

Research Article

The Relationship of Autonomic Tone and Sympathoadrenal System in The Growing Organism

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ABSTRACT:

The autonomic nervous system in children undergoes significant structural and functional changes, followed by tension of the compensatory mechanisms of the cardiovascular system caused by their adaptation to physical and mental stress. Studying the functional state of the sympathetic-adrenal system with taking into account the features of vegetative regulation of heart rate allows us to register early functional changes in the state of neurohumoral regulation of autonomic functions. Objective of the research was to determine the characteristics of the functional state of the sympathetic-adrenal system in primary school children with different initial autonomic tone. We selected boys and girls aged 7, 8 and 9 years, each group of 60 persons. To assess the initial autonomic tone, we used the method of variation pulsometry, the state of the sympathetic-adrenal system was determined by the content of epinephrine, norepinephrine, dopamine and DOPA in batch urine based on the fluorimetric method. To assess the significance of differences, standard Student t-test values were calculated.

Based on histogram data we have found that the vast majority of primary school children have sympathicotonic \variant of the initial autonomic tone, characterized by a decrease in the mode, variation range, an increase in the mode and the tension index. Kids with a predominance of sympathetic influences show significantly higher levels of excretion of norepinephrine, increase in the norepinephrine / epinephrine ratio and a persistent reduction in dopamine, which indicates the tension in the system of catecholamine's biosynthesis and decrease in their reserves, as well as allows us to consider such features to be authentic humeral criteria for assessing autonomic tone in children aged 7-9 years.

Keywords: autonomic tone, catecholamine's, boys and girls aged 7-9 years.

INTRODUCTION

The initial autonomic tone (IAT) is one of the integral parameters of the autonomic nervous system, characterized by the relative permanence of the autonomic functions [1]. In childhood, the autonomic nervous system (ANS) undergoes significant structural and functional changes [2], in 7-10 years, children have a dramatic increase in the density of cholinergic and adrenergic plexus, increased vagal tone of heart [3], however, the sympathetic influence on heart prevail, and there is a tension of the

compensatory mechanisms of the cardiovascular system caused by their adaptation to physical and mental stress [4, 5]. There is also observed a so-called vegetative lability, which is manifested in the predominance of sympathetic tone and parasympathetic ANS [6], able to transform into some form of vegetative disorders under the influence of adverse conditions [7]. Undoubtedly, it is important in disease prevention to early detect functional changes and the borderline states of the child's

body. The sympathetic-adrenal system (SAS), being a part of the ANS, plays a crucial role in the maintenance of the neuro-autonomic balance [8] and the regulation of adaptive reactions of the growing organism. At the same time, ANS imbalance may be associated with both SAS hyperactivity, and with the increased sensitivity to catecholamine's (CA) α and β -adrenergic receptors of the heart and blood vessels [9]. Identification of biologically active substances - the sympathetic-parasympathetic metabolites in the human blood and secretions gives an idea about the tone and reactivity of ANS [10], allows estimating the neural and humeral interrelations in the mechanism of regulation of physiological functions, disturbance of which is a preliminary to abnormal reaction of the body [7]. Studying the functional state of the sympathetic-adrenal system with taking into account the features of vegetative regulation of heart rate in healthy children, in our opinion, will allow us to register early functional changes in the state of neurohumoral regulation of autonomic functions. Subject to the above, an objective was set to determine the characteristics of the functional state of the sympathetic-adrenal system in primary school children with different initial autonomic tone.

METHODS

The study involved boys and girls aged 7, 8 and 9 years of I and II health groups, studying at the secondary school of Kazan. Total 60 persons were selected from each gender group, which were staying under observation for three years. Investigation of the features of autonomic regulation of heart rate was performed by the method of variation pulsometry [1], using an automated cardio-pulmonary complex REACARD (Russia). Cardiac rhythm was recorded for 3 minutes in the supine position, the mode (Mo) values, mode amplitude (MoA), variation range (Δx) and the tension index ($TI = MoA/2Mo \times \Delta x$) were analyzed. IAT was assessed on the basis of TI values subject to its age grading: sympathotonics were the children with TI over 95.0 c.u. normotonics - with TI in the range of 46.0 to 68.0 c.u., and vagotonics - with TI less than 46.0 c.u. SAS state was

determined based on epinephrine (E), norepinephrine (NE), dopamine (DA), and DOPA content in batch urine by fluorimetric method [11], using BIAN-130 (M-800) and KA standards (Sigma). The collected urine was acidified with sulfuric acid and kept in a refrigerator, and was adjusted with ammonia before the tests to pH 8.2 in the presence of EDTA. In addition, we determined the NE/E ratio, which increase indicates growing activity of a mediator component of SAS, and decrease - of hormonal component. Urine was collected in children with various IAT at relative rest, in the morning hours, at the beginning of the school year (October). Statistical processing of the data was carried out by conventional methods of variation statistics with the use of program package Microsoft Exel Windows 2007. To assess the significance of differences, standard Student t-test values were calculated.

RESULTS

It has been shown that the vast majority of the surveyed 7-year-old pupils have a shift in the autonomic balance towards the predominance of sympathetic influences on cardiac rhythm with the inclusion hypersympathicotonic states ($TI > 120$ c.u.) - these are 67.00% of boys and 62.50% of girls (Fig. 1). Eutonic state, i.e. the optimum ratio of sympathetic and parasympathetic influences occurs only in 16.50% and 12.50% of cases of both gender groups, respectively. During the age period from 7 to 8 years, the number of children with different IAT variants varies, but the prevailing group, as well as in 7-year-olds are pupils with severe sympathetic influence on heart rate, counting for 56.50% of boys and 49.90% of girls. Meanwhile, the number of vagotonics increase by 9.6% and 13.8% in both gender groups, respectively. At the age of 9 years, there is an increase in the number of normotonic boys due to reduction in the number of boys with sympathetic- an vagotonic variants of IAT, however, the group of sympathotonics remains predominant (47.70%). 9-year-old girls stand out against other age groups with the greatest number of pupils with eutonic state - 39.90%. According to the literature, an autonomic instability in

primary school children may be associated with a variety of causes and initiating factors such as age heterophony of functional maturation of ANS divisions [12], influence of stress factors

of educational activity [4,10], and the constitutional-genetic imbalance of regulating mechanisms of the autonomic functions [13].

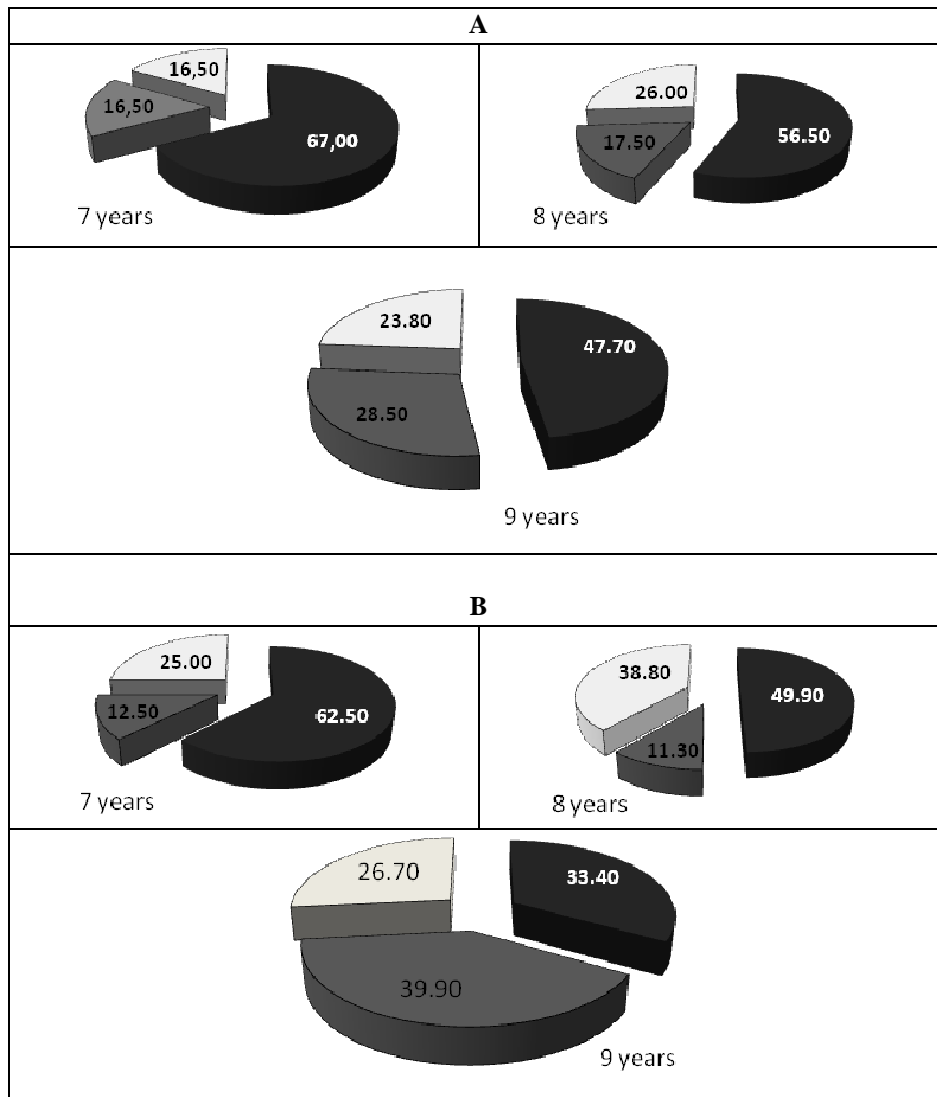


Fig. (1). The ratio of the different variants of the initial autonomic tone in boys (A) and girls (B) of 7-9 years old (%)

Sympathicotonia - , Normotonia - , Vagotonia - ,

It was found that the children with sympathotonic state are characterized by relatively low values of Mo and Δx (Table 1), equal to 636.00 ± 11.24 and 182.12 ± 3.09 ms in 7-year-old boys as compared with vagotonics, who have the same values by 52.00 ms ($p < 0.01$) and 124.24 ms ($p < 0.01$) higher than in the state of sympathicotonia. At the same time, children with sympathotonic IAT have MoA and TI values prevailing, equal to 30.01 ± 0.65 % and 131.29 ± 2.15 c.u., which exceeds values of normo- and vagotonics by 4.01 % ($p < 0.05$) and 66.56 c.u. ($p < 0.01$), as well as by 8.83 % and 84.79 c.u. ($p < 0.01$), respectively. The same MoA and TI values are observed in the girls. At the age of 8 and 9 years, the ratios between the characteristics of the various IAT variants are similar, which confirms the literature data, according to which sympathicotonia is characterized by a decrease in Mo, Δx, and an increase in MoA, while vagotonic state leads to increase in first two indicators of cardiointervalography, and decrease in the third [1,14].

Table 1. Characteristics of various options baseline autonomic tone in boys of 7-9 years ($M \pm m$)

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IV T	Indicators											
	Mo, ms			AMo, %			Δx, ms			TI, c.u..		
	7years	8years	9years	7years	8years	9years	7years	8years	9years	7years	8years	9years
S	636.0	659.5	656.1	30.01	29.65	30.33	182.1	221.3	194.2	131.2	107.2	121.8
	0 ±	3 ±	0 ±	±	±	±	2 ±	8 ±	0 ±	9 ±	8 ±	6 ±
	11.24	13.98	10.27	0.65	1.95	2.16	3.09	4.94	4.71	2.15	2.87	24.90
N	629.0	589.2	705.0	26.00	24.87	22.81	232.0	393.0	278.0	64.73	63.37	58.06
	0 ±	5 ±	0 ±	±	±	±	0 ±	0 ±	0 ±	± 1.30	± 1.36	± 6.98
	10.31	10.64	11.75	1.59	2.09	1.18	3.99	9.87	5.99			
V	688.0	716.6	765.6	21.18	15.86	18.22	309.3	435.0	359.2	46.50	27.75	33.90
	0 ±	6 ±	0 ±	±	±	±	6 ±	0 ±	0 ±	± 1.33	± 0.90	± 1.86
	14.92	15.82	16.51	0.95	0.97	0.93	5.93	10.21	7.06			
S/N		**	**	*		**	**	**	**	**	**	**
N/ V	**	**	**	*	**	**	**	*	**	**	**	**
S/V	**	*	**	**	**	**	**	**	**	**	**	**

Remark: differences are significant between IVT groups: «*» $p < 0,05$; «**» - $P < 0,01$ and above.

IVT - initial vegetative tone, S - sympathicotonia, N - normotonia, V - vagotonia.

Mo - mode, AMo- amplitude of mode, Δx - variation range, TI - tension index

Analysis of the functional state of SAS in children aged 7-9 years showed that the excretion of catecholamine's depends on IAT, and has differences in the age groups (Table 2). 7-year-old boys with sympathicotonic IAT show higher level of NE excretion - 20.66 ± 1.35 ng/min, which is higher by 3.38 ng/min ($p < 0.05$) and 4.63 ng/min ($p < 0.05$) than in normo- and vagotonics, as well as an increase in NE/E ratio equal to 2.43 ± 0.09 , while the same in normo- and vagotonics - 1.86 ± 0.07 and 1.08 ± 0.05 , respectively.

There are no differences in A excretion, except for vagotonics, who have its level 1.5 times higher than the rest. We should note that children aged 7 years with sympathicotonic IAT have a significantly lower level of DA excretion, which is 33.07 ng/min ($p < 0.01$), and 32.94 ng/min ($p < 0.01$) less than the same in normo- and vagotonics. Probably, a high demand for NE in sympathotonic boys is not provided by adequate replenishment of its predecessor [8, 11]. Further analysis showed that the pupils aged 8 and 9 years, in contrast to 7-year-olds, show no statistically significant differences in NE excretion.

An increasing activity of the mediator component of SAS in the group of pupils with sympathicotonic IAT is indicated by the NE/E ratio, which is higher and amounts to 3.00 ± 0.07 and 2.72 ± 0.08 , respectively, while the normo- and vagotonics have values equal to 2.05 ± 0.05 ; 2.04 ± 0.04 and 1.72 ± 0.06 ; 1.96 ± 0.07 in both ages, respectively. As well as in the 7-year-olds, there is a relative reduction in DA excretion, which level does not exceed 115.07 ± 3.37 ng/min, and 136.29 ± 5.04 ng/min, which is significantly lower than in the normo- and vagotonics ($p < 0.01$) and may indicate SAS tension and reduction of its functional reserves [10].

This is also indicated by a lower level of DOPA excretion, which is 6.27 ng/min less in 8-year-old sympathotonics than in the norm tonics ($p < 0.05$), and in 9year-olds - 8.89 ng/min less ($p < 0.05$) than in the vagotonics.

Table 2. The excretion of catecholamine's and DOPA in boys and girls of 7-9 years old with different initial vegetative state (M±m)

Age	Sex	IVT	Indicators				
			E (ng/min)	NE (ng/min)	DP (ng/min)	DOPA (ng/min)	NE/E
7 years	Boys	S	8.49±0.78	20.66±1.35	124.33±4.73	22.17±1.33	2.43±0.09
		N	8.66±0.30	16.13±1.28	157.40±8.22	20.34±1.80	1.86±0.07
		V	14.83±0.42	16.03±1.36	157.27±7.34	13.94±1.62	1.08±0.05
		S/N		*	**		
		N/V	**			*	
		S/V	**	*	**	**	
	Girls	S	7.24±0.84	16.85±1.19	111.57±3.27	12.15±1.08	2.32±0.06
		N	6.97±0.41	13.71±0.93	124.33±5.12	15.52±1.24	1.96±0.09
		V	7.19±0.51	15.35±1.31	133.01±5.84	22.17±2.16	2.13±0.06
		S/N		*	*		
		N/V				**	
		S/V			**	**	
8 years	Boys	S	5.99±0.49	18.00±1.75	115.07±3.37	15.27±1.04	3.00±0.07
		N	9.99±0.65	20.56±1.90	142.47±7.62	21.54±2.10	2.05±0.05
		V	8.49±0.72	17.33±1.53	167.14±9.11	15.84±1.76	2.04±0.04
		S/N	**		**	*	
		N/V			*	*	
		S/V	*		**		
	Girls	S	9.08±0.88	18.71±1.69	111.99±3.08	19.82±2.81	2.24±0.07
		N	8.99±0.64	16.05±1.36	167.63±8.66	13.35±1.19	1.81±0.05
		V	7.94±0.59	14.44±1.28	146.74±6.73	23.05±2.40	2.09±0.06
		S/N			**	*	
		N/V				**	
		S/V		*	**		
9 years	Boys	S	6.83±0.37	18.58±1.94	136.29±5.04	13.35±1.02	2.72±0.08
		N	10.55±0.76	18.15±1.68	151.23±8.35	15.42±1.59	1.72±0.06
		V	8.33±0.34	17.89±1.32	167.17±8.94	20.24±2.24	1.96±0.07
		S/N	**				
		N/V	*				
		S/V	**		**	*	
	Girls	S	10.46±0.45	23.13±1.45	143.74±7.66	16.37±1.98	2.21±0.09
		N	9.00±0.57	16.99±0.96	141.64±7.42	13.99±1.50	1.88±0.07
		V	11.50±0.97	21.83±1.02	163.75±8.15	15.26±1.64	1.89±0.07
		S/N		**			
		N/V		*	*		
		S/V					

Remark: differences are significant between IVT groups: «*» p- <0,05; «**» - P <0,01.

S - sympathicotonia, N - normotonia, V - vagotonia.

IVT - initial vegetative tone, E –epinephrine, NE –norepinephrine, DP – dopamine.

The primary school girls as well as boys generally have similar shifts in SAS indicators and their dependence on the IAT features, however, there are some differences related to the intensity of their manifestation from 7 to 9

years. 7-year-old girls, as well as boys with sympathicotonia show higher NE excretion than the vagotonics and norm tonics, equal to 16.85 ± 1.19 ng/min, which is 3.14 n/min and 1.50 ng/min higher than in the rest (the differences

are significant as compared with the normotonics). Similar changes occur with the NE/E coefficient, reaching its maximum in girls with a predominance of sympathetic influences on cardiac rhythm (2.32 ± 0.06 as compared to 1.96 ± 0.09 and 2.13 ± 0.06).

In relation to A, there are virtually no differences, its excretion level ranges from 6.97 ± 0.41 to 7.24 ± 0.84 ng/min in different IAT groups. The increase in NE in girls with sympathicotonia, as well as in boys is accompanied by a decreased number of its predecessors - DA excretion level is 111.57 ± 3.27 ng/min, which is 1.20 and 1.11 times lower than in the normo- and vagotonics. Similar differences were observed with DOPA. We should note that with aging, from 7 to 9 years, the girls, unlike boys, continue showing the significant differences in the level of NE excretion between the IAT groups, namely its dominance in schoolgirls with an increased tone of the sympathetic division of the ANS. At the age of 8 years, the significant differences were observed between the sympatho- and vagotonics - 18.71 ± 1.69 ng/min and 14.44 ± 1.28 ng/min ($p < 0.05$), at 9 - between the sympatho- and normotonics - 23.13 ± 1.45 and 16.99 ± 0.96 ng/min ($p < 0.05$).

Moreover, the mean group values of NE excretion reach their maximum in a group of 9-year-olds, and correspond to the first peak of its age growth during the ontogeny. As well as boys, the girls aged 8 and 9 years with an increased tone of the sympathetic division of the ANS have predominance of SAS mediator component over hormonal one, resulting in the increased NE/E coefficient, which is 2.24 ± 0.07 and 2.21 ± 0.09 , respectively, and is 1.15 - 1.72 times higher than in the normo- and vagotonics. Simultaneously with the increase in the NE excretion there is a reduction in the excretion of DA and DOPA.

The excretion of DA in schoolgirls aged 8 and 9 years is 111.99 ± 3.08 ng/min and 143.74 ± 7.66 ng/min, which in the first and in the second case is 1.49 and 1.30 ($p < 0.01$), and 1.15 and 1.14 ($p < 0.05$) times smaller than in normo- and vagotonics, respectively.

SUMMARY:

The conducted study allows us to make the following conclusion:

1. The vast majority of children aged 7-9 years have sympathicotonic variant of the initial autonomic tone, characterized by a decrease in Mo and Δx , and increase in MoA and TI. At the same time, the girls, unlike boys, have an increased activity of vagus influence on the sinus node despite the higher TI values.

2. Children with the prevailing sympathetic influences on cardiac function as compared with normo- and vagotonics have higher levels of excretion of norepinephrine, an increasing norepinephrine/epinephrine ratio, and a decreasing dopamine level.

According to S. Nottin et al. (2002); R. Perini, A. Veicsteinas (2003), there is a strengthening of cholinergic effects on cardiac function occurring with aging. However, R.M. Baevskii et al. (2001) note that at the age of 7-9 years there is a trend towards cardiac cycle shortening, and significant reduction in the variation range, which indicates the relative predominance of sympathetic tone. According to our study, the boys show earlier (by age of 8 years) reduction of centralization of heart rhythm control (TI) on the background of increased vagal influences (Δx) and the growing activity humoral regulation channel (Mo). In girls aged 7 and 8 years, unlike boys, an increase in TI values is accompanied by compensatory strengthening of vagal influences that may indicate a more balanced state of ANS divisions. The established autonomic instability of children at a given interval of ontogeny (prevalence of sympatho- or parasympathetic effects) confirms the multifactorial nature of this phenomenon: the age and sex heterochrony of functional maturation of the ANS divisions [12], a genetic imbalance of the autonomic regulation mechanisms [3], and the impact of stress factors of educational activities [4].

It was shown for the first time that the increase in tone of the sympathetic division of the ANS in children of primary school age is accompanied by a significant increase in absolute values of NE excretion and in NE/E ratio as compared with the normo- and

vagotonics. This indicates a close contingency of IAT, determined by cardiointervalography, with the level of excretion of catecholamine's and DOPA, and is consistent with the concept of SAS as part of ANS, regulating the neuro-automatic balance [2,7,8].

CONCLUSION:

Thus, our study has shown that the vast majority of children aged 7-9 years have sympatheticotonic variant of the initial autonomic tone, which is formed during the period of adaptation to educational process in schools and is characterized by a predominance of the activity of the SAS mediator component over hormonal one, and a persistent decrease in dopamine level. This indicates the tension in the system of catecholamine biosynthesis and reduction in their reserves, and suggests that the autonomic instability, associated with the neurohumoral shifts, results to a large extent from the adaptive-compensatory relations of children's body with the environment.

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REFERENCES

1. *Baevskii R.M., Ivanov G.G.* Heart rate variability: the theoretical aspects and clinical application potential // *Ultrasound and functional diagnostics.* - 2001. - No.3. - 108 p.
2. *Nottin S., Vinet A., Mandigout S. et al.* Left ventricular dynamics during early recovery from maximal exercise in boys and men // *Med. Sci Sports Exerc.* - 2002. - V.34. - No.12. - P.1951-1957.
3. *Perini R., Veicsteinas A.* Heart rate variability and autonomic activity at rest and during exercise in various physiological conditions // *Eur. Journal Appl. Physiol.* - 2003. - V.90. - No.3-4. - P.379-325.
4. *Bezrukikh M.M.* Age physiology. - M.: Pedagogics, 2002. - 225 p.
5. *Martinelli F.S., Chacon-Mikahil M.P., Martins L.E. et al.* Heart rate variability in athletes and nonathletes at rest and during head-up tilt // *Braz. Journal Med Biol. Res.* - 2005. - V.38. No.4. - P.639-647.
6. *Spivak E.M., Pechnikova N.V.* Features of the autonomic regulation of the cardiovascular system at a primary arterial hypertension in adolescents // *Yaroslavl Pedagogical Bulletin.* 2012. V.3. No.3. 155 p.
7. *Sharapov A.N.* Neuroendocrine regulation of autonomic functions and vascular dystonia in children // *Physiology of child development.* - M.: Education from A to Z, 2000 - Pp. 127-142.
8. *Tseng Y.T., Wadhawan R., Stabila J.R. et al.* Molecular interactions between glucocorticoid and catecholamine signaling pathways // *Journal Allergy clin. Immunol.* - 2002. - V. 110. - No.6. - P.247-254.
9. *Manukhin B.* Adrenoceptor physiology. - L.: Nauka, 1968. - Pp. 200-208.
10. *Shaikhelislamova M.V., Sitdikov F.G., Dikopolskaya N.B. et al.* Age- and sex-related characteristics and mechanisms of adaptations during the prepubertal and pubertal periods of development // *Human Physiology.* - 2009. - T.35. - No.6. - P.747-754.
11. *Matlina E.Sh., Menshikov V.V.* Clinical biochemistry of catecholamines. - M.: Nauka, 1967. - 131 p.
12. *Raczac G., Pinna G.D., La Rovere M.T.* Cardiovagal response to acute mild exercise in young healthy subjects // *Circ. Journal.* 2005. V.69.- No.8. - P.976-980.
13. *Resmini E., Casu M., Patrone V. et al.* Sympathovagal imbalance in acromegalic patients // *Journal of Clinical Endocrinology & Metabolism.* - 2006. - V.91. - No.1. P.115-120.
14. *Kmit G.V.* The duration of the individual phases and periods of the cardiac cycle based on the type of autonomic regulation of heart rate in children aged 7-8 years // *New investigations. Almanac.* - 2005. - No.1. - Pp. 78-83.