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THE EFFECT OF VARIOUS MODES OF IMMOBILIZATION STRESS ON ORGANISM LESION IN HIGH-RESISTANT AND LOW-RESISTANT TO HYPOXIC HYPOXIA FEMALE AND MALE RATS

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SUMMARY. Introduction. We are followed by everyday stress the response to which depends on gender, age, individual reactivity, the state of various body functions.

The aim of the study – to determine interrelation between the stomach lesion, cytokines system and regulation mechanisms as concerns to autonomous nervous system (ANS) in high-resistant and low-resistant to hypoxic hypoxia (HRH, LRH) rats of different gender in response to various conditions of immobilization stress.

Materials and Methods. The experiments were carried out on 144 high-resistant and low-resistant (HRH, LRH) to hypoxia female and male rats. The first group – control group, the second and the third – stress 1 and stress 2 (an hour-long immobilization each 72 or 24 hours, 4 times). Interleukin (IL) content, necrosis swelling factor alpha (FSN-alpha) were determined in blood. The amount of hemorrhages, erosions , ulcers, their rate and multiplicity were determined in mucous membrane of the stomach. Variational cardiointervalometer method was carried out for examination of variation range (VR), mode (Mo), mode amplitude(AMo), stress index(SI). Statistical processing of digital data was done by means of «Excel» and «STATISTICA» 6.0 programs.

Results. In control group of HRH-males compared to LRH concentration of IL-1 beta was less, IL-4 concentration was higher. The increase of FSN-alpha, IL-10 is marked in males under stress 1. Under stress 2 in HRH IL-1 beta, FSN-alpha, IL-10 were increased; in LRH FSN-alpha indices were increased. Higher concentration of IL-10 was marked in control group of HRH-females compared to LRH. IL-10 beta, FSN-alpha were increased in HRH under stress 1, IL-1beta, IL-4, FSN-alpha were increased in LRH under stress 1; IL-10 indices were higher in HRH. Under stress 2 FSN-alpha, IL-6 were increased in HRH, in LRH IL-10 and FSN-alpha were increased.

In cardiointervalometry study indices of AMo and Is were higher in control group of of LRH-males) were revealed in LRH-males of control group. Under stress 1 Mo was increased; indices of AMo and SI remained higher in LRH; VR remained higher in HRH. Under stress 2 Mo indices were increased in HRH, AMo and SI was decreased in LRH. Mo indices were less compared to HRH. AMo and SI were higher in control group of HRH-females. Under stress 1 in LRH Mo,VR were decreased , IS indices were increased. Indices of Mo, VR were less in LRH females compared to HRH, but AMo and SI were higher. Under stress 2 AMo indices were increased in HRH; in LRH Mo and AMo were decreased. Mo was less in LRH-females compared to HRH.

Chronic stress was accompanied by ulcers of mucous membrane of the stomach, critical distinctions of ulcerogenesis indices which depend on gender, hypoxia resistance and mode of stress were observed.

Conclusions. 1. The highest activity of anti-inflammatory cytokines of intact rats is revealed in HRL-males that persists during various modes of stress.

The highest activity of proinflammatory cytokines was marked in LRH-females under stress 1, in HRH males – under stress 2. Individual sensitivity to various modes of stress was revealed in HRH and LRH rats: sympathetic impacts by humoral canals are decreased under stress 1 in males, in LRH sympathetic regulation by humoral canals is increased but parasympathetic is decreased; the activity of sympathetic nervous system due to humoral impacts decreases in HRH males under stress 2. As for nervous impacts, they are decreased in LRH males but increased in HRH females. The activity of sympathetic nervous system by nervous canals is decreased in LRH- females and by humoral canals is increased.

Macroscopic injuries of mucous membrane of the stomach were marked in all groups of animals under chronic stress.

KEY WORDS: stress; hypoxia; stomach; autonomous regulation.

Introduction. We are followed by everyday stress [1] which usually has adaptive action but strong and long-term stress causes lesion of different organs and systems of the human body. It is well known that stress identical in force and duration influences each person differently. Reaction on stress depends on gender, age, individual body reactivity, endocrine, central and autonomous nervous systems condition [2]. Psychosocial factors, genetically-induced neurobiological peculiarities of individual, epigenetic influences are determinant factors to stress vulnerability or resistance [3]. In addition to disturbances of higher nervous system [4] disorders of internal organs especially endocrine, cardiovascular systems [5], gastrointestinal tract etc. may occur among people. Inflammatory diseases of internal organs often develop. The determination of genetic links which would have revealed the mechanisms of injured influence of various stress rates for persons with different reactivity, may contribute to the elaboration of individual methods of their correction.

The aim of the study is to determine interrelation between the stomach lesion, cytokines system and regulation mechanisms as concerns to autonomous nervous system (ANS) in high-resistant and low- resistant to hypoxic hypoxia (HRH, LRH) rats of

different gender in response to various conditions of immobilization stress.

Materials and Methods. The experiments were carried out on 144 high-resistant and low- resistant (HRH, LRH) female and male rats of Wistar line of different gender aged 5.5-6 months. Animals were divided into 3 groups: the control group and 2 pilot groups (undergone 2 types of stress). Each group comprised 12 male rats and 12 females. The separation of individuals with various hypoxia resistance from general group of animals was performed by technique of Berezovskyi V. Y. (1978) [6]. Chronic stress 1 was simulated by an hour-long immobilization of rats their back down 4 times in 72 hours interval between each stress episodes; stress 2 was simulated by an hour-long immobilization of rats their back down 4 times in 24 hours interval between each stress episodes. Predominance of tolerant and resistant adaptation strategies is typical for these conditions [7].

All experiments were carried out before noon at specialized premises, at 18-22OC, relative humidity 40–60 %, brightness 250 lux. Experiments were carried out according to European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (Strasbourg, 03.18.1986), decision of the First National Bioethics Congress (Kyiv, 2001) and the Decree of Public Health Care Ministry of Ukraine No 690 of 09.23.2009.

Euthanasia of rats was performed by total heart blood letting after previous sodium thiopental anaesthesia (60 mg/kg of animal body weight intraperitoneally). The stomach and blood were taken for further pilot research. The following interleukins (IL): IL-1beta, IL-2, IL-4, IL-6, IL-10,the factor of swelling necrosis-alpha (FSN-alpha) by means of immunoenzyme method using assay kits of "Granum" Company were determined in blood. In macroscopic examination of the stomach mucous membrane (MMS) changes of mucous membrane, the amount of hemorrhages, erosions and ulcers in each animal's stomach were determined. The rate (percent of animals available) and multiplicity of hemorrhages, erosions, ulcers (quantity per one animal) were estimated [8, 9].

Variational cardiointervalometer method was used for examination of cardiac rhythm variability [10]. The device "Cardiolab"(Kharkiv, Ukraine) was used for registration. 1000 cardiointervals consistently arranged R-R were recorded. By means of computer program the following indices were estimated: variation range of cardiointervals (VR, c); modes (Mo, c); amplitude modes (AMo, %); stress index (SI).

Statistical processing of digital data was done by means of «Excel» ("Microsoft", USA) and "STATISTICA"6.0. ("Statsoft", USA). Reliability of values difference between independent quantities was determined at normal distribution according to Student criterion (statistic), in other cases by means of non-parametric methods.

Results and Discussion. Lower concentration of IL-1beta in 2.05 times ($p<0.001$) and larger concentration of IL-4 for 24.73 % ($p<0.001$) were revealed in control group of HRH males in comparison with LRH (table 1).

Under stress 1in comparison with control in HRH considerable decrease of IL-1 beta indices (for 22.8 %, $p<0.02$) and IL-4 (for 31.9 %, $p<0.001$), increase of FSN-alpha (in 2.9 times, $p<0.002$), IL-10 (for 25.6 %, $p< 0.02$) were marked. In LRN notable decrease of IL-1 beta (for 39.5 %, $p<0.001$), IL-6 (for 44.5 %, $p<0.001$), IL-4 (for 25.9 %, $p<0.001$), the increase of FSN-alpha (in 5.2 times, $p<0.001$), IL-10 (for 46.9 %, $p<0.001$) were observed. Concentrations of IL-1 beta in HRH were smaller (in 1.6 times, $p<0.001$), IL-10 (for 37.6 %, p.0.001), but IL-6 were larger (for 50.2 %, p.0.001), IL-4 (for 18 %, $p<0.001$).

Under stress 2 compared with control group in HRH considerable increase of IL-1 beta indices (in 2.3 times, $p<0.001$), FSN-alpha (in 8.2 times, $p<0.001$), IL-10 (for 40.2 %, $p<0.001$) were marked, IL-4 indices were decreased (by 22.7 %, $p<0.001$); in LRH notable decrease of IL-1 beta (by 54.7 %, $p<0.001$), IL-4 (by 20.4 %, $p<0.01$) and the increase of FSN-alpha(in 5.9 times, $p<0.001$) were observed, while IL-1 beta indices were higher(by 60.4 %, $p<0.001$), IL-6 (by 34 %, $p<0.001$) and IL-4 (by 22.5 %, $p<0.01$) in HRH.

Under stress 1 compared with stress 2 in HRH indices of IL-6 were higher by 33.8 % ($p<0.01$), IL-1 beta indices were 3 times less ($p<0.001$), FSN-alpha in 2.8 times less ($p<0.001$), IL-4 were smaller by 13.7 % ($p<0.001$); in LRH indices of IL-10 were higher by 27.1 % ($p<0.001$).

Concentration of IL-10 is higher by 37.36 % ($p<0.001$) in HRH females of control group compared with LRH.

Considerable increase of IL-1 beta (by 25.9 %, $p<0.05$), FSN-alpha(in 3.2 times higher, $p<0.01$), but decrease of IL-2 (by 38.1 %, $p<0.01$), IL-6 (by 62.7 %, $p<0.001$) were marked under stress 1 in HRH compared with control group; considerable increase of IL-1beta (by 26.9 %, $p<0.05$), IL-4 (by 10.8 %, $p<0.001$), FSN-alpha(in 5,7 times higher, $p<0.001$) were observed in LRH; while IL-2 indices were less (by 96.7 %, $p<0.001$), IL-6 (by 91.8 %, $p<0.001$), IL-4 (by 18.5 %, $p<0.001$) and IL-10 were higher(by 38.1 %, $p<0.001$) in HRH.

Under stress 2 compared to control in HRH considerable increase of FSN-alpha (3.4 times higher, $p<0.01$) and decrease of IL-1beta (by 30 %, $p<0.001$), IL-6 (by 59.7 %, $p<0.01$) were marked; considerable increase of IL-10 (by 37.7 %, $p<0.001$), FSN-alpha (7.3 times higher, $p<0.001$) were observed in LRH while IL-2 were

Table 1. Variations of interleukin indices in blood of HRH and LRH animals of different gender, caused by various modes of stress, M±m (n=12)

Group	Index					
	IL-1beta, pg/ml	IL-2, x10^{-3}, pg/ml	IL-6, pg/ml	FSN-alpha, pg/ml	IL-4, pg/ml	IL-10, pg/ml
Males						
HRH						
Control	40.45±3.83	6.92±1.11	3.33±0.57	0.063±0.002	1.74±0.08	7.79±0.67
Stress 1	31.25±0.62*	7.75±0.82	3.73±0.46	0.181±0.037*	1.18±0.01*	9.79±0.49*
Stress 2	95.11±2.77$^{*,\&}$	6.00±0.61	2.47±0.08$^{\&}$	0.517±0.088$^{*,\&}$	1.35±0.03$^{*,\&}$	10,92±0,85*
LRH						
Control	83.26±5.23**	8.25±1.42	3.35±0.39	0.068±0.002	1.31±0.03**	9.17±0.61
Stress 1	50,34±3.71*,**	6.67±0.80	1.86±0.10*,**	0.350±0.085*	0.97±0.03*,**	13.47±0.43*,**
Stress 2	37.69±5.38*,**	5.00±0.88	1.63±0.11*,**	0.396±0.056*,	1.04±0.100*,**	9.82±0.62$^{\&}$
Females						
HRH						
Control	55.79±5.04$^{\#}$	8.08±0.84	1.67±0.24$^{\#}$	0.056±0.001$^{\#}$	1.15±007$^{\#}$	15.04±1.00$^{\#}$
Stress 1	70.25±3.91$^{*,\#}$	5.00±0.68$^{*,\#}$	0.62±0.07$^{*,\#}$	0.183±0.047*	1.13±0.03	16.66±1.45$^{\#}$
Stress 2	39.07±3.10$^{*,\&,\#}$	7.17±0.50$^{\&}$	0.67±0.05$^{*,\#}$	0.189±0.048$^{*,\#}$	1.14±006$^{\#}$	15.61±1.35$^{\#}$
LRH						
Control	47.48±2.28$^{\#}$	9.50±0.73	1.53±0.11$^{\#}$	0.056±0.003$^{\#}$	1.21±0.06	9.42±0.86**
Stress 1	60.24±3.85*	9.83±1.20$^{**,\#}$	1.19±0.15$^{**,\#}$	0.324±0.084*	1.34±0.03$^{*,**,\#}$	10.31±0.48$^{**,\#}$
Stress 2	42.38±4.74$^{\&}$	11.08±0.72$^{**,\#}$	1.23±0.19**	0.411±0.093*,**	1.07±0.06$^{\&}$	12.97±0.50$^{*,\&,\#}$

Footnotes: 1. * – indices are reliable in comparison with control;
2. ** –indices are reliable in comparison with HRH;
3. # – indices are reliable in comparison with males of relevant group;
4. & – indices are reliable in comparison with stress 1group.

less (by 54.6 %, p<0.001), IL-6 (by 83.4 %, p<0.001), FSN-alpha (2.2 times less, p<0.05) in HRH.

Under stress 1 compared to stress 2 in HRH, indices of IL-1 beta were higher by 44.4 % (p<0.001), IL-2 indices were less by 43.3 % (p<0.01); in LRH indices of IL-1 beta were higher by 29.6 % (p<0.001), IL-4 by 20.3 % (p<0.001), indices of IL-10 were less by 25.8 % (p<0.001).

In HRH males of control group compared to females, IL-1 beta were less (by 37.9 %, p<0.02) and IL-10 (by 93.1 %, p<0.001; indices of IL-4 were higher (by 33.9 %, p<0.001), IL-6(by 49.9 %, p<0.01), FSN-alpha (by 16.4 %, p<0.002).

Under stress 1 in HRH males compared to females IL-1 beta were less (2.2 times, p<0.001) and IL-10 (by 70.3 %, p<0.001); IL-2 indices were higher (by 35.5 %, p<0.01), IL-6 (higher by 83.3 %, p>0.001). Under stress 1 in LRH males compared to females indices of IL-10 were higher (by 23.4 %, p<0.001), IL-6 (higher by 35.9 %, p<0.001); indices of IL-2 were less (by 47.5 %, p<0.05), IL-4 (less 38.1 %, p<0.001).

Under stress 2 in HRH males compared to females, indices of IL-10 were less (by 42.9 %, p<0.02), IL-1 beta were higher (by 58.9 %, p<0.001), IL-4 (higher by 15.4 %, p<0.02), IL-6 (higher by 72.8 %, p<0.001), FSN-alpha (higher by 63.4 %, p<0.002). Under stress 2 in LRH males compared to females indices of IL-10 were less (by 32.1 %, p<0.001), IL-2 (2.2 times less, p<0.001).

Therefore, the greatest activity of anti-inflammatory cytokines is revealed in HRH-females of intact rats that also persists under various stress conditions (regimes).The greatest activation of (anti-) proinflammatory cytokines was in LRH-females under stress 1 and in HRH-males under stress 2.

In cardiointervalography study of indices, higher indices of AMo (by 70.1 %, p<0.001) and SI (2.5 times higher, p<0.001) were revealed in LRH-males of control group. Under stress 1 Mo was increased both in HRH and LRH (respectively by 7.9 %, p<0.05 and 8.7 %, p<0.01); values of AMo and SI remained higher in LRH (respectively by 44.2 %, p<0.001 and 84.4 %, p<0.001), but VR were higher in HRH (by 25.3 %, p<0.02). Under stress 2 in HRH compared to control group Mo increased precisely (by 20.6 %, p<0.02); in LRH AMo decreased (by 31.7 %, p<0.001), SI also decreased (by 38.9 %, p<0.02), Mo was less (by 15.9 %, p<0.05) compared to HRL; compared to stress 1 in LRH indices of Mo were less (by 7.3 %, p<0.005), AMo (less by 28.8 %, p<0.001), SI (less by 28.0 %, p<0.05).

In LRH females of control group indices increase of AMo (by 39 %, p<0.05) and SI (by 65 %, p<0.05) were also revealed. Indices changes under stress 1 were marked only in LRH: Mo was decreased (by 16 %,

p>0.05), VR was less (by 24.5 %, p<0.05), Si was decreased (by 54.4 %, p<0.05).In LRH females compared to HRH indices of Mo were less(by 10.6 %, p<0.05), VR were less (by 58.6 %, p<0.05), but AMo, IS were higher (by 99 %, p<0.05, 4.3 times higher, p<0.05). The following changes of cardiointervalography indices were observed under stress 2: in HRH AMo was increased (by 17.1 %, p<0.05); in LRH Mo was decreased (by 9.5 %, p<0.05), AMo was less (by 24.5 %, p<0.05).In LRH females compared to HRH Mo indices were less (by 8.4 %, p<0.05). Under stress 1 compared to stress 2 in HRH, indices of AMo were less (by 54.3 %, p<0.05) and SI (2.2 times less, p<0.05), but higher indices were of VR (by 44 %, p<0.05); as for LRH indices were lower of Mo (by 7.7 %, p<0.05), VR (by 37.5 %, p<0.05), higher were AMo (by 30.6 %, p<0.05) and SI (by 41.1 %, p<0.05).

Table 2. Variations of cardiointervalography indices, caused by stress in HRH and LRH animals' heart of different gender (M±m)

Group	Index			
	Mode, seconds	Amplitude mode, %	Variation range, $x10^{-2}$, second	Stress index, $x10^3$, SU.
Males				
HRH(n=12)				
Control (n=12)	0.128±0.002	28.32±1.75	0.69±0.07	18.20±2.70
Stress 1 (n=12)	0.138±0.004*	32.03±1.45	0.60±0.05	20.89±2.76
Stress 2 (n=9)	0.154±0.011*	33.13±4.48	0.78±0.11	22.47±5.93
LRH(n=12)				
Control (n=12)	0.129±0.002	48.17±2.27**	0.80±0.03	45.36±5.47**
Stress 1 (n=12)	0.140±0.003*	46.20±1.73**	0.47±0.04**	38.52±3.59**
Stress 2 (n=9)	0.130±0.002$^{**,\&}$	32.91±2.77$^{*,\&}$	0.60±0.10	27.72±4.44$^{*,\&}$
Females				
HRH(n=12)				
Control (n=11)	0.144±0.003$^{\#}$	32.57±1.37	0.57±0.03	20.72±2.05
Stress 1 (n=12)	0.138±0.004	24.72±2.98$^{\#}$	0.97±0.12$^{\#}$	12.19±2.48$^{\#}$
Stress 2 (n=12)	0.145±0.001	38.15±1.79$^{*,\&}$	0.54±0.04$^{\&}$	26.89±3.44$^{\&}$
LRH(n=12)				
Control (n=10)	0.147±0.003$^{\#}$	45.27±2.80**	0.53±0.06	34.19±5.33**
Stress 1 (n=12)	0.123±0.003$^{*,**,\#}$	49.20±1.96**	0.40±0.02*,**	52.79±4.43$^{*,**,\#}$
Stress 2 (n=12)	0.133±0.003$^{*,**,\&}$	34.16±3.53$^{*,\&}$	0.55±0.07$^{\&}$	31.12±6.12$^{\&}$

Footnotes: 1. * – indices are reliable in comparison with control;
2. ** –indices are reliable in comparison with HRH;
3. # – indices are reliable in comparison with males of relevant group;
4. & – indices are reliable in comparison with stress 1group.

In indices comparison of HRH males and females lower indices of Mo (by 12.3 %, p<0.05) were revealed in males of control group, but under stress 1AMo indices were higher (by 22.8 %, p<0.05), SI were higher (by 41.6 %, p<0.05); indices of VR were lower (by 54.7 %, p<0.05). There were no reliable changes under stress 2. In LRH males of control group compared to females indices of Mo were also less (by 13.9 %, p<0.05), but under stress 1 AMo index was higher (by 6.5 %, p<0.05) and SI was lower (by 37 %, p<0.05). There were no reliable changes under stress 2.

Chronic stress was accompanied by ulcers of mucous membrane of the stomach (table 3). Critical distinctions of ulcerogenesis indices were observed. These indices depend on gender, hypoxia resistance and mode of stress.

The most significant changes of mucous membrane of the stomach were observed in LRH females: thinning and folding of mucous membrane (in rats these are signs of gastritis), hemorrhages, ulcers. Received data are matched with the increase of adrenalin discharge by adrenal glands. Therefore activity progress of sympathetic part of ANS in LRH females contributes to the hardest lesion of the stomach.

Conclusions. 1. The highest activity of anti-inflammatory cytokines of intact rats is revealed in HRL-males that persists during various modes of stress.

The highest activity of anti-inflammatory cytokines was marked in LRH-females under stress 1, in HRH males – under stress 2.

2. Individual sensitivity to various modes of stress was revealed in HRH and LRH rats: sympathetic impacts by humoral canals are decreased under stress 1 in males, in LRH sympathetic regulation by humoral canals is increased but parasympathetic is decreased; the activity of sympathetic nervous system due to humoral impacts decreases in HRH males under stress 2. As for nervous impacts, they are de-

Table 3. Macroscopic changes of mucous membrane of the stomach caused by stress in high-resistant and low- resistant to hypoxia (HRH, LRH) animals of different genders

Group	Males		Females	
	HRH(n=12)	LRH(n=12)	HRH(n=12)	LRH(n=12)
Control				
Changes	No pathologic changes			
Stress 1				
Thinning of stomach wall, (%)	-	-	-	75
The number of animals with folding of mucous membrane	9	6	6	9
Rate of hemorrhage, %	50	50	50	75
Rate of erosion, %	25	25	-	-
Rate of ulcers, %	25	30	30	25
Multiplicity of hemorrhage	4.5	3.75	2.25	5.25
Multiplicity of erosion	0.75	1.00	-	-
Multiplicity of ulcers	0.25	0.75	0.75	1.50
Stress 2				
Thinning of stomach wall, %	-	-	-	25
The number of animals with folding of mucous membrane	4	2	-	-
Rate of hemorrhage, %	50	50	25	75
Rate of erosion, %	8.3	-	8.3	-
Rate of ulcers, %	8.3	16.6	16.6	8.3
Multiplicity of hemorrhage	1.5	2.25	1.5	15
Multiplicity of erosion	0.25	-	0.25	-
Multiplicity of ulcers	0.25	0.5	0.25	5
The number of animals with pallor mucous membrane	2	7	9	6

creased in LRH males but increased in HRH females. The activity of sympathetic nervous system by nervous canals is decreased in LRH and by humoral canals is increased.

3. Macroscopic injuries of mucous membrane of the stomach were marked in all groups of animals under chronic stress. LRH females are the most vulnerable due to activation of proinflammatory cytokines and sympathetic nervous system by humoral canals.

Prospective Study. Microscopic analysis of mucous membrane of the stomach and rats' myocardium, depending on various stress conditions will be carried out.

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ВПЛИВ РІЗНИХ РЕЖИМІВ ІММОБІЛІЗАЦІЙНОГО СТРЕСУ НА ПОШКОДЖЕННЯ ОРГАНІЗМУ ВИСОКО- ТА НИЗЬКОСТІЙКИХ ДО ГІПОКСИЧНОЇ ГІПОКСІЇ САМЦІВ І САМИЦЬ ЩУРІВ

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РЕЗЮМЕ. Вступ. Постійно нас супроводжують стреси, реакція на які залежить від статі, віку, індивідуальної реактивності, стану різних систем організму.

Мета – визначити взаємозв'язок між ураженням шлунка, системою цитокінів і механізмами регуляції з боку автономної нервової системи у високо- і низькостійких до гіпоксичної гіпоксії (ВГ і НГ) щурів різної статі у відповідь на різні режими іммобілізаційного стресу.

Матеріал і методи. Досліди проведено на 144 високо- і низькостійких до гіпоксії (ВГ і НГ) самцях і самицях щурів. Перша група – контроль, друга і третя – стрес 1 і стрес 2 (одногодинна іммобілізація кожні 72 або 24 години 4 рази). У крові визначали вміст інтерлейкінів (ІЛ), фактора некрозу пухлин-альфа (ФНП-альфа). У слизовій оболонці шлунка рахували кількість крововиливів, ерозій і виразок, їх частоту та множинність. Проводили варіаційну кардіоінтервалометрію, визначали варіаційний розмах (ВР), моду (Мо), амплітуду моди (АМо), індекс напруження (ІН). Статистичну обробку цифрових даних виконано за допомогою програм «Excel» та «STATISTICA» 6.0.

Результати. У контрольних ВГ-самців, порівняно з НГ, була меншою концентрація ІЛ-1бета, більшою – ІЛ-4. При стресі 1 у самців відмічено зростання ФНП-альфа, ІЛ-10. При стресі 2 у ВГ зросли ІЛ-1бета, ФНП-альфа, ІЛ-10, у НГ – збільшився ФНП-альфа. У контрольних ВГ-самиць, порівняно з НГ, була вища концентрація ІЛ-10. При стресі 1 у ВГ зросли ІЛ-1бета, ФНП-альфа, у НГ – ІЛ-1бета, ІЛ-4, ФНП-альфа; у ВГ були більшими ІЛ-10. При стресі 2 у ВГ збільшилися ФНП-альфа, ІЛ-6, у НГ – ІЛ-10, ФНП-альфа.

При кардіоінтервалометрії були більші показники АМо та ІН у контрольних НГ-самців. При стресі 1 зросла Мо; значення АМо та ІН залишалися вищими у НГ, а ВР – у ВГ. При стресі 2 у ВГ збільшилася Мо; у НГ зменшилися АМо та ІН, а порівняно з ВГ була меншою Мо. У контрольних НГ-самиць були більші АМо та ІН. При стресі 1 у НГ зменшилися Мо, ВР, та зріс ІН. Порівняно з ВГ у НГ самиць показники Мо, ВР були меншими, а АМо, ІН – більшими. При стресі 2 у ВГ зросла АМо; у НГ зменшилися Мо, АМо. Порівняно з ВГ, у НГ-самиць Мо була меншою.

Хронічний стрес супроводжувався розвитком виразок слизової оболонки шлунка, спостерігалися суттєві відмінності показників ульцерогенезу, які залежать від статі, стійкості до гіпоксії та режиму стресу.

Висновки. В інтактних щурів найбільша активність протизапальних цитокінів відмічена у ВГ-самиць, що зберігається і при різних режимах стресу. Найбільша активація прозапальних цитокінів при стресі 1 відбулася у НГ-самиць, при стресі 2 – у ВГ-самців. Виявлено індивідуальну чутливість ВГ і НГ щурів до різних режимів стресу: при стресі 1 у самців зменшуються симпатичні впливи гуморальними каналами, у НГ-самиць – зростає симпатична регуляція гуморальними каналами, зменшується парасимпатична; при стресі 2 у ВГ-самців зменшується активність симпатичної нервової системи за рахунок гуморальних впливів, у НГ-самців – нервових, у ВГ-самиць вплив останніх збільшується, у НГ-самиць – зменшується активність симпатичної нервової системи нервовими і зростає гуморальними шляхами. У всіх групах тварин, які зазнали хронічного стресу, відмічено макроскопічні пошкодження слизової оболонки шлунка, але найбільш уразливими є НГ самиці.

КЛЮЧОВІ СЛОВА: стрес; гіпоксія; шлунок; автономна регуляція.

ВЛИЯНИЕ РАЗЛИЧНЫХ РЕЖИМОВ ИММОБИЛИЗАЦИОННОГО СТРЕССА НА ПОВРЕЖДЕНИЕ ОРГАНИЗМА ВЫСОКО- И НИЗКОСТОЙКИХ К ГИПОКСИЧЕСКОЙ ГИПОКСИИ САМЦОВ И САМОК КРЫС

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РЕЗЮМЕ. Введение. Постоянно нас сопровождают стрессы, реакция на которые зависит от пола, возраста, индивидуальной реактивности, состояния различных систем организма.

Цель – определить взаимосвязь между поражением желудка, системой цитокинов и механизмами регуляции со стороны вегетативной нервной системы у высоко- и низкоустойчивых к гипоксической гипоксии (ВГ и НГ) крыс разного пола в ответ на различные режимы иммобилизационного стресса.

Материал и методы. Опыты проведены на 144 высоко- и низкоустойчивых к гипоксии (ВГ и НГ) самцах и самках крыс. Первая группа – контроль, вторая и третья – стресс 1 и стресс 2 (одночасовая иммобилизация каждые 72 или 24 часа 4 раза). В крови определяли содержание интерлейкинов (ИЛ), фактора некроза опухолей-альфа (ФНО-альфа). В слизистой оболочке желудка считали количество кровоизлияний, эрозий и язв, их частоту и множественность. Проводили вариационную кардиоинтервалометрию, определяли вариационный размах (ВР), моду (Мо), амплитуду моды (АМо), индекс напряжения (ИН). Статистическую обработку цифровых данных выполняли с помощью программ «Excel» и «STATISTICA» 6.0.

Результаты. У контрольных ВГ-самцов, в сравнении с НГ, была меньше концентрация ИЛ-1бета, больше – ИЛ-4. При стрессе 1 у самцов отмечен рост ФНО-альфа, ИЛ-10. При стрессе 2 в ВГ выросли ИЛ-1бета, ФНО-альфа, ИЛ-10, у НГ – увеличился ФНО-альфа. У контрольных ВГ-самок, по сравнению с НГ, была выше концентрация ИЛ-10. При стрессе 1 у ВГ выросли ИЛ-1бета, ФНО-альфа, у НГ – ИЛ-1бета, ИЛ-4, ФНО-альфа; у ВГ были большими ИЛ-10. При стрессе 2 у ВГ увеличились ФНО-альфа, ИЛ-6, у НГ – ИЛ-10, ФНО-альфа.

При кардиоинтервалометрии были большие показатели АМо и ИН у контрольных НГ-самцов. При стрессе 1 выросла Мо; значение АМо и ИН оставались высокими в НГ, а ВР – у ВГ. При стрессе 2 у ОГ увеличилась Мо; у НГ уменьшились АМо и ИН, а по сравнению с ВГ была меньше Мо. У контрольных НГ-самок были больше АМо и ИН. При стрессе 1 у НГ уменьшились Мо, ВР, и вырос ДР. По сравнению с ВГ, у НГ самок показатели Мо, ВР были меньше, а АМо, ИН - больше. При стрессе 2 у ВГ выросла АМо; у НГ уменьшились Мо, АМо. По сравнению с ВГ, у НГ-самок Мо была меньше.

Хронический стресс сопровождался развитием язв слизистой оболочки желудка, наблюдались существенные различия показателей ульцерогенеза, которые зависят от пола, устойчивости к гипоксии и режима стресса.

Выводы. У интактных крыс наибольшая активность противовоспалительных цитокинов, отмеченная у ВГ-самок, сохраняется и при различных режимах стресса. Наибольшая активация провоспалительных цитокинов при стрессе 1 состоялась у НГ-самок, при стрессе 2 у ВГ-самцов. Выявлено индивидуальную чувствительность ВГ и НГ крыс к различным режимам стресса: при стрессе 1 у самцов уменьшаются симпатические влияния гуморальными каналами, у НГ-самок – растет симпатичная регуляция гуморальными каналами, уменьшается парасимпатическая; при стрессе 2 у ВГ-самцов уменьшается активность симпатической нервной системы за счет гуморальных воздействий, у НГ-самцов – нервных, у ВГ-самок влияние последних увеличивается, у НГ-самок – уменьшается активность симпатической нервной системы нервными и растет – гуморальными путями. Во всех группах животных, подвергшихся хроническому стрессу, отмечено макроскопические повреждения слизистой оболочки желудка, но наиболее уязвимыми являются НГ самки.

КЛЮЧЕВЫЕ СЛОВА: стресс; гипоксия; желудок; автономная регуляція.

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