PHYSIOLOGY

Regulation of Pumping Function of the Heart in Developing Body under Changing Regimens of Motor Activity

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We analyzed parameters of the pumping function of the heart in rats subjected to enhanced motor activity after a preliminary 70-day hypokinesia under conditions of α- and β-adrenergic receptor stimulation with norepinephrine followed by blockade of β-adrenergic receptor with propranolol (obsidian) and α_1-adrenergic receptors with doxazosin. After norepinephrine administration, the HR and cardiac output were higher in rats with enhanced physical activity after preliminary hypokinesia than in rats with low physical activity. After propranolol administration, stroke volume and cardiac output in 100-day-old rats with limited activity were lower, and HR higher was than in rats with enhanced physical activity after preliminary 70-day hypokinesia. After administration of doxazosin, rats with limited motor activity demonstrated more pronounced changes in HR than rats with enhanced physical activity after preliminary 70-day hypokinesia.

Key Words: *heart rate; stroke volume; cardiac output; hypokinesia*

Regulation of the pumping function of the heart in the developing organism exposed to different modes of physical activity was analyzed in some studies [1,5]. Hypokinesia delays the age-related development, while enhanced physical activity accelerates the development of pumping function of the heart [2-5].

Here we studied the pumping function and the mechanisms of its regulation during transition from hypokinesia to intensive exercise.

MATERIALS AND METHODS

The experiments were carried out on 70- and 100-day-old albino rats. Group 1 included animals with limited physical activity (LPA, hypokinesia); group 2 comprised rats during the transition from LPA to enhanced physical activity (EPA) (LPA-EPA). Growing rats were placed in immobilization cages to limit motor activity [1]. After preliminary 7-week hypokinesia, the rats were subjected to progressively increasing physical exercise. The rats were forced to swim for 10 min on day 1; then the time of swimming increased by 5 min during the 1st week and by 10 min during the 2nd and the 3rd weeks. By the end of the 3rd week, the duration of the training session reached 80 min. During the 4th week, the training session lasted 90 min including 30 min with a load of 3% body weight.

Differential rheograms were recorded in rats narcotized with urethane (800 mg/kg intraperitoneally) during spontaneous respiration using an RPG-204 rheoplethysmograph developed and made at the experimental production workshop of the Russian Academy of Medical Sciences. Pharmacological preparations were applied against the background of the previous

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drug in the following order: norepinephrine (non-selective stimulation of α-and β-adrenergic receptors), propranolol (non-selective blockade of β-adrenergic receptors), and doxazosin mesylate (antagonist of α_1-adrenergic receptors). The drugs were infused via the femoral vein catheter.

The results were analyzed using Chart, ClarisWorks and Statistica 6.0 SR softwares. The data were statistically processed using common methods of variation statistics. Significance of differences was evaluated by Student's *t* test.

RESULTS

HR remained elevated in 70-day-old rats and 100-day-old rats with LPA before dissection with natural breathing (Table 1). HR in 100-day-old rats subjected to EPA after preliminary hypokinesia (LPA-EPA) decreased by 95.8 bpm in comparison with that in 100-day-old rats with LPA ($p\leq0.05$). In 70-day-old rats subjected to hypokinesia, norepinephrine increased HR by 43.9 bpm and in 100-day-old rats by 70.3 bpm ($p\leq0.001$). HR increased by 107.9 bpm after norepinephrine administration in 100-day-old rats with LPA-EPA ($p\leq0.01$). Propranolol decreased HR in rats with LPA: in 70-day-old rats by 97.7 bpm and in 100-day-old rats by 153.1 bpm ($p\leq0.01$). After propranolol administration, HR in 100-day-old rats with LPA-EPA decreased by 128.2 bpm ($p\leq0.01$). Doxazosin administration reduced HR by 18 bpm in 70-day-old rats with LPA; in 100-day-old rats, this reaction was more pronounced (107.8 bpm).

Stroke volume (SV) before dissection under conditions of natural breathing in 100-day-old rats with LPA-EPA increased by 0.123 ml in comparison with that in coeval animals with LPA ($p\leq0.05$). Age-related increase in SV was found in rats with LPA after norepinephrine administration: by 0.033 ml in 70-day-old rats and by 0.041 ml in 100-day-old animals ($p\leq0.05$). Norepinephrine increased SV by 0.021 ml in 100-day-old rats with LPA-EPA. Transition from LPA to EPA significantly reduced SV response to norepinephrine at the age of 70 days. In rats subjected to hypokinesia, SV decreased after propranolol administration by 0.066 ml in 70-day-old rats and by 0.062 ml in 100-day-old rats. In 100-day-old rats with LPA-EPA, SV after propranolol administration decreased by 0.098 ml in comparison with that after norepinephrine infusion ($p\leq0.05$). Doxazosin reduced SV by 0.009 ml in 70-day-old rats with LPA and by 0.013 ml in 100-day-old rats. In 100-day-old rats with LPA-EPA, SV after doxazosin administration decreased by 0.040 ml ($p\leq0.01$).

Cardiac output (CO) in 100-day-old rats with LPA-EPA was higher than in 100-day-old rats with

TABLE 1. Parameters of Pumping Function of the Heart in Rats with LPA and LPA-EPA after Norepinephrine, Propranolol, and Doxazosin Administration (*M*±*m*)

Conditions of registration	Age 70 days (*n*=26)			Age 100 days (*n*=46)					
	LPA			LPA (*n*=25)			LPA-EPA (*n*=21)		
	HR	SV	CO	HR	SV	CO	HR	SV	CO
At rest with natural breathing (without drugs)	415.4±4.4	0.152±0.007	56.50±5.60	400.2±4.6°	0.162±0.009	65.27±8.10	304.4±8.9$^{\circ x}$	0.285±0.007$^{\circ x}$	85.52±4.72$^{\circ x}$
At rest with natural breathing after dissection of the femoral vein (without drugs)	414.8±4.7	0.157±0.001	65.39±5.50	392.6±6.0°	0.155±0.009	61.01±3.73	301.4±9.2$^{\circ x}$	0.281±0.005$^{\circ x}$	86.43±6.01$^{\circ x}$
In 5 min after norepinephrine administration	458.7±4.3^{*+}	0.190±0.008^{*+}	67.28±6.19	462.9±1.2^{*+}	0.196±0.008^{*+}	89.35±6.07^{*+}	409.3±7.9$^{*+\circ x}$	0.302±0.009°	122.06±7.90$^{*+\circ x}$
In 10 min after propranolol administration	361.0±7.1^{*+}	0.124±0.008^{+}	46.35±5.56	309.8±4.0$^{+\circ}$	0.134±0.005^{+}	42.32±9.32^{+}	281.1±4.4$^{+\circ x}$	0.204±0.009$^{*+\circ x}$	57.56±4.41^{+}
In 10 min after doxazosin administration	379.0±5.3^{*+}	0.115±0.005^{+}	43.50±3.27	202.0±9.6$^{+\circ}$	0.121±0.011^{+}	24.59±2.27^{+}	261.6±5.5$^{+\circ x}$	0.164±0.002$^{*+\circ x}$	42.98±3.38^{+x}

Note. $p<0.05$ in comparison with: *previous drug, $^{+}$baseline, $^{\circ}$parameters in 70-day-old rats, ^{x}parameters in 100-day-old rats.

LPA by 20.2 ml/min ($p \leq 0.05$), which is consistent with previous findings [3]. After norepinephrine injection CO increased by 28.3 ml/min in 100-day-old rats with LPA and by 35.6 ml/min in 100-day-old rats with LPA-EPA ($p \leq 0.05$). Propranolol reduced CO by 20.9 ml/min in 70-day-old rats with LPA and by 47 ml/min in 100-day-old rats ($p \leq 0.05$). After propranolol administration to 100-day-old rats with LPA-EPA, CO was reduced by 64.5 ml/min ($p \leq 0.05$). Administration of doxazosin decreased CO by 2.8 ml/min in 70-day-old rats with LPA and by 14.5 ml/min in 100-day-old rats with LPA-EPA ($p \leq 0.05$).

Thus, 100-day-old rats showed significantly reduced HR and increased SV and CO upon transition to enhanced exercise after preliminary 70-day hypokinesia compared with rats with LPA. After norepinephrine administration, HR and CO in rats subjected to EPA after preliminary hypokinesia was higher than in rats with LPA. SV and CO were lower under conditions of propranolol treatment and HR was higher than in rats with EPA after preliminary 70-day limitation. HR changed more markedly in rats with LPA after doxazosin administration compared to rats with EPA after preliminary 70-day hypokinesia.

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