

Participation of catecholamines and corticosteroids in regulation of the autonomic tone in children

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ABSTRACT

Aim: The article presents the results of the research of sympathetic-adrenal system and adrenal cortex (AC) functions, taking into account the features of heart rate vegetative regulation. **Methods:** They allowed to reveal a close contingency of excretion of catecholamines (CAs), metabolites of androgens and glucocorticoids, with the initial autonomic tone of children. It has been shown that children of both genders, with a predominance of sympathetic influences on cardiac rhythm, contrary to the normo- and vagotonics, had higher levels of norepinephrine (NE) excretion, combined with the increased secretion of 17-oxycorticosteroids (OCS) and 17-ketosteroids. 8–9-year-old girls are the exceptions. **Results:** They have relative decrease in activity of the glucocorticoid function of the AC in the sympathicotonia state. Furthermore, the boys - vagotonics, 11–12 years old, are the exceptions. Their intensity of the NE and 17-OCS excretion practically does not differ from that in the sympathotonics group. **Conclusion:** Thus, functional synergism of autonomic nervous system departments, coming out in the process of maintaining the autonomic balance, is accompanied by characteristic humoral-hormonal reactions of the organism in the form of simultaneous increase in levels of CAs and corticosteroids.

KEY WORDS: Boys and girls 7–12 years old, Catecholamines, Corticosteroids, Initial vegetative tone

INTRODUCTION

It is known that two groups of biochemical factors - catecholamines (CAs) and corticosteroids (CSs) - play an exceptional role in maintaining of neurovegetative balance and regulation of adaptive reactions of the body. The functions of the sympathetic-adrenal system (SAS), in its hormonal and mediator departments, are connected with the CAs; and functions of the hypothalamic-pituitary-adrenocortical system in its terminal phase are connected with the CSs.^[1,2]

Hypothalamus, due to the presence of direct connections with the centers of sympathetic and parasympathetic innervation of the heart, and anatomical functional connection with the pituitary, interrelates the autonomic nervous system (ANS) and endocrine system in the process of neurohumoral regulation of blood circulation.^[3] That is, some

changes in the state of vegetative balance of the cardiovascular system may be connected with a change in the biochemical parameters of its neuroendocrine regulation. The question of the possible participation of CSs in the activity of peripheral vegetative lines is of particular importance because glucocorticoids have a direct influence on the functions of the afferent link of the vegetative reflex, increasing the excitability of the reflex structures, affecting synaptic transmission in the sympathetic ganglion, and increasing the rate of synaptic conduction.^[4] The functional relationship between the hypothalamic zone of the brain, the pituitary gland, adrenal cortex (AC), and SAS is came out at different levels of the neurohumoral regulatory mechanism. The greatest number of studies is devoted to the central nervous level of these interrelations, which prove, in particular, that the CA, along with other central nervous system mediators, perform the humoral conduction of nerve influences at the hypothalamus level, thereby affects the secretion of corticoliberin, adrenocorticotrophic hormone, and glucocorticoids.^[5,6] There is also some information about the central adrenergic inhibitory mechanism in the regulation of the output of the corticotropin-

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releasing factor and, accordingly, adrenocorticotrophic hormone.^[7] It has been shown that the disorders of the ANS in children can be accompanied by both hyperfunctions of the SAS and increased sensitivity to CA of α - and β -adrenergic receptors of vessels, and also came out as changes in basal secretion of cortisol and sex hormones.^[7,8]

The investigation of the functional state of SAS and the AC, taking into account the peculiarities of vegetative regulation of the heart rhythm in healthy children, will allow registering early functional changes in the state of neurohumoral regulation of vegetative functions.

The aim of the study is to study the specific features of excretion of CAs and CSs in children with different tonus of the ANS.

METHODS

The study involved boys and girls, 7–12 year old, who studied in the secondary school of Kazan, belonging to the I and II groups of health. In total, 110 people were selected from each gender group, which were monitored continuously for 6 years. The study of the features of vegetative regulation of the heart rhythm was carried out by the method of variational pulsometry^[9] using the automated cardiopulmonary complex REACARD (Russia). The cardiac rhythm was recorded for 3 min in the prone position. The mode (Mo), mode amplitude (AMo), variation range (Δx), and tension index ($TI = AMo/2Mo \times \Delta x$) were analyzed. The initial vegetative tonus (IVT) was assessed on the basis of TI values, taking into account its age gradation: The children with TI more than 95.0 relative units belonged to the sympathotonics, normotonics - were the children with TI from 46.0 to 68.0 relative units, and vagotonics - were the children with TI <46.0 relative units. The state of SAS was judged by the content of norepinephrine (NE) and adrenaline (A) in daily urine, on the basis of the fluorometric method.^[10] The state of AC was assessed for urinary content of 17-oxy corticosteroids (17-OCS), which are the main metabolites of cortisol, cortisone, and their derivatives, as well as the content of 17-ketosteroids (17-KS), 2/3 of which are synthesized from androgens of AC, and 1/3 - from androgen gonads. For the quantitative measurement of 17-KS, the colorimetric method of N.V. Samosudova and Zh.Zh. Bass was used, based on the reaction of W. Zimmerman in the modification of Krekhova.^[11] The measurement of 17-OCS was carried out by the method of Silber and Porter, on the basis of the reaction with phenylhydrazine after enzymatic hydrolysis.^[11] Daily urine collection was performed at the beginning of the school year (October).

Statistical processing of the obtained data was carried out by the standard methods of variation statistics,

using the Microsoft Excel Windows 2007 software package. To assess the reliability of the differences, *t*-test, based on Student's *t*-criterion, was used.

RESULTS

Comparative analysis of the functional state of SAS and AC in 7–12-year-old children showed that excretion of NE, metabolites of glucocorticoids and androgens, is characterized by close contingency. It depends on the IVT and has some differences in age-gender groups.^[12] Thus, in 7-year-old boys with the sympathotonic type of IVT, a higher level of NE excretion is combined with increased excretion of 17-OCS and 17-KS. This parameter in sympathotonic boys is 227.00 ± 12.00 nmol/h and $980.00 \pm 57, 00$ nmol/h, respectively, that is, 1.19 and 1.18 ($P < 0.05$) times higher than that of schoolchildren with the vagotonic variant of the IVT [Table 1]. A similar ratio of the studied parameters is also observed among 7-year-old girls [Table 2]. They have increased activity of the sympathetic link of SAS, which is accompanied by an increase in the glucocorticoid and androgenic functions of AC and is expressed in relatively higher excretion values of 17-OCS and 17-KS, 293.00 ± 12.60 nmol/h and 790.30 ± 40.00 nmol/h, respectively. These values exceed the parameters of girls in the state of vagotonia, on the average of 1.2 times ($P < 0.01$ and $P < 0.05$). Further, analysis showed that in 8, 9, and 10-year-old boys, the differences in the excretion rates of metabolites of glucocorticoids and androgens between IVT groups, as a whole, are similar to the 7-year-old boys. However, they are mathematically less significant and are observed in the absence of significant differences in the excretion of NE. The excretion of 17-OCS in 8-year-old boys belonging to sympathotonic and vagotonic groups significantly differs. In the first case, it is 237.00 ± 14.30 nmol/h, and in the second case, it is 193.30 ± 10.60 nmol/h ($P < 0.05$). In 9-year-old boys, significant differences exist only in excretion of 17-KS, which is 1164.00 ± 84.60 nmol/h in sympathotonics. It is more than in boys with a vagotonic type of IVT by 190.00 nmol/h. However, a reliable difference is noted only in comparison with normotonics ($P < 0.05$). More significant differences are observed in 10-year-old schoolchildren. The group of sympathotonic has the greatest excretion of metabolites of androgens and glucocorticoids. This is higher than the values of boys in the state of vagotonia at 80.51 nmol/h and 30.64 nmol/h (the differences are significant for 17-OCS).

In 8, 9, and 10-year-old girls, the differences in the level of excretion of CA, between the IVT groups, correspond to those of 7-year-old schoolgirls. However, unlike boys, the ratio between the SAS and AC values varies. The previously established differences in the content of metabolites of glucocorticoids between the IVT groups

Table 1: Urinary catecholamines, metabolites of androgens and glucocorticoids in 7–12-year-old boys with different initial vegetative tones (M±m)

Age, years	№	IVT	Indicators			
			A, ng/min	NE, ng/min	17-KS, nm/h	17-OCS, nm/h
7	1	s	4.49±0.78	20.66±1.35	980.00±57.00	227.00±12.00
	2	n	8.66±0.30	16.13±1.28	906.30±53.00	293.30±10.30
	3	v	14.83±0.42	16.03±1.36	837.00±36.60	190.00±10.00
		1/2		*		
		2/3	**			*
		1/3	**	*	*	*
8	1	s	5.99±0.49	18.00±1.75	1032.00±72.00	237.00±14.30
	2	n	9.99±0.65	20.56±1.90	964.60±50.30	227.66±13.00
	3	v	8.49±0.72	17.33±1.53	1100.30±96.00	193.30±10.60
		1/2	**			
		2/3	*			
		1/3	*			*
9	1	s	6.83±0.37	18.58±1.94	1164.00±84.60	336.00±24.00
	2	n	10.55±0.76	18.15±1.68	930.66±49.00	338.00±22.30
	3	v	8.33±0.34	17.89±1.32	974.00±55.60	300.30±21.00
		1/2	**		*	
		2/3	*			
		1/3	**			
10	1	s	6.96±0.43	17.58±1.82	946.30±44.00	230.60±13.30
	2	n	7.81±0.56	16.74±1.65	930.00±43.00	238.00±15.00
	3	v	7.35±0.62	17.32±1.75	865.00±30.00	200.00±11.00
		1/2				
		2/3				*
		1/3			*	
11	1	s	7.65±0.57	22.84±2.09	1324.00±72.00	270.30±36.00
	2	n	6.65±0.23	16.34±1.45	1302.30±65.30	380.60±38.00
	3	v	6.94±0.31	19.36±1.64	1212.00±72.00	265.00±15.60
		1/2		*		
		2/3		*		*
		1/3				*
12	1	s	6.96±0.34	21.08±1.16	1570.00±60.00	360.00±26.00
	2	n	8.68±0.41	16.08±1.21	1480.60±42.30	270.00±18.00
	3	v	7.96±0.60	19.24±1.00	1590.60±58.00	384.00±15.00
		1/2		**		*
		2/3				*
		1/3				

-, Differences are significant for the groups IVT: * $P \leq 0.05$; ** $P \leq 0.01$. s: Sympathotonics, n: Normotensive, v: Vagotonics, IVT: Initial vegetative tonus, A: Adrenalin, NE: Norepinephrine, 17-KS: 17-Ketosteroids, 17-OCS: 17-oxycorticosteroids

acquire the opposite character: In girls, in the state of sympathicotonia, significantly increased excretion of NE unexpectedly combines with a significantly lower excretion of 17-OCS. Hence, in 8-year-old girls, it is 180.66 ± 9.00 nmol/h, which is 1.40 times less than in schoolgirls with normo- and vagotonic types of IVT ($P < 0.05$), in which the exertion of NE is correspondingly lower. Similar differences are observed in 9–10-year-old schoolgirls. In case of increased sympathetic influences on the cardiac rhythm, the excretion index of 17-OCS becomes, respectively, 86.00 nmol/h and 155.70 nmol/h lower than that of the vagotonics ($P < 0.05$). Probably, the danger of depletion of glucocorticoids in the state of increased tone of the sympathetic department of ANS ($\alpha 1$ -adrenoreceptor mechanism at the hypothalamic level) is prevented in girls by temporary regulatory inhibition of hormone synthesis (and, as a consequence of decreased 17-OCS excretion).^[4]

The differences between SAS and CN parameters in the IVT groups are another for 11–12-year-old boys. There are no significant differences in the excretion of NE, 17-KS, and 17-OCS between sympathotonic and vagotonic patients. Thus, 11-year-old boys, with sympathotonic and vagotonic types of IVT, have the content of NE in the portioned urine in the range from 19.36 ± 1.64 ng/min to 22.84 ± 2.09 ng/min, that is, 1.30 and 1.19 times more than in normotonics. The nature of excretion of androgens and glucocorticoids metabolites is identical: In the first case, its level varies from 1212.00 ± 72.00 nmol/h to 1324.00 ± 72.00 nmol/h in different groups of IVT, and in the second case - the values of sympatho- and vagotonics practically do not differ from each other, while they are 1.50 times less than in boys normotonics. For schoolchildren of 12 years, the balance between studied hormones and hormonal metabolites has its

Table 2: Urinary catecholamines, metabolites of androgens and glucocorticoids in 7–12-year-old girls with different initial vegetative tones (M±m)

Age, years	№	IVT	Indicators			
			A, ng/min	NE, ng/min	17-KS, nm/h	17-OCS, nm/h
7	1	s	7.24±0.84	16.85±1.19	790.30±40.00	293.00±12.60
	2	n	6.97±0.41	13.71±0.93	780.00±32.30	272.66±12.00
	3	v	7.19±0.51	15.35±1.31	700.00±28.00	200.60±10.30
		1/2		*		
		2/3			*	**
8		1/3			*	**
	1	s	9.08±0.88	18.71±1.69	794.00±50.00	180.66±9.00
	2	n	8.99±0.64	16.05±1.36	862.00±49.60	253.00±25.60
	3	v	7.94±0.59	14.44±1.28	680.66±30.00	320.00±19.30
		1/2			*	*
9		2/3			*	*
		1/3		*	*	*
	1	s	10.46±0.45	23.13±1.45	980.00±62.00	334.00±21.00
	2	n	9.00±0.57	16.99±0.96	1003.00±100.00	324.30±19.60
	3	v	11.50±0.97	21.83±1.02	976.30±68.30	420.00±28.00
10		1/2		**		
		2/3				*
		1/3				*
	1	s	8.46±0.63	24.13±1.92	996.00±65.00	224.30±13.00
	2	n	8.00±0.53	16.34±1.62	989.00±75.00	234.00±14.00
11	3	v	7.32±0.44	22.45±1.26	980.30±63.60	280.00±29.00
		1/2				
		2/3		*		*
		1/3		*		*
	1	s	8.09±0.58	23.64±1.50	1569.00±88.00	450.30±40.00
12	2	n	7.34±0.43	14.85±1.22	1365.00±60.60	314.00±20.00
	3	v	8.21±0.60	19.33±1.47	1372.00±65.30	371.00±22.00
		1/2		*		**
		2/3		*		
		1/3		*		
12	1	s	6.82±0.45	19.63±1.94	1532.00±55.00	464.00±38.00
	2	n	-	-	-	-
	3	v	6.91±0.33	16.75±1.18	1564.60±50.00	317.60±20.00
		1/2				
		2/3				
		1/3				**

-. Differences are significant for the groups IVT: * $P \leq 0.05$; ** $P \leq 0.01$. s: Sympathotonics, n: Normotensive, v: Vagotonics, IVT: Initial vegetative tonus, A: Adrenalin, NE: Norepinephrine, 17-KS: 17-Ketosteroids, 17-OCS: 17-Oxycorticosteroids

own peculiarities - the excretion of NE, 17-KS, and 17-OCS in children sympathotonics and vagotonics is relatively higher than in boys normotonics. There are the following figures: Excretion of NE - 5.00 ng/min ($P < 0.05$) and 3.16 ng/min, excretion of 17-KS - 89.36 nmol/h and 109.74 nmol/hour, and excretion of 17-OCS - 90.30 nmol/hour ($P < 0.05$) and 113.62 nmol/h ($P < 0.05$), respectively. The unexpectedly high excretion of NE and 17-OCS is observed in boys with a predominance of parasympathetic influences on the cardiac rhythm. Its intensity hardly differs from that in the sympathotonic group. This is probably a natural evidence of the functional synergy of the ANS divisions, mutually reinforcing biological activity in the process of maintaining the vegetative balance.^[1,4] This is accompanied by characteristic humoral-hormonal reactions of the organism, in the

form of simultaneous increase in the activity of the SAS mediator link and the glucocorticoid function of AC. The differences between the IVT groups are similar for 11–12-year-old girls. Against the backdrop of significant increase in the excretion of NE in the state of sympathicotonia, a relatively higher level of excretion of glucocorticoids is observed: The content of 17-OCS in schoolgirls with a sympathotonic type of IVT is 78.58 nmol/h and 147.00 nmol/h ($P < 0.05$) exceeds the values of vagotonics (and it is significantly higher in 11-year-old children than in normotensive state).

Hence, the sympathicotonic type of IVT formed in children during their adaptation to school, as well as in the prepubertal and pubertal periods of development, is characterized by a simultaneous and significant

increase in the excretion of NE and 17-OCS, reflecting the functional relationship between the nerve link of SAS and the glucocorticoid function of AC, because of their mutually reinforcing biological action increased tonic sympathetic influences on cardiac activity.

SUMMARY

1. High level of NE excretion is observed with the increased excretion of 17-OCS and 17-KS among 7-year-old schoolchildren of both genders, with a predominance of sympathetic influences on the cardiac rhythm.
2. 8-year-old and 9-year-old girls, unlike normo- and vagotonics, have a significant decrease in 17-OCS excretion, as a result of regulatory inhibition of hormone synthesis, to prevent the depletion of glucocorticoids in the state of increased tone of ANS sympathetic department.
3. 11–12-year-old boys, with a predominance of parasympathetic influences on the cardiac rhythm, have a high excretion of NE and 17-OCS, which does not differ from that in the sympathotonic group and is an evident of functional synergy of ANS departments.

CONCLUSION

Hence, the vegetative tone of 7–12-year-old children is provided by a certain ratio of CAs and CSs excretion. The sympathicotonic variant of IVT, in comparison with normo- and vagotonic, is characterized by a higher level of NE in combination with increased excretion of 17-OCS. The exception is for 11-year-old boys and 8–9-year-old girls, because in the first case, the activity of the nervous link of SAS and glucocorticoid function of AC in the group of sympatho- and vagotonics is equivalent, and in the second case, it has a multidirectional character.

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