

# Reaction of the Adrenal Cortex to Graded Exercise in Children with Different Initial Tonus of the Autonomic Nervous System

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It was found that the response of the adrenal cortex to graded bicycle exercise in children depends on the initial autonomic tonus and is adequate to the background excretion level of hormone metabolites. Seven-year-old sympathotonic girls with increased excretion of 17-hydroxycorticosteroids at rest demonstrated the lowest increase in this parameter after exercise in comparison with more pronounced increment in vagotonics with relative low initial level of glucocorticoid metabolites. Enhanced excretion of glucocorticoid metabolites with a decrease in androgens observed in 9-year-old sympathotonic girls attests to predominance of catabolic processes over anabolic ones and low efficiency of switching from muscle exercise to recovery in children.

**Key Words:** adrenal cortex; initial autonomic tone; exercise; junior schoolchildren

Autonomic instability manifesting in predominant tonus of the sympathetic or parasympathetic nervous system is typical of the vast majority of children [5,8] that are considered conventionally healthy with exhausted adaptation reserve [3]. Corticosteroids play an exceptional role in the regulation of neuroautonomic balance. Disorder of the autonomic nervous system can manifest in altered basal secretion of cortisol and sex hormones [9]. Glucocorticoids play a key role in the regulation of muscle activity ensuring transition of immediate adaptive responses to full-value long-term adaptation and preventing excessive tissue response to stress [12]; adrenal androgens can act as defense mechanism reducing high cortisol levels by inhibiting enzymes involved in their synthesis [11]. In children, the relative immaturity of the adrenal cortex against the background of instability of neurohumoral regulation mechanisms makes them more vulnerable to inadequate physical activity that can induce transformation of age-related evolution rearrangements into endocrine and neurovascular dysfunction.

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Here we studied peculiarities of adaptation of the adrenal cortex to graded exercise in 7-9 year-old children with different initial autonomic tone (IAT).

## MATERIALS AND METHODS

We performed 3-year monitoring of 7-, 8-, and 9-year-old schoolgirls ( $n=82$ , Kazan residents, health groups I and II).

IAT was determined based on the study of heart rhythm by the method of variational pulsometry using a REACARD automated cardiopulmonological complex. Heart rhythm was recorded over 3 minutes in the supine position. HR, mode (Mo), amplitude mode (AMo), variation rate ( $\Delta X$ ), and tension index (TI) were analyzed. Parameters of histograms were physiologically interpreted according to conception of R. M. Bayevskiy on two-circuit level of heart rhythm control [1]. Assessing IAT, we focused on the integral indicator TI calculated as  $TI=AMo/2Mo \times \Delta X$ . Children with TI more than 68.0-95.0 arb. units were attributed to sympathotonics; with TI more than 46.0-68.0 arb. units, to normotonics; with TI less than 46.0 arb. units, to vagotonics.

State of the adrenal cortex was assessed by urinary 17-hydroxycorticosteroids (17-OHCS), the main metabolites of cortisol, cortisone and their derivatives as well as by levels of 17-ketosteroids (17-KS), androgen metabolites of adrenal cortex. 17-KS was measured by the colorimetric method proposed by N. V. Samosudova and Zh. Zh. Bass based on the reaction of W. Zimmerman modified by M. A. Krekhova [4]. Urine was collected without preservative and stored at 0 to 12°C. Then, hydrolysis, extraction with ether (2×10 ml), purification of the extract, and the reaction with *m*-dinitrobenzene were carried out, after which the mixture was allowed to develop color. Absorbance of the solution was measured with FEC-56PM photoelectric colorimeter at  $\lambda=500-560$  nm (0.5 cm optical pass). The level of 17-OHCS was evaluated by the method of R. N. Silber and C. C. Porter [4], which involved enzymatic hydrolysis of urine, chloroform extraction, and reaction with phenylhydrazine. To develop the color, the sample was incubated in a water bath at 60°C. Absorbance of the solution was measured using SF-16 spectrophotometer at  $\lambda=410$  nm in cuvettes with a thickness of 10 mm.

Graded physical exercise (1.5 W per 1 kg body weight) was performed for 3 minutes on a RITM VE-05 bicycle ergometer in the sitting position. The urine was collected before and 1 h after the test.

The resulting material was treated with conventional methods of variation statistics. The significance of differences was assessed by Student's *t* test.

## RESULTS

Sympathicotonia was characterized by relatively low values of Mo and  $\Delta X$  (Table 1): 605.00±6.24 and 152.00±2.75 msec in 7-years-old children (*i.e.* by 25.00 msec and 79.00 msec lower than in normotonics

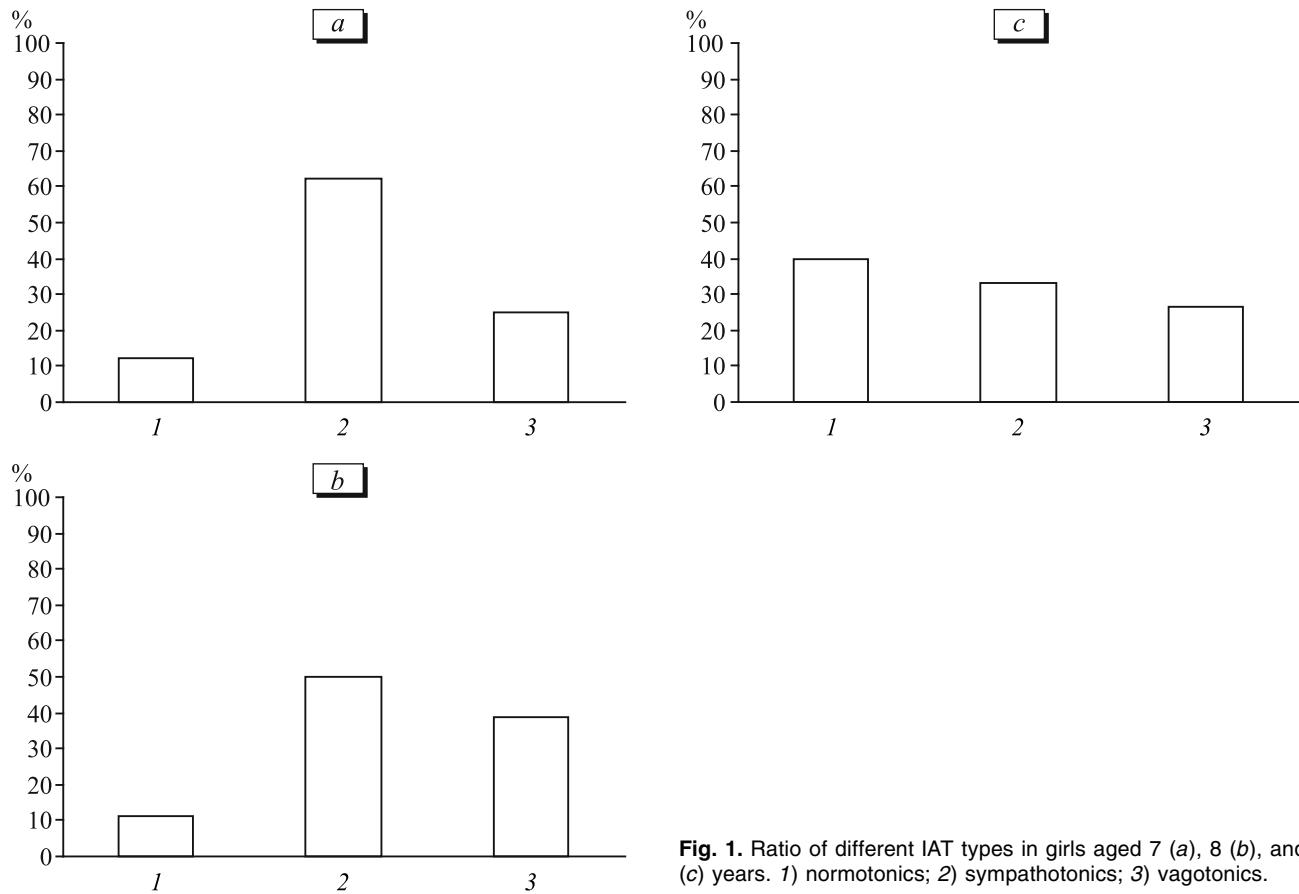
and by 173.00 and 242.33 msec lower than in vagotonics, respectively;  $p<0.05$  and  $p<0.01$ ). In girls with sympathotonic type of IAT, AMo and TI predominated and were 35.60±2.69% and 205.00±4.16 arb. units, *i.e.* surpassed the corresponding parameters in vagotonics by 16.98 and 168.18 arb. units and in normotonics by 11.20% and 136.78 arb. units, respectively ( $p<0.01$ ). In girls aged 8 and 9 years, the relationship between IAT type characteristics was similar ( $p<0.05$  and  $p<0.01$ ) except for Mo parameters; the differences between them were insignificant in 9-years-old girls. Sympathotonics prevailed (62.5%) among the girls of 7 years (Fig. 1) whereas eutonic state was recorded only in 12.5% of cases in this age group. At the age of 8 years, sympathotonics also prevailed (49.9%), but the number of girls with vagotonic type of IAT increased by 13.8%. In 9-year-aged girls, regulation of heart rate was more balanced. The number of normotonics increased by 28.6% and the number of sympathotonics and vagotonics decreased by 16.5% and 12.1%, respectively. Autonomic instability in young school girls may be due to several factors, such as constitutional imbalance of mechanisms regulating autonomic functions [10], heterochrony in the functional maturation of the departments of autonomic nervous system [3] and, finally, the impact of stress factors of learning during adaptation to school [2].

Analysis of the functional state of the adrenal cortex at rest (before load) showed (Table 2) that excretion of 17-OHCS and 17-KS in normotonic 7-year-old schoolgirls was 272.66±12.00 nmol/h and 780.00±32.30 nmol/h; in sympathotonic the corresponding values were 293.00±12.60 nmol/h and 790.30±40.00 nmol/h, respectively, *i.e.* by 1.2 times higher than in vagotonic girls ( $p<0.01$  and  $p<0.05$ ). At the age of 8 and 9 years, the differences between IAT types in the levels of glucocorticoid metabolites were opposite: excretion of 17-

**TABLE 1.** Characteristics of Different IAT Types in Girls Aged 7 to 9 Years ( $M\pm m$ ;  $N=10-51$ )

IAT; age		HR, bpm	Mo, msec	AMo, %	$\Delta X$ , msec	TI, arb. units
Normotonics	7	103.99±1.47	630.00±10.62	24.40±1.03	231.00±2.68	68.22±1.99
	8	96.00±2.14	630.00±12.36	24.40±1.94	231.00±5.39	82.85±2.25
	9	85.74±1.58	708.83±12.02	22.55±1.74	256.66±4.95	62.03±5.57
Sympathotonics	7	100.84±2.15	605.00±6.24*	35.60±2.69**	152.00±2.75**	205.00±4.16**
	8	98.62±1.12	614.00±12.20	30.51±2.41	189.11±3.79**	145.24±5.65**
	9	91.04±1.34*	690.20±11.11	28.20±1.91*	223.60±5.42**	99.10±13.45*
Vagotonics	7	101.65±1.78	778.00±19.86****	18.62±0.67****	394.33±7.64****	35.82±1.28****
	8	87.28±2.35****	697.00±14.28****	17.12±1.93***	365.57±7.69****	36.67±1.88****
	9	86.50±1.62 <sup>+</sup>	725.75±12.95	17.97±0.59***	446.25±11.89****	29.17±1.45****

**Note.** \* $p<0.05$ , \*\* $p<0.01$  compared with normotonics; \* $p<0.05$ , \*\* $p<0.01$  compared with sympathotonics.



**Fig. 1.** Ratio of different IAT types in girls aged 7 (a), 8 (b), and 9 (c) years. 1) normotonics; 2) sympathotonics; 3) vagotonics.

OHCS in 8 year-old sympathotonics was  $180.66 \pm 9.00$  nmol/h, *i.e.*, by 1.4 times lower than in normotonic and vagotonic girls ( $p < 0.05$  and  $p < 0.01$ ). At the age of 9 years, 17-OHCS excretion was by 86.00 nmol/h lower than in vagotonics ( $p < 0.05$ ) against the background of enhanced sympathetic influences. It can be hypothesized that the risk of glucocorticoid depletion in individuals with elevated tonus of the sympathetic nervous system ( $\alpha_1$ -adrenoreceptor mechanism at the hypothalamic level) [6] is prevented by temporary suppression of hormone synthesis (resulting in reduced excretion of 17-OHCS).

The reaction of the adrenal cortex to graded exercise was adequate to background values of hormone metabolite excretion. Thus, in vagotonic girls aged 7 years with relatively low excretion at rest ( $200.60 \pm 10.30$  nmol/h), the increase in 17-OHCS excretion after exercise was maximum ( $61.89$  nmol/h;  $p < 0.05$ ), whereas in sympathotonics these changes were less pronounced ( $38.36$  nmol/h) and the level of 17-OHCS before the load was higher ( $293.00 \pm 12.60$  nmol/h;  $p < 0.01$ ). These reactions are explicable in terms of the law on the initial level of homeostasis [7]. Irrespective of IAT, physical exercise significantly increased 17-KS excretion in all 7-year-old girls from 366.70 to 483.56 nmol/h ( $p < 0.05$  and  $p < 0.01$ ), which

pointed to the dominant role of adrenal androgens in the regulation of adaptive responses of younger schoolgirls. In sympathotonics at the age of 8 and 9 years unlike 7-year-old sympathotonics, the increase in 17-OHCS excretion was maximum: 73.70 and 112.02 nmol/h, respectively ( $p < 0.01$  and  $p < 0.05$ ). The temporary regulatory inhibition of the adrenal glucocorticoid function at rest probably maintained its reserve capacity. Relative suppression of the adrenal cortex was observed in normotonics and vagotonics. The increase in 17-OHCS was insignificant and did not exceed 24.32 nmol/h. In 9-year-old vagotonics, this parameter tended to decrease from  $420.00 \pm 28.00$  to  $408.80 \pm 20.66$  nmol/h. In 9-year-old sympathotonic girls, the shifts in the content of metabolites of glucocorticoids and androgens were opposite: 17-OHCS increased by 112.02 nmol/h ( $p < 0.05$ ) and 17-KS decreased by 233.71 nmol/h ( $p < 0.05$ ). This may indicate predominance of catabolic processes over anabolic ones and low efficiency of the switching from muscle exercise to recovery.

Thus, girls of primary school age are characterized by functional instability of the adrenal cortex during physical exercise against the background of autonomic balance shifts towards sympathetic or parasympathetic effects. Suppression of the glucocorticoid function of

**TABLE 2.** Excretion of Androgen and Glucocorticoid Metabolites before and after Physical Activity in Girls with Different IAT Types Aged from 7 to 9 Years ( $M \pm m$ ;  $N=10-14$ )

Age; IAT	17-KS, nmol/h		17-OHCS, nmol/h	
	before	after	before	after
7 years	normotonics	780.00 $\pm$ 32.30	1263.56 $\pm$ 74.62**	272.66 $\pm$ 12.00
	sympathotonics	790.30 $\pm$ 40.00	1157.33 $\pm$ 70.37*	293.00 $\pm$ 12.60
	vagotonics	689.39 $\pm$ 28.00 <sup>++</sup>	1120.61 $\pm$ 65.46**	200.60 $\pm$ 10.30 <sup>++</sup>
8 years	normotonics	862.00 $\pm$ 49.60	982.32 $\pm$ 57.44	253.00 $\pm$ 25.60
	sympathotonics	794.00 $\pm$ 50.00	994.35 $\pm$ 60.37	180.66 $\pm$ 9.00 <sup>+</sup>
	vagotonics	680.66 $\pm$ 30.00 <sup>+</sup>	784.72 $\pm$ 39.92	320.00 $\pm$ 22.10 <sup>++</sup>
9 years	normotonics	1003.00 $\pm$ 100.00	1090.00 $\pm$ 80.82	324.30 $\pm$ 19.60
	sympathotonics	980.00 $\pm$ 62.00	746.29 $\pm$ 30.00*	334.00 $\pm$ 21.00
	vagotonics	976.30 $\pm$ 68.30	1546.00 $\pm$ 140.30*	420.00 $\pm$ 28.00 <sup>++</sup>
				408.80 $\pm$ 20.66

**Note.** \* $p<0.05$ , \*\* $p<0.01$  compared with values before exercise; <sup>+</sup> $p<0.05$ , <sup>++</sup> $p<0.01$  compared with normotonics; \* $p<0.05$ , <sup>++</sup> $p<0.01$  compared with sympathotonics.

the adrenal cortex in normotonics and vagotonics aged 9 years plays a protective role protecting the organism against catabolic effects and limiting the duration of intense muscular work.

## REFERENCES

1. R. M. Bayevskiy and G. G. Ivanov, *Ultrazvuk. Funktsionaln. Diagnost.*, No. 3, 108 (2001).
2. R. M. Bezrukikh, *Age Physiology* [in Russian], Moscow (2002).
3. A. M. Veyn, *Autonomic Disorders* [in Russian], Moscow (2003).
4. V. G. Kolb and V. S. Kamyshnikov, *Clinical Biochemistry* [in Russian], Minsk, (1976).
5. S. M. Kushnir, *Vestn. Aritmol.*, No. 18, 40 (2000).
6. N. S. Sapronov, *Pharmacology of the Pituitary-Adrenal System* [in Russian], St. Petersburg (1998).
7. E. M. Spivak, *Autonomic Dystonia Syndrome at Early Age and in Pre-School Childhood* [in Russian], Yaroslavl (2003).
8. M. V. Shayhelislamova and F. G. Sitzdikov, *Hormonal Status and Autonomic Tonus in Children of 7 to 15 Years of Age* [in Russian], Kazan (2008).
9. A. N. Sharapov, *Physiology of Development of the Child* [in Russian], Ed. M. M. Bezrukikh et al., Moscow (2000).
10. I. N. Shlyk, *Computer Electrocardiography at the Turn of the Centuries*, Moscow (1999).
11. G. P. Chrousos, *Endocr. Res.*, **26**, No. 4, 513-514 (2000).
12. M. M. Ostander, Y. M. Ulrich-Lai, and D. C. Choi, *Endocr. Res.*, **147**, No. 4, 2008-2017 (2006).