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Changes of electrocardiograms and heart morphology of animals with different resistance to hypoxia under influences of stress

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Abstract

Stress is a process that increases a person's adaptive capacity and leads to the various diseases, such as hypertension, coronary artery disease, heart attack, cardiac arrest, stroke, mental disorders such as depression and anxiety and even sudden death. Individual response to stress may depend on age, gender, features of autonomic regulation, state of the central nervous system, endocrine systems, higher nervous activity. With excessive stress, the work of internal organs is disturbed, in particular, the cardiovascular system. Determination of the damaging effect of stress on the cardiovascular system in individuals with different reactivity will contribute to the development of individual correction methods.

The aim of the study was to analyze the changes in electrocardiograms (ECG) and morphological feachers after stress in animals with different resistance to hypoxia.

Material and methods of investigation. Experiments were performed on 48 Wistar rats, with high and low resistance to hypoxia (HRH, LRH), aged 5–6 months. Animals were divided into two groups – control and experimental (after immobilization stress). Individuals with different resistance to hypoxia were selected by method of V. Ya. Berezovsky. Stress was modeled by three one-hour immobilization of rats, which were immobilized on their backs with an interval of 24 hours between each stressful episode. Investigation we did after 24 hours after third immobilization. Under anesthesia were registrated ECG and taken heart for morphological investigation. Sections were stained with hematoxylin and eosin.

Results. In examining the ECG in control HRH and LRH animals, no significant difference in the analyzed ECG indicators was established. 24 hours after the last 1 hour three-time immobilization in HRH rats were noted an increase in heart rate, a decrease of the duration of the RR interval, a decrease of the amplitude of the R wave, an increase of QTc interval, an increase of the amplitude of the T wave, an increase in the deviation of the ST segment from the isoline. In LRH rats, stress caused an increase in heart rate, a decrease in the duration of the RR interval, a decrease in the duration of the PQ interval, a decrease in the amplitude of the R wave, an increase in the amplitude of the T wave, an increase in the deviation of the ST segment from the isoline.

When comparing the parameters of HRH and LRH rats, in LRH were found a smaller amplitude of the P wave, a smaller amplitude of the R wave, a smaller value of the QTc interval, greater deviation of the ST segment from the isoline.

Physiological changes on ECG can also connected with morphological feaches.

Conclusions. Stress leads to changes in functional and histological properties of heart, which depends on resistance to hypoxia. In the ECG 24 hours after the last 1 hour three-time immobilization in HRH and LRH rats were noted an increase in heart rate, a decrease of the duration of the RR interval, a decrease of the amplitude of the R wave, an increase of the amplitude of the T wave, an increase in the deviation of the ST segment from the isoline. In HRH rats were also an increase of QTc interval, in LRH rats – a decrease in the duration of the PQ interval. Indxes changes were grater in LRH rats. Mophological changes was higher also in LRH animals.

Key words: electrocardiogram; morphology; heart; stress; resistance to hypoxia.

Introduction. Stress is a process that increases a person's adaptive capacity and leads to the psychological and biological changes [1]. The stress could be short-term acute stress and long-term chronic stress.Magnification of the duration of stress, strength action of stressors, can caused distress, which can be potential risks for diseases. Stress is a significant risk factor for various diseases, such as hypertension, coronary artery disease, heart attack, cardiac arrest, stroke, mental disorders such as depression and anxiety and even sudden death [2].

During stress, the activation of the sympatho-adrenal system with an increase of the frequency of heart contractions is noted. Therefore, the analysis of heart rate variability makes it possible to assess both the degree of stress and the degree of adaptation to it. Each of us reacts individually to the same stress. Individual response to stress may depend on age, gender, features of autonomic regulation, state of the central nervous system, endocrine systems, higher nervous activity, etc. [3]. Stress is an integral part of our life [4]. It can lead to both adaptation and its disruption, the development of various diseases [5], which is different and depends on reactivity. With excessive stress, the work of internal organs is disturbed, in particular, the cardiovascular system [6]. Hypodynamia, lack of time for work, unemployment lead to the development of distress. Determination of the damaging effect of stress on the cardiovascular system in individuals with different reactivity will contribute to the development of individual correction methods.

The aim of the study was to analyze the changes in electrocardiograms and morphological feachers after stress in animals with different resistance to hypoxia.

Material and methods of investigation. Experiments were performed on 48 Wistar rats, with high and low resistance to hypoxia (HRH, LRH), aged 5–6 months. Animals were divided into two groups – control and experimental (after immobilization stress). There were 24 male rats in each group. Individuals with different resistance to hypoxia were selected from the general cohort of animals according to the method of V. Ya. Berezovsky [7]. Stress was modeled by three one-hour immobilization of rats, which were immobilized on their backs with an interval of 24 hours between each stressful episode [8]. Investigation we did after 24 hours after third immobilization.

All experiments were conducted in the first half of the day in a specially designated room at a temperature of 18–22 °C, relative humidity of 40–60%, and illumination of 250 lux. The experiments were carried out in compliance with the norms of the European Convention on the Protection of Vertebrate Animals Used for Research and Other Scientific Purposes (Strasbourg, 1986), the resolution of the First National Congress on Bioethics (Kyiv, 2001) and the order of the Ministry of Health of Ukraine dated September 23, 2009 No 690.

In order to determine the degree of impairment of the functional state of the heart using the device "Cardiolab" (Kharkiv, Ukraine) in animals under thiopental-sodium anesthesia (40 mg/kg of animal weight), electrocardiograms were recorded with computer analysis of heart rate (HR), durations of RR interval, PQ interval, QT interval, QTc interval, amplitudes of waves P, R, and T, durations of waves P and T, deviation of the ST segment from the isoline.

The animals hearts were also subjected to a morphological study of pieces of the heart, taken under thiopental-sodium anesthesia (60 mg/kg weight) and stained with hematoxylin and eosin. Transverse sections of the heart, made at the level of both ventricles. The preparations were taken immediately after taking blood from the heart of the animal, fixed in a 10% solution of neutral formalin. No earlier than two weeks later, the preparations were washed in tap water and held in alcohol, poured into paraffin blocks. Sections were stained with hematoxylin and eosin, and examined under a light microscope [9].

The significance of the obtained differences between the results (minimum level of significance $p<0.05$) was assessed using the Kruskal–Wallis and Newman–Keuls tests (BioStat program, AnalystSoft Inc.). All results prresented in M±σ.

Results and discussion. In examining the ECG (table 1) in control high- and low-resistant to hypoxia animals, no significant difference in the analyzed ECG indicators was established. 24 hours after the last 1 hour three-time immobilization in HRH rats were noted an increase in heart rate by 5.8% ($p<0.05$), a decrease of the duration of the RR interval by 5.8% ($p<0.05$), a decrease of the amplitude of the R wave by 10.9% ($p<0.02$), an increase of QTc interval by 6.8% ($p<0.02$), an increase of the amplitude of the T wave by 27.2% ($p<0.002$), an increase in the deviation of the ST segment from the isoline by 36.4% ($p<0.001$).

Table – Stress-induced changes in electrocardiograms in animals with high and low resistance to hypoxia (M±σ)

Index	Group			
	contol		stress	
	HRH	LRH	HRH	LRH
HR, min^{-1}	455.18±10.53	469.84±9.23	481.48±9.29*	497.69±8.26*
RR, mc	130.23±3.14	128.12±3.26	123.08±2.78*	121.58±2.25*
P, mc	10.56±1.02	11.74±1.28	11.26±1.40	12.16±1.38
P, mV	0.101±0.014	0.110±0.012	0.121±0.011	0.105±0.010**
PQ, mc	38.23±2.46	42.47±2.31	36.08±2.11	36.16±2.43*
R, mV	0.621±0.031	0.591±0.033	0.560±0.028*	0.501±0.031*,**
QT, mc	76.07±3.12	74.08±3.24	72.03±3.09	71.14±2.96
QTc, mc	144.68±1.57	142.15±1.63	154.51±1.43*	143.28±1.27**
T, mc	12.42±1.03	13.07±1.12	13.05±1.13	13.91±1.12
T, mV	0.213±0.022	0.225±0.021	0.271±0.026*	0.275±0.027*
ST, mV	0.022±0.002	0.026±0.003	0.030±0.004*	0.058±0.009*,**
Notes. * – indicators are reliable compared to the control. ** – indicators are reliable compared to HRH animals.				

In LRH rats, stress caused an increase in heart rate by 5.9% ($p<0.05$), a decrease in the duration of the RR interval by 5.4% ($p<0.05$), a decrease in the duration of the PQ interval by 17.4% ($p<0.01$), a decrease in the amplitude of the R wave by 18.0% ($p<0.01$), an increase in the amplitude of the T wave by 22.2% ($p<0.002$), an increase in the deviation of the ST segment from the isoline by 2.2 times ($p<0.001$).

When comparing the parameters of HRH and LRH rats, a smaller amplitude of the P wave by 15.2% ($p<0.01$) was found in LRH, a smaller amplitude of the R wave by 11.8% ($p<0.02$) was in LRH, a smaller value of the QTc interval by 7.8 % ($p<0.05$) was in LRH, greater deviation of the ST segment from the isoline by 93.3% ($p<0.001$) was in LRH.

Similar results were obtained by other authors under stress. So, stressed group of rats showed a significant decrease in QRS amplitude and a shortening of the RR, QT, and QTc intervals with an elevation of the ST segment [10]. Analyses of ECG on human showed that QT and ST intervals are able to differentiate stressful from non-stressful events [11].

The QTc can be the main in the prognosis of rapid death. Stable prolonged QTc in patients with stress-induced cardiomyopathy leads to the increase of Short-term mortality [12].

The changes of P wave after exercise-induced is more in patient with corinry heart disease. The results of the study show that an addition of P-wave duration changes assessment to ST-depression analysis and other exercise-induced abnormalities increase sensitivity of exercise stress test, especially for left coronary artery disease and 3-vessel coronary disease. We have also provided evidence for the negative influence of the presence of arterial hypertension on the predictive value of P-wave changes in the stress test [13].

Psychological stress can lead to atrial and ventricular arrhythmias. T-wave alternans, as well as other ECG measures of heterogeneity of repolarization, increases with emotional and cognitive stress. In the atrium, stress impacts components of the signal-averaged ECG [14]. Acute coronary syndrome can show changes of ST segment, new-onset left bundle branch block, presence of Q waves, and new T-wave inversions. [15].

Physiological changes on ECG can also connected with morphological feaches. When examining the preparations of the myocardium of the HRH of a male rat that was subjected to immobilization stress (Fig. 1). Contractile cardiomyocytes kept their typical shape and location, the nuclei were located mostly on the periphery of the cell, contoured against the background of unevenly illuminated sarcoplasm. It was special that the changes were not the same in all cardiomyocytes: between the vacuolated cells there were individual cells of a darker color with a better structured sarcoplasm. In the layers of connective tissue between muscle fibers, fibroblasts with large euchromatic nuclei and small-sized fibrocytes with intensively basophilic oval-shaped nuclei were visible. Tincture heterogeneity of cardiomyocytes was observed in the myocardium. Areas were also visible in the cells of which the nucleus was not visible, or it was shifted to the periphery. Most of the fibers were swollen, destruction of cardiomyocytes was noted. Heterogeneous accumulations of formed blood elements, leukocyte infiltration were visible in the lumens of blood vessels.

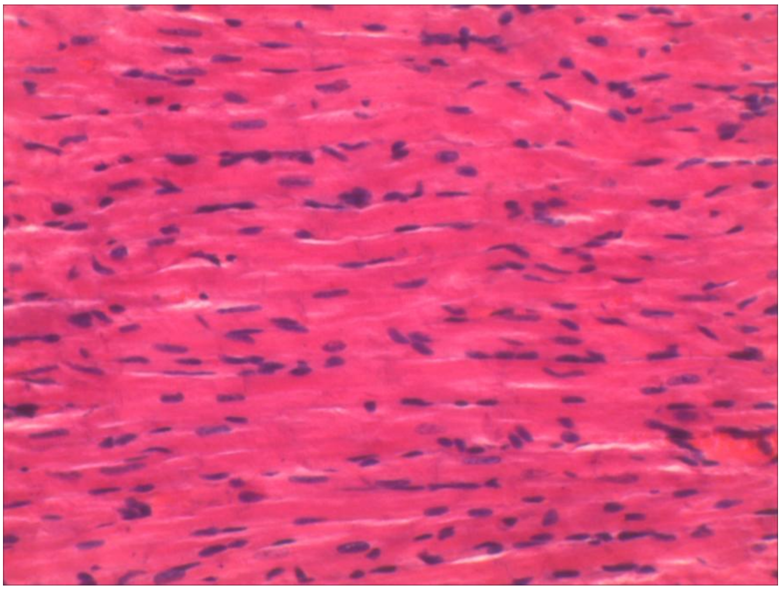

Figure 1 – A fragment of the HRH myocardium of a male rat subjected to immobilization stress. Staining with hematoxylin and eosin. Magnification x 200

In LRH males (Fig. 2), which were subjected to stress, the changes were most pronounced. A significant expansion of the elements of the hemomicrocirculatory channel and their significant blood filling was noted, which was accompanied by the exit of formed blood elements outside the vascular channel. Damage in the myocardium was characterized by small foci of altered cells that merged in places. The staining of the sarcoplasm of such cardiomyocytes was uneven. Against the background of the described changes, homogeneous areas of the myocardium with intense oxyphilic staining were also detected. Cell nuclei of such areas of the myocardium were not visualized. Defibrillation of cardiomyofibrils, stromal edema was noted. Violations of the tinctorial properties of the myocardium in NG males under stress 1 were most pronounced.

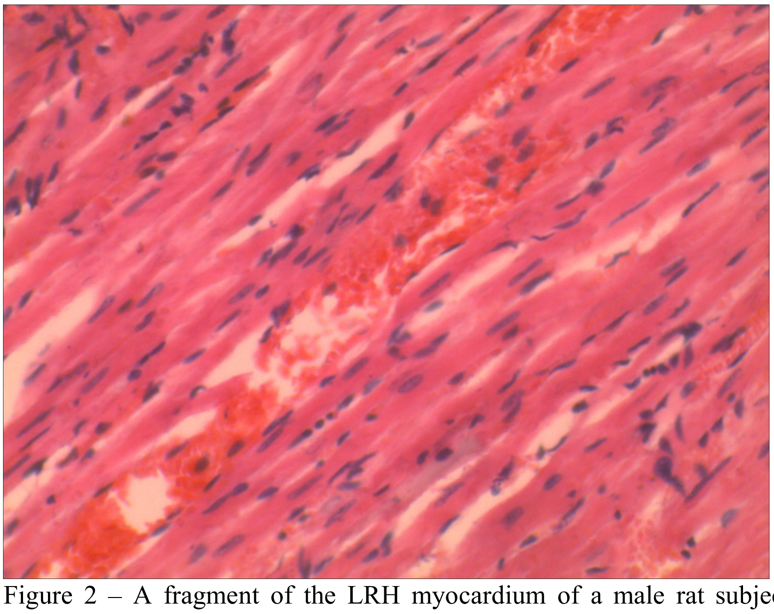

Figure 2 – A fragment of the LRH myocardium of a male rat subjected to immobilization stress. Staining with hematoxylin and eosin. Magnification x 200

Thus, significant morphological changes, in addition to functional ones, were noted. All detected changes were greater in rats with low resistance to hypoxia.

Conclusions. Stress leads to changes in functional and histological properties of heart, which depends on resistance to hypoxia. In the ECG 24 hours after the last 1 hour three-time immobilization in HRH and LRH rats were noted an increase in heart rate**,** a decrease of the duration of the RR interval, a decrease of the amplitude of the R wave, an increase of the amplitude of the T wave, an increase in the deviation of the ST segment from the isoline. In HRH rats were also an increase of QTc interval, in LRH rats – a decrease in the duration of the PQ interval. Indxes changes were grater in LRH rats. Mophological changes was higher also in LRH animals.

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