ORIGINAL RESEARCHES

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HEMODYNAMIC AND HEART RATE CHANGES THAT OCCUR IN RESPONSE TO AN ACTIVE ORTHOSTATIC TEST IN YOUNG MALE RESIDENTS OF DIFFERENT DISTRICTS OF RUSSIA'S FAR EASTERN REGION

The **purpose** of this research was to study the restructuring of the cardiovascular system, hemodynamics and heart rate in response to an active orthostatic test.

Material and methods: 69 young men who are students of the North-Eastern State University (Magadan) and 43 male students of the educational institutions of Chukotka Autonomous Okrug (Anadyr) took part in the research. The subjects were examined to study the main indices of the cardiovascular system and heart rate variability at rest (lying down) and in the process of performing an active orthostatic test.

Results: The conducted studies have shown that the process of prompt adaptation happens through the reorganization of the cardiovascular system and the parameters of the heart rate, which differ in persons living in different districts of the Far Eastern region.

Discussion: It has been found that autonomic maintenance of cardiac activity in response to an active orthostatic test is carried out by reducing the activity of the parasympathetic link, which is aimed at maintaining a sympathetic prevalence of vascular tone and heart necessary to realize the reserve capabilities of the cardiovascular system. Changes in the cardiovascular system in response to the orthostatic test were provided by a hypertensive reaction of diastolic blood pressure with a normotensive reaction vs. systolic blood pressure which was more pronounced in the group of Anadyr subjects. Of note that at the moment of transition to a vertical position, a significant decrease in the HF component of the heart rate was registered, which allowed to increase the activity of the sympathetic system and was more pronounced in the group of Anadyr young men. Against the background of a decrease in the LF component of the heart rate spectrum in the Anadyr subjects, also aimed at decreasing the inhibitory parasympathetic effect on sympathetic activity followed by activation of the tone of sympathetic vasoconstrictor fibers, this resulted in an increase in vasomotor tone and was manifested by a pronounced increase in diastolic blood pressure and total peripheral vascular resistance. Such post-exercise rearrangements in hemodynamics against the background of a decrease in the stroke volume with unchanged cardiac output testify to the vascular mechanism of maintaining hemodynamic parameters in response to the active orthostatic test. In the Magadan group the reaction to AOT was not noted. At the same time insignificant decrease in stroke volume against the background of post-exercise tachycardia led to a significant increase in cardiac output, which is a reflection of the circulatory mechanism for maintaining cardiovascular homeostasis.

Conclusion: The obtained results suggest the differences in the changes of hemodynamic parameters and heart rate in response to active orthostatic test can be considered as the regional feature of the functioning of cardio hemodynamics among representatives of the two far eastern regions of the seaside climatic zone.

Keywords: young male residents of the northeast of Russia, cardiovascular system, heart rate indicators, active orthostatic test.

Introduction. Being a method of influencing the venous return of blood to the heart, active orthostatic test (AOT) allows studying compensatory hemodynamic and autonomic shifts and thus to assess the function of the circulatory system as a whole [5]. Orthostatic tension causes consistent compensatory cardiovascular reactions to maintain homeostasis while the sympathetic nervous system, the parasympathetic nervous system, and the baroreflex mechanisms play an important role in this homeostatic response [17].

With a sharp movement of the body from a lying position to a standing position, due to the action of gravitational forces and greater venous compliance, a larger volume of blood remains in the lower part of the body, which leads to a decrease in venous return and unloading of arterial baroreceptors.

As a result, the sympathetic activation of both the heart and the vascular smooth muscle cells increases, and a significant decrease in the parasympathetic activity occurs, which in turn causes compensatory changes in the Heart Rate and the level of arterial pressure [16]. In this regard, the **purpose** of this work was to study the hemodynamic and cardiorhythm rearrangements in response to an Active Orthostatic Test (AOT) demonstrated by vago-normotonia Caucasoid young men living in the coastal climatic zone in two regions of Russia's Far East, Magadan Region and Chukotka Autonomous District.

Materials and methods. The study involved 69 young men aged 17–19 (18.1 ± 0.1 yrs) with an average body mass of 68.2 ± 0.4 kg and body length of 177.8 ± 0.2 cm being students in the Northeast State University (the city of Magadan) and 43 young men aged 17–19 (18.3 ± 0.2 yrs) with an average body mass of 67.8 ± 0.5 kg and body length of 178.1 ± 0.3 cm being students of educational institutions of Chukotka Autonomous District (the city of Anadyr). Cardiointervalograms were recorded continuously for 5 minutes at rest (lying position, baseline) and 5 minutes in a standing position (orthostasis). The recording of the cardiointervalogram was performed using the Varicard unit and the VARICARD-KARDi software [8] taking into account the guidelines of the group of Russian experts [1].

The Total Power of the heart rate spectrum (TP) was calculated without taking into account the Ultra-Low Frequency component (ULF) based on the requirements of the correctness of the analysis of short time series using the Fourier transform method [4]. The following Heart Rate Variability (HRV) parameters were analyzed: mode (Mo, ms) as the most common value of the R-R interval; the difference between the maximum and minimum values of cardiointervals (MxDMn, ms); the number of pairs of cardiointervals with a difference of more than 50 ms in % of the total number of cardiointervals (pNN50, ms); standard deviation of the complete range of cardiointervals (SDNN, ms); mode amplitude with a class width of 50 ms (AMo50%, ms); Stress Index of regulatory systems (SI, standard units); Total Power of heart rate spectrum (TP, ms^2), spectrum power of the high-frequency component of Heart Rate Variability in the range of 0.4–0.15 Hz (respiratory waves) (HF, ms^2,%); spectrum power of the low-frequency component of Heart Rate Variability in the range of 0.15–0.04 Hz (LF, ms²,%); the power of the spectrum of the Very Low-Frequency component of heart rate variability in the range of 0.04–0.015 Hz (VLF, ms²,%). At the same time, the period of the first minute of "active orthostasis" was excluded from the results presented below, since it represents a pronounced transient process, the analysis of which was not part of the objectives of our study.

Blood Pressure indicators were recorded with an automatic "Nessei DS – 1862" tonometer (Japan) at rest (lying position) and at 1st minute after going to the vertical position. At each stage of the experiment, the Starr Stroke Volume (SV, mL), the Cardiac Output (CO, L/min), the Total Peripheral Vascular Resistance (TPVR, dyne² • s • cm⁻⁵) [13] were determined by calculation.

The initial type of autonomic regulation was determined at rest on the basis of the values of the following indicators: MxDMn, SI, TP, where the range of eutonia (normotonia) for MxDMn we took into account was from 200 to 300 ms, for SI - from 70 to 140 arb. units, for TP - from 1000 to 2000 ms² [9]. If the studied indices of MxDMn and TP were below these ranges, the autonomic balance was considered as sympathotonic, but with an increase in the values of this corridor it suggested to be vagotonia featured. On the contrary, as regards to the SI with an increase in its values of more than 140 arb. units (taking into account the other two indicators), the autonomic balance was referred to sympathicotonic one, and with a decrease of less than 70 const. units, it was vagotonia featured. Due to the small number of sympathotonics in the sample, the functional indicators of young male subjects of this type were not analyzed in this series of studies. The sample for statistical analysis included individuals with the vagonormotonic type of autonomic regulation.

All examinations were carried out in a room with a comfortable temperature of 19-21° C, in the morning. The study was carried out in accordance with the principles of the Helsinki Declaration. The study protocol was approved by the Ethical Committee for Biomedical Research at the NESC of the Fareastern Branch of the Russian Academy of Sciences (No. 004/013 dated December 10, 2013). Prior to inclusion in the study, all participants gave their written informed consent.

The results were statistically processed using the application package of Statistica 7.0. The check on the normal distribution of the measured variables was carried based on the Shapiro-Wilk test. The results of non-parametric processing methods are presented in the form of a median (Me) and an interquartile range of 25 and 75 percentiles. The results of parametric processing methods are presented as an average value and its error (M ± m). In the case of comparing related samples, the statistical significance of differences was determined using the t-Student criterion for dependent samples with a normal distribution as well as using the non-parametric Wilkinson test for samples with a distribution other than normal. When comparing unrelated samples, the statistical significance of differences was determined using the t-Student test for independent samples with a parametric distribution and we used the non-parametric Mann-Whitney test for samples with a distribution other than normal. The critical level of significance (p) in the work was assumed to be equal to or less than 0.05 [3].

Results and discussion. It is known that the Blood Pressure rate is one of the main indicators of the cardiovascular system functionality, and keeping it optimal is provided by a complex set of neurohumoral processes united by a network of interconnections. The evaluation of their individual contribution to the overall structure of regulatory mechanisms is very difficult [7]. Table 1 presents the main indicators of the cardiovascular system at rest and in the process of performing an active orthostatic test in young Caucasians from various districts of the Far Eastern region. As the data presented in the table indicate, the young men of the Chukotsky Autonomous District and Magadan Region have differences in the main characteristics of hemodynamics at rest which is manifested in significantly lower indices of systolic (BP_S) and diastolic (BP_D) blood pressure, as well as the TPVR in the Caucasian group of Anadyr subjects, which in general may indicate the formation of region-related features of the functioning of the cardiovascular system depending on the region of residence. In response to AOT in the young men of the two groups, there was a statistically significant increase in the BP_D and

Table 1

Indicators of the cardiovascular system in the young males of the FED in baseline and in the process of active orthostatic test (AOT), M ± m

Studied parameter	Magadan Region (MR)			Chukotsky Autonomous District (ChAD)			Significance of difference baseline MR– baseline ChAD	Significance of difference AOT MR – AOT ChAD
	Stage of Experiment		Significance of difference baseline – AOT	Stage of Experiment		Significance of difference baseline – AOT		
	Indicators at rest (lying)	AOT		Indicator at rest (lying)	AOT			
BPS, mm Hg	123.9±1.0	125.7±1.7	p=0.17	118.9±2.0	118.5±2.2	p=0.75	p<0.05	p<0.01
BPD, mm Hg	64.4±0.9	76.6±0.9	p<0.001	61.4±1.2	76.7±1.2	p<0.001	p<0.05	p=0.94
HR, bpm	65.2±1.2	84.0±2.2	p<0.001	65.8±1.8	85.4±2.3	p<0.001	p=1.00	p=0.66
SV, mL	81.0±1.1	68.5±1.1	p<0.001	81.0±1.1	64.5±1.3	p<0.001	p=0.58	p<0.05
CO, L/min	5263.4±105.7	5721.4±163.7	p=0.07	5362.9±167.3	5490.7±167.3	p=0.38	p=0.61	p=0.69
TPVR, dyne2 • s • cm-5	1420.8±36.4	1430.7±42.1	p=0.30	1311.9±41.0	1419.0±53.2	p<0.05	p<0.05	p=0.+86

Table 2

Indicators of the Heart Rate Variability at rest and with AOT in young male vagonormotonic Caucasians residing in the FED, Me (25; 75-percentile)

Studied parameter	Magadan Region (MR)			Chukotsky Autonomous District (ChAD)			Significance of difference baseline MR– baseline ChAD	Significance of difference AOT MR – AOT ChAD
	Stage of Experiment		Significance of difference baseline – AOT	Stage of Experiment		Significance of difference baseline – AOT		
	Indicators at rest (lying)	AOT		Indicator at rest (lying)	AOT			
MxDMn, ms	330.4 (263.0;400.1)	280.6 (225.7;379.4)	p<0.05	370.0 (246.3;416.3)	228.0 (178.8;274.8)	p<0.001	p=0.80	p<0.01
RMSSD, ms	54.0 (38.5;63.4)	24.7 (16.6; 39.9)	p<0.001	60.1 (937.0; 82.5)	21.4 (16.3;28.9)	p<0.001	p=0.21	p=0.14
pNN50, %	30.0 (16.3;44.6)	4.5 (1.3;15.8)	p<0.001	37.7(11.6;55.2)	3.2 (1.0;7.6)	p<0.001	p=0.23	p=0.20
SDNN, ms	59.8 (45.9;71.2)	47.3 (36.9; 64.0)	p<0.001	70.6 (47.5;83.7)	48.9 (36.5;55.7)	p<0.001	p=0.13	p=0.59
Mo, ms	922.3 (824.4; 980.7)	631.8 (580.2; 724.2)	p<0.001	916.5 (772.0;997.5)	650.0 (606.0;691.3)	p<0.001	p=0.48	p=0.75
AMo50, ms	36.0 (28.1; 42.6)	45.4 (37.3; 51.7)	p<0.001	28.7 (23.3;44.0)	47.3 (39.5;57.9)	p<0.001	p=0.20	p=0.12
SI, arb. units	58.8 (37.6; 90.4)	122.7 (66.3; 182.8)	p<0.001	40.0 (30.4;127.2)	139.7 (100.0;263.8)	p<0.001	p=0.49	p<0.05
TP, ms2	2816.2 (1810.6; 4373.7)	1832.0 (1063.0; 3560.1)	p<0.01	3697.7 (1615.0;4103.0)	1685.3 (930.8;2163.3)	p<0.001	p<0.05	p=0.17
HF, ms2	921.3 (613.6; 1519.0)	231.9 (107.7; 454.2)	p<0.001	1244.3 (510.1;2 463.3)	224.3 (115.8;304.9)	p<0.001	p<0.05	p=0.56
LF, ms2	950.0 (647.3; 1325.5)	899.5 (504.6; 1714.3)	p=0.17	1346.8 (633.8;1 677.7)	1003.8 (423.7;1361.0)	p<0.05	p<0.05	p=0.65
VLF, мс2	395.6 (249.9; 711.7)	291.6 (187.6; 686.0)	p=0.47	715.3 (355.1;1086.1)	321.1 (196.1;473.6)	p<0.001	p<0.05	p=0.81
LF/HF, arb. units	1.0 (0.6;1.6)	4.6 (2.8;7.6)	p<0.001	1.2 (0.6;1.5)	4.7 (3.2;6.4)	p<0.001	p=0.98	p=0.96
IC, arb. units	1.5 (1.0; 2.3)	6.8 (3.8;10.6)	p<0.001	1.5 (1.1;2.3)	6.6 (5.0;8.3)	p<0.001	p=0.63	p=0.99

HR against the background of a decrease in Stroke Volume (SV), and the degree of their change was more marked in the Anadyr group. It is necessary to note the different nature of the responses to the test of Cardiac Output (CO) and TPVR in representatives of the two groups: in the group of Magadan young men, a statistically significant increase in the CO circulation was observed against the background of constant TPVR, whereas in the group of Anadyr surveyed, on the contrary, in response to AOT the increase in TPVR and the maintained CO baseline values were seen.

Studies have shown the increased diastolic blood pressure BP_D in response to AOT. The mechanisms underlying orthostatic hypertension remain poorly understood. D. H. Streeten and co-workers (1985) in their work [22] in patients with orthostatic hypertension found excessive accumulation of venous blood in the lower extremities and high levels of the blood noradrenaline in the standing position. This was apparently due to the fact that pronounced venous deposition had led to a significant reduction in cardiac output, with further sympathoactivation (possibly due to cardiopulmonary receptors) and excessive constriction of arterioles, but not venules, and increased BP_D. A higher level of norepinephrine and vasopressin in the standing position in persons with orthostatic hypertension compared with orthostatically normotensive subjects were also noted in studies by K. Kario and co-authors (2009, 2013) [18, 19].

Despite the fact that the vector of the general directionality of hemodynamic shifts in response to AOT in the two groups was similar with respect to the Blood Pressure and Heart Rate, we noted different mechanisms for maintaining the BP. So the transition to a standing position leading to a decrease in venous return and as a consequence of this decrease in the SV of the blood circulation, to a lesser extent expressed in the group of Magadan young male subjects. A less significant decrease in SV in this group due to an increase in the HR led to a significant increase in the CO of the blood circulation. This was not observed in the group of Anadyr boys.

Table 2 presents the characteristics of the heart rate variability at rest and at the peak of AOT in the subjects with the vagotonia-normotonia initial type of autonomic regulation from Caucasians living in different regions of the Far Eastern District. The analysis of the received data of the frequency characteristics of the HR in response to orthostasis allowed us to establish a decrease in the activity of the parasympathetic ANS which manifests a statistically significant decrease in MxDMn, RMSSD, pNN50, SDNN, Mo, with a more pronounced decrease in the group of Anadyr young male subjects.

An analysis of the rearrangements of the HR spectral characteristics in the young men of the two groups revealed certain differences in the nature of the responses to orthostatic testing. The obtained results indicate that in response to the test in young men of the two groups, the high-frequency component of the HR decreases, but the decrease in this value was slightly more pronounced in the group of Anadyr young males. It is known that the reduction of parasympathetic activity during orthostatic exercise allows for relative sympathetic activation. This vagal “brake” is necessary so that the body can effectively respond to environmental disturbing factors. That is why vagal control of the heart manifested in the restructuring of the HRV indices can reflect not only autonomous and adaptive “flexibility”, but also indicates the body’s somatoregulatory capabilities [14].

It is indicated that after moving to a vertical position and redistributing the blood flow, afferentation from the baroreceptor zones of the main arteries decreases, their inhibitory effect on the vasomotor center of the brain stem decreases leading to an increase in sympathetic activity and a decrease in the efferent tone of the vagus nerves, while the main function of the sympathetic nervous system is maintaining the adequate blood circulation [10]. It is necessary to note the pronounced tendency of decrease in high-frequency oscillations of the Heart Rate in response to AOT, which reached 74% in the Magadan group, and 81% in the Anadyr group. In the work of A. N. Fleischman (1999, 2009) it was shown that a significant, more than 50% of the baseline values in the supine position, a decrease in the HF index in response to orthostasis indicates the compensatory nature of changes and, in turn, may indicate a violation of adaptation mechanisms. But a moderate decrease in this indicator, on average by 30% from the initial level in the supine position, is a reflection of the decrease in the tonic effect of the vagus on the heart and causes an increase in the chronotropic function of the heart [11, 12]. Apparently, such a significant decrease in parasympathetic activity during the orthostatic loading in young men can be considered, after the theory of “accented antagonism” [20], as aimed at providing a certain level of sympathetic activation the main function of which will be maintaining optimal blood circulation.

LF-frequencies of the cardiorhythm spectrum are currently considered to be an activator of arterial pressure rhythm oscillations implemented through baroreflex mechanisms [6]. In the 2nd group of young men, in contrast to the representatives of the 1st group, in response to AOT, there was a decrease in the LF component of the Heart Rate general spectrum, which is currently regarded as a manifestation of autonomic failure and may indicate a violation of sympathetic vasomotor innervation [12]. Based on the above, the nature of the resulting changes in the spectral characteristics of the Heart Rate in the Anadyr group indicates a decrease in impulses from baroreceptors (decrease in LF) at orthostasis, which in turn reduces the inhibitory vagotonic effect on sympathetic activity and activates the tone of sympathetic vasoconstrictive fibers [15], which leads to activation of vasomotor tone and is manifested by a pronounced increase in BP_D and TPVR. Apparently, baroreflex regulation activates sympathetic activity that is more pronounced in the Anadyr group as evidenced by higher values of the SI-test / SI-baseline ratio, the numerical value of which was 3.5 arb. units, against 2.1 arb. units in the group of Magadan subjects, that should be, based on the recommendations of N. A. Belokon’ and M. B. Kuberger (1987), interpreted as “hypersympathicotonic reactivity” and “normal autonomic reactivity”, respectively [2].

The dynamics of the Heart Rate spectral analysis in response to the AOT VLF components of the heart rhythm in the group of Anadyr boys, unlike the group of Magadans, was negative with a significant degree (by 55%), which may reflect the presence of energy-deficient processes at the tissue level [12].

Conclusion. Thus, the intergroup differences which we revealed in chronotropic, inotropic and vasomotor responses to orthostatic stress cause different degrees of rearrangements of hemodynamic parameters. A more pronounced afterload reduction in Stroke Volume in the group of Anadyr young men which was apparently associated with blood deposition in the peripheral veins and a decrease in venous return with an inadequate increase in heart rate due to insufficient sympathetic activation, leads to a constant load Cardiac Output as compared to the indicator at rest. Maintaining the blood pressure at an optimal level while reducing the Stroke Volume should be compensated by the baroreflex mechanisms, which in turn should lead to an increase in total peripheral resistance (as was observed in the Anadyr group), otherwise blood pressure will decrease and may lead to syncope [21]. In this case we can see the vascular mechanism for maintaining hemodynamic values in response to the orthostatic test in the subjects of this sample. In the group of Magadan Caucasians, due to the high baseline values of the Total Peripheral Vascular Resistance, there was no vasoconstrictor reaction to Active Orthostatic Test. At the same time, a not so significant decrease in Stroke Volume against the background of the exercise tachycardia led to a significant increase in Cardiac Output as the integral characteristics of the blood circulation. Based on this, we can assume the formation of a circulatory mechanism for maintaining cardiovascular homeostasis in response to AOT among representatives of this group.

In general, at the moment of transition to the vertical position, the young men examined by us recorded an excessive decrease in the cholinergic HF component of the cardiac rhythm, which allowed us to increase the activity of the sympathetic system. This was largely revealed in the group of Anadyr youths and was expressed in a more significant increase in diastolic blood pressure, which, against the background of a decrease in the LF component of the heart rhythm spectrum, leads to an increase in the tone of the sympathetic vasoconstrictive fibers [15] and is manifested by a pronounced increase in diastolic blood pressure and TPVR.

It was established that the pattern of the Heart Rate Variability rearrangement is aimed at reducing the tonic inhibitory effect of the parasympathetic link of the Autonomic Nervous System, where urgent compensatory reactions are realized by reducing MxDMn, RMSSD, pNN50, SDNN, Mo, TP, and HF, which in turn made it possible to maintain sympathetic prevalence on vascular tone and heart, as well as to use baroreceptor regulation, which is generally aimed at the realization of the reserve capabilities of the cardiovascular system.

Based on this it can be assumed that the maintenance of Blood Pressure at a significant decrease in Stroke Volume among representatives of the Anadyr Caucasians is partly compensated by baroreflex mechanisms, which in turn leads to an increase in Total Peripheral Vascular Resistance, as well as a decrease in the low-frequency component of the heart rate. The data obtained during the work enable us to conclude that the vector of rearrangements of the Heart Rate indicators in response to orthostatic load consists in the activation of sympathetic activity arising against the background of a significant decrease in parasympathetic influence with varying degrees of activation of the baroreceptor regulation of compensatory rearrangements of the cardiovascular system in representatives of the two groups. This result can be considered as a region-related feature of the rearrangements of hemodynamic parameters and heart rate in response to the orthostatic test among representatives of two Far Eastern regions of the seaside climatic zone of residence.

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