Peculiarities of Regulation of Heart Rate and Stroke Volume in Rats during Ontogeny

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Changes in heart rate and stroke volume after successive blockade of cardiac adreno- and cholinoceptors were examined on rats of different age. It was established that irrespective of animal age the heart rate remained unchanged under conditions of total adreno- and cholinergic blockade of the heart. Stroke volume under conditions of total adreno- and cholinergic blockade increased with age.

Key Words: *cardiac pumping function; stroke volume; heart rate; adrenoreceptors; cholinoceptors*

Adrenergic and cholinergic mechanisms regulating pumping function of the heart during ontogeny under conditions of muscle training and hypokinesia are extensively studied [2-6]. At the same time, the degree of changes in functional state of adrenergic and cholinergic receptors during physical exercise, and changes in heart rate (HR), stroke volume (SV), and cardiac output (CO) at rest and under the effect of muscle training and hypokinesia requires further investigation.

Here we examined the peculiarities of adrenergic and cholinergic mechanisms of regulation of the pumping function of the heart and the responses of HR, SV, and CO to successive and relatively complete blockade of adrenergic and cholinergic receptor structures in the heart.

MATERIALS AND METHODS

The experiments were carried out on 21-, 30-, 42-, 49-, 70-, and 100-day old albino rats (n=182) narcotized with chloral hydrate (40 mg/kg body weight) kept under conditions of unrestricted motor activity and on 70-day old rats subjected to regular muscle training (swimming) as described previously [1].

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Differentiated rheogram was recorded using a 4RG-2M rheograph coupled with a MacLab-4e digitizer (ADInstruments). The results were analyzed using original software. Needle electrodes were fixed subcutaneously.

Changes in the pumping function were examined after successive injection of the test agents into the femoral vein: selective β_1-adrenoreceptor (AR) blocker atenolol (0.2 mg/kg), non-selective β-AR blocker propranolol (0.8 mg/kg), selective α_1-AR blocker prazosin (Adversuten, 0.2 mg/kg), non-selective α-AR blocker phentolamine (0.5 mg/kg), and muscarinic cholinoceptor blocker atropine (0.6 mg/kg). Each blocker was injected against the background of pronounced effect produced by the previously applied agent. SV was determined using a modified method of tetrapolar rheography [1].

The data were analyzed by Student's t test.

RESULTS

The group of rats trained for 70 days demonstrated the lowest HR (41.6 bpm) resulting from the block of β_1-AR (p<0.05, Table 1). Propranolol injected against the background of β_1-AR blockade changed HR depending on animal age: decreased this parameter in young animals (up to the age of 42 days), but increased it in older rats (from the age of 49 days). Prazosin injected against the back-

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TABLE 1. Effect of Successive Blockade of Adrenergic and Cholinergic Cardiac Receptors in Rats of Various Age on HR (bpm, *M*±*m*)

Observation periods		Age, day						
		21	30	42	49	70 (non-trained)	100	70 (trained)
Initial	before surgery	455.73±5.42	485.48±5.78^{+}	433.31±5.60^{+}	431.16±5.21	417.32±3.39^{+}	361.58±11.59^{+}	371.81±10.09^{x}
	after surgery	469.66±3.12	489.25±7.10	437.36±4.29^{+}	431.73±1.53	410.02±3.21^{+}	372.23±8.57^{+}	376.11±7.19^{x}
After injection of	atenolol	349.09±6.94*	333.69±4.06^{*+}	355.61±8.52^{*+}	332.42±4.33^{*+}	332.51±6.22*	302.31±8.67^{*+}	334.51±4.28
	propranolol	324.11±4.80*	322.39±4.78	350.98±2.31^{+}	302.35±5.86^{*+}	297.43±7.83*	271.50±9.56^{*+}	277.20±3.68^{x}
	prazosin	308.97±4.03*	296.47±5.96*	335.17±4.68^{*+}	304.81±10.17^{+}	285.75±7.94^{+}	269.89±7.51	250.40±6.04^{x}
	phentolamine	270.01±4.44*	223.38±2.84^{*+}	295.78±4.55^{*+}	264.79±4.72^{*+}	248.49±8.63^{*+}	225.29±6.96^{*+}	221.30±4.57^{x}
	atropine	284.81±8.01*	280.82±1.90*	295.78±3.15^{+}	278.81±7.90^{+}	281.23±6.54*	270.19±5.33*	270.09±7.32*

Note. Here and in Tables 2: $p<0.05$ compared to *preliminary injection, $^{+}$the next age group, and ^{x}non-trained 70-day rats.

TABLE 2. Effect of Successive Blockade of Adrenergic and Cholinergic Cardiac Receptors in Rats of Various Age on SV (ml, *M*±*m*)

Observation periods		Age, day						
		21	30	42	49	70 (non-trained)	100	70 (trained)
Initial	before surgery	0.062±0.003	0.071±0.001^{+}	0.130±0.003^{+}	0.154±0.005^{+}	0.208±0.005^{+}	0.290±0.002^{+}	0.347±0.008^{x}
	after surgery	0.059±0.005	0.072±0.003^{+}	0.127±0.006^{+}	0.146±0.010^{+}	0.202±0.002^{+}	0.285±0.004^{+}	0.334±0.004^{x}
After injection of	atenolol	0.029±0.004*	0.062±0.003^{*+}	0.099±0.006^{*+}	0.092±0.007*	0.149±0.004^{*+}	0.280±0.006^{+}	0.313±0.007^{*x}
	propranolol	0.027±0.003	0.039±0.004^{*+}	0.108±0.009^{+}	0.077±0.009^{*+}	0.135±0.010^{*+}	0.272±0.014^{+}	0.308±0.008^{x}
	prazosin	0.026±0.003	0.034±0.002^{+}	0.105±0.008^{+}	0.082±0.010^{+}	0.133±0.009^{+}	0.265±0.010^{+}	0.291±0.007^{x}
	phentolamine	0.016±0.002*	0.028±0.002^{*+}	0.105±0.005^{+}	0.066±0.006^{*+}	0.120±0.010^{*+}	0.247±0.014^{*+}	0.258±0.013^{*x}
	atropine	0.029±0.003*	0.045±0.004^{*+}	0.129±0.010^{*+}	0.142±0.007^{*+}	0.157±0.009^{*+}	0.266±0.012^{+}	0.298±0.009^{*x}

ground of propranolol decreased HR in 21-day old rats by 15.14 bpm ($p<0.05$); in 30-and 42-day old rats HR decreased by 25.92 and 15.81 bpm ($p<0.05$), respectively. The dependence of HR on α_1-AR decreased with age. Phentolamine produced different HR decrease in different age groups. The response of HR to successive block of β-AR was more pronounced than the response to similar block of α-AR. In all age groups of rats with blocked cardiac AR, atropine increased HR. In 21- and 100-day old rats, it increased HR by 14.8 and 44.9 bpm ($p<0.05$). In rats with muscarinic cholinoceptors blocked against the background successive block of cardiac β- and α-AR, HR remained at the same level despite different age and muscle training (swimming). Thus, HR does not significantly change in rats with successive block of the adrenergic and cholinergic influences irrespective of the differences in age and muscle training. It can be concluded that the development of age-related and exercise-related bradycardia results mainly from changes in extracardiac adrenergic and cholinergic mechanisms regulating cardiac function.

Successive block of β-AR with atenolol and propranolol decreased SV in 21- and 30-day old rats by 0.032 ml (Table 1). The block of α-AR with prazosin and phentolamine decreased SV by 0.011 ml.

In 49- and 70-day old rats, β-AR blockade decreased SV by 0.069 and 0.067, respectively ($p<0.05$). The respective reactions of SV to the block of α-AR were 0.011 and 0.015 ml ($p<0.05$). In 100-day old rats, the block of β-AR produced less pronounced changes in SV (0.013 ml) than those induced by blockade of α-AR (0.025 ml). Atropine increased SV in all groups of rats, and this effect increased with age ($p<0.05$). SV was 2 times greater in 70-day trained rats than in the rats with unrestricted motor activity. During successive block of adrenergic and cholinergic cardiac receptors, SV increased with age. At the same time, the dependence of SV on extracardiac influences decreased with age.

Thus, HR remains constant during ontogeny under conditions of successive blockade of adrenergic and cholinergic cardiac receptors. By contrast, SV in rats with successive blockade of adrenergic and cholinergic cardiac receptors increases with age.

REFERENCES

1. R. A. Abzalov, in: *Motion and the Developing Heart* [in Russian], Moscow (1985), pp. 14-18.
2. R. A. Abzalov and F. G. Sitdikov, *The Developing Heart and Motion Regimen* [in Russian], Êàzàn (1998).
3. I. Kh. Vakhitov, L. T. Minnakhmetova, and O. P. Mart'yanov, *Byull. Eksp. Biol. Med.,* **139**, No.9, 484-486 (2005).
4. T. L. Zefirov and N. V. Svyatova, *Ibid.,* **126**, No. 12, 612-614 (1998).
5. R. R. Nigmatullina, R. A. Abzalov, B. S. Kulaev, and N. I. Abzalov, *Arkh. Klin. Eksp. Med.,* **9,** No.1, 106-109 (2000).
6. R. R. Nigmatullina, R. A. Abzalov, and N. I. Abzalov, *Ross. Fiziol. Zh*., **86**, No. 12, 1580-1586 (2000).