably stronger resonance response. In general, the 0.1-Hz generation is a powerful process because the absolute powers of the 0.1-Hz component of the HRV spectrum were the highest at all stages of the orthostatic test.

The roles of the LF and HF components of the HRV spectrum in determining the changes in the SANCH functional state. The considerable orthostatic changes in HR suggest that the general autonomic status characterizing the effector part of the SANCH alters upon the change in body position. Thus, it is possible to study the changes in the HRV spectrum components associated with changes in SANCH characteristics, with the mean HR serving as a marker of the system's functional state at different stages of the study.

We did not find significant changes in the power of the LF component during the orthostatic test under the conditions of spontaneous breathing, which indicates that the power parameters of this spectral component are not related to the changes in mean HR in the case of spontaneous breathing. Therefore, it is impossible to estimate the changes in the SANCH functional state by the orthostatic changes in the LF component under the conditions of spontaneous breathing. The importance of the HF component of the HRV spectrum for describing the properties of the system considerably increases under the conditions of controlled respiratory disturbance at a frequency of 0.1 Hz.

However, the vectors of orthostatic changes in the LF component were considerably smaller than those for the HF range in the cases of both spontaneous and controlled breathing, the values of the vectors of orthostatic changes in the HF component being independent of the type of respiratory disturbance (spontaneous or controlled). This might allow us to assume that the change in the HF component reflects the shift of the internal parameters of the SANCH better than the change in the LF component does. However, the correlation analysis did not show substantial differences between the relationships of the changes in the LF and HF components with the HR increment during the orthostatic test.

Thus, analysis of the results of the orthostatic test demonstrated that the orthostatic changes in the LF component of HRV in spontaneously breathing subjects do not reflect the changes in the SANCH activity expressed as an increase in mean HR and a decrease in HRV. The orthostatic test altered the strength of the response of the 0.1-Hz spectral component to controlled breathing. The data obtained indicate that the time course of the response of the SANCH 0.1-Hz generation to a controlled external 0.1-Hz respiratory disturbance can be used for studying the internal characteristics of the system and their changes caused by certain external and internal factors.

Taking into account that the power of the HF component of the HRV spectrum changes much more during the orthostatic test, when the functional parameters of the SANCH are altered, this parameter seems to deserve consideration with regard to its use for estimat-

ing the pattern of changes in the characteristics of the SANCH, along with the power of the 0.1-Hz component.

Note that we did not find correlations between the absolute values of components of the same range (LF and LF, HF and HF) of the HRV spectrum. This indicates that the absolute spectral powers do not reflect their possible changes in response to varying the internal characteristics of the SANCH. The correlations between absolute LF and HF powers at different stages of functional tests indicate interactions between them. The stronger correlations in spontaneously breathing subjects compared to those in the case of controlled periodic breathing reflect significant relationships between mechanisms determining the formation of the LF and the HF powers in the HRV spectrum under the conditions of spontaneous breathing. The slight decrease in correlation coefficients under the conditions of controlled breathing with a period of 10 s may be determined by differences in the mechanisms of formation of generation data, which are likely to be caused by the resonance effect in the 0.1-Hz region, whose strength is entirely determined by the characteristics of the main oscillatory process of the system at this frequency. Therefore, it is preferable to study the HF component of the HRV spectrum in the absence of external disturbances in the LF range.

If we accept this working hypothesis, then the results of our study suggest that the mechanisms forming the LF and the HF components of the HRV spectrum under the conditions of controlled breathing with a period of 10 s become considerably more common as a subject assumes an orthostatic (vertical) position, which is probably accounted for by a decrease in the power of the resonance response in the 0.1-Hz region. This finding indicates that the orthostatic test causes changes in the activity of 0.1-Hz oscillations of the SANCH. Therefore, the 0.1-Hz generation of the system can change its functional parameters under the action of varying external factors, which confirms its importance for adequate functioning of the heart.

Note that the tests performed in this study did not show any sex-related differences in the pattern of changes in the spectral components of the HRV, which indicates the uniformity of the structural organization of the SANCH in humans.

The importance of HRV spectral parameters for estimating the adaptive potential of HR autonomic control. The results of correlation analysis of mean HRs at different stages of the functional test indicate that the higher the initial HR (at the start of the functional test), the lower the probability of its subsequent increase, which reflects a lower sensitivity of the SANCH to changes in the external conditions under which the cardiovascular system is functioning. The decrease in the SANCH sensitivity to such changes in external conditions indicates a decreased capacity for adequate changes in its functional parameters, which is expressed in a decrease in adaptability of the system. This assumption may serve as a basis for determining the adaptive potential of the SANCH using data on the parameters characterizing its internal state, including the HRV spectral components.

The absolute values of the LF and the HF components are associated with the absolute HRs, the correlation between them being the strongest under orthostatic conditions. At the same time, the HR negatively correlates with the HRV spectral power. Therefore, we may hypothesize that the higher the spectral power, the more pronounced the adaptability of the system, according to the assumption put forward in the preceding paragraph. Thus, the absolute values of the LF and the HF powers characterize the functional state of the SANCH, with its output signal in the form of the mean HR serving as its marker. The functional state of the SANCH directly determines the changes in its functional parameters in response to the variation of the external conditions.

However, the powers of the HRV spectral components have no significant prognostic value in terms of the prediction of the subsequent increment in HR during the functional test. Therefore, it can be concluded that the HF and LF generations characterize the state of the SANCH at a given moment and cannot be used directly for describing its adaptation reserve.

CONCLUSIONS

(1) The spectral components of HRV do not bear significant signs of sex differentiation, which indicates that a uniform structural organization of the human SANCH is common to both sexes.

(2) The LF component of the HRV spectrum is a marker of the functional state of the SANCH; it should be studied under the conditions of controlled breathing at a frequency of 0.1 Hz.

(3) The HF and LF components of the HRV spectrum characterize the state of the SANCH at a given moment and cannot be used directly for describing its adaptation reserve.

(4) The HF component of the HRV spectrum is interesting in terms of its possible use for estimating changes in the adaptation reserve of the SANCH. It is advisable to analyze this component in the absence of external disturbances in the LF range of the spectrum.

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