Age-Related Differences in the Response of Blood Stroke Volume to Stimulation of the Sympathetic Ganglion in Rats with β-Adrenoceptor Blockade

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Blood stroke volume in rats aging 21 and 56 days decreased during β-adrenoceptor blockade with propranolol, but increased again by the 15th minute after treatment. Suprathreshold stimulation of the stellate ganglion decreased the stroke volume and increased the heart rate in control animals. Electrical stimulation after β-adrenoceptor blockade was followed by a further decrease in stroke volume in young rats. In 100-day-old animals this parameter remained unchanged, while the cardiac output improved.

Key Words: *β-adrenoceptors; propranolol; stroke volume; stellate ganglion; ontogeny*

The number of cardiac β-adrenoceptors undergoes significant changes during ontogeny and depends on the strength of stimulation. The higher is activity of the sympathetic nervous system and catecholamine content in receptor areas, the greater is the decrease in adrenoceptor density [9,10]. The density of adrenoceptors decreases during the development of sympathetic adrenergic innervation [12]. Administration of exogenous norepinephrine and increase in catecholamine content in the myocardium are accompanied by a decrease in the sensitivity and increase in reactivity of the heart [7]. High threshold current for the heart rate (HR) and stroke volume (SV) in adult animals reflects the reduced sensitivity of adrenoceptors to sympathetic influences [1]. The chronotropic response involves cardiac β- and α_1-adrenoceptors. The positive ionotropic effect is realized via α_1-adrenoceptors. Published data show that β-adrenoceptors are involved in the regulation of this cardiac function [4,6]. Here we studied the role of β-adrenoceptors in the sympathetic regulation of SV in rats during the early postnatal ontogeny.

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MATERIALS AND METHODS

Experiments were performed on outbred albino rats aging 21, 56, and 100 days (late succling puberty and maturity). The animals were anesthetized with 1.3 g/kg urethane and fixed on an operation table. The right stellate ganglion was prepared under a MBS-2 binocular microscope. Differential rheogram and electrocardiogram (ECG) were recorded to study cardiac activity. The data were monitored on an electrophysiological device and analyzed by means of Conan software. Electrical stimulation of the stellate ganglion was performed with platinum electrodes on an ESL-2 device (10 Hz pulse frequency, 5 V current amplitude, 1 msec duration). ECG was analyzed as described elsewhere [3]. SV was determined by the method [11] with modifications [5]. The cardiac output (CO) was calculated. The nonselective β-adrenoceptor antagonist propranolol (0.8 mg/kg) was injected into the femoral vein. Parameters were recorded over 15 min postinjection. Amplitude and temporal characteristics of differential rheogram were estimated [4] to increase the informativeness of tetrapolar thoracic rheography and study of the mechanisms of cardiac output regulation.

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RESULTS

Control stimulation of the right stellate ganglion for 30 sec decreased SV, but increased HR in all rats. Published data show that most pronounced changes in HR are observed during stimulation of sympathetic nerves at a frequency of 8-10 Hz. The inotropic effect develops at a lower frequency of stellate ganglion stimulation. We found that SV in rats aging 21, 56, and 100 days decreased by 15, 19, and 17%, respectively. CO underwent insignificant changes (Fig. 1). Probably, the constant level of CO is provided by opposite changes in HR and strength of cardiac contractions. Acceleration of cardiac contractions leads to a decrease in the end-diastolic volume, which can result in the reduction of SV. CO can slightly increase or even decrease under these conditions. CO in rats aging 56 and 100 days retuned to normal 5 and 7 min after stimulation, respectively. However, CO in 21-day-old animals was not normalized even by the 10th minute after treatment. The amplitude of rheogram (Ad) and blood ejection time (Tu) decreased in rats of different groups ($p<0.01$).

SV and HR decreased after treatment with the β-adrenoceptor antagonist, which reflects the existence of tonic sympathetic influences [2]. By the 15th minute SV in rats aging 21, 56, and 100 days surpassed the baseline level by 45 ($p<0.01$), 32 ($p<0.05$), and 5%, respectively (Table 1). It should be emphasized that CO increased in rats aging 21 and 56 days (by 11 and 14%, respectively), but decreased in 100-day-old animals (by 7%). This parameter remained unchanged to the end of observations. Immediately after treatment with propranolol the amplitude of rheogram in rats aging 21, 56, and 100 days decreased by 7, 6, and 5%, respectively. By the 15th minute Ad in 21- and 56-day-old animals increased by 20 ($p<0.05$) and 26% ($p<0.05$), respectively. The time of blood ejection remained practically unchanged in rats aging 57 and 100 days, but increased by 19% in 21-day-old animals. SV decreased after α_1-adrenoceptor blockade, which reflects the existence of a constant positive effect realized via these receptors [4,8]. Previous studies showed that propranolol produced a positive inotropic effect and increased SV via blockade of β-adrenoceptors [8]. Other authors reported that blockade of one adrenoceptors was followed by activation of other adrenoceptors. The data on reflex stimulation of α_1-adrenoceptors with propranolol probably confirm our results. We showed that SV increases 15 min after administration of the preparation. The increase in the mode amplitude reflects activation of the sympathetic regulatory mechanism. SV underwent most pronounced changes in 21- and 56-day-old rats ($p<0.05$). Published data show that sympathetic regulatory influences on SV prevail in 100-day-old animals [4]. We found that changes in SV are least significant in adult rats. The mode amplitude significantly increased in 56-day-old rats ($p<0.05$), but decreased in adult animals. These changes reflect suppression of sympathetic regulatory influences.

In 21-day-old rats suprathreshold electrical stimulation (30 sec) of the stellate ganglion during β-adrenoceptor blockade with propranolol was followed by a decrease in SV by 30% ($p<0.05$). This parameter remained 22% below the baseline level by the 10th minute. SV in 56-day-old animals decreased only by 15% and returned to normal after 5 min. SV in 100-

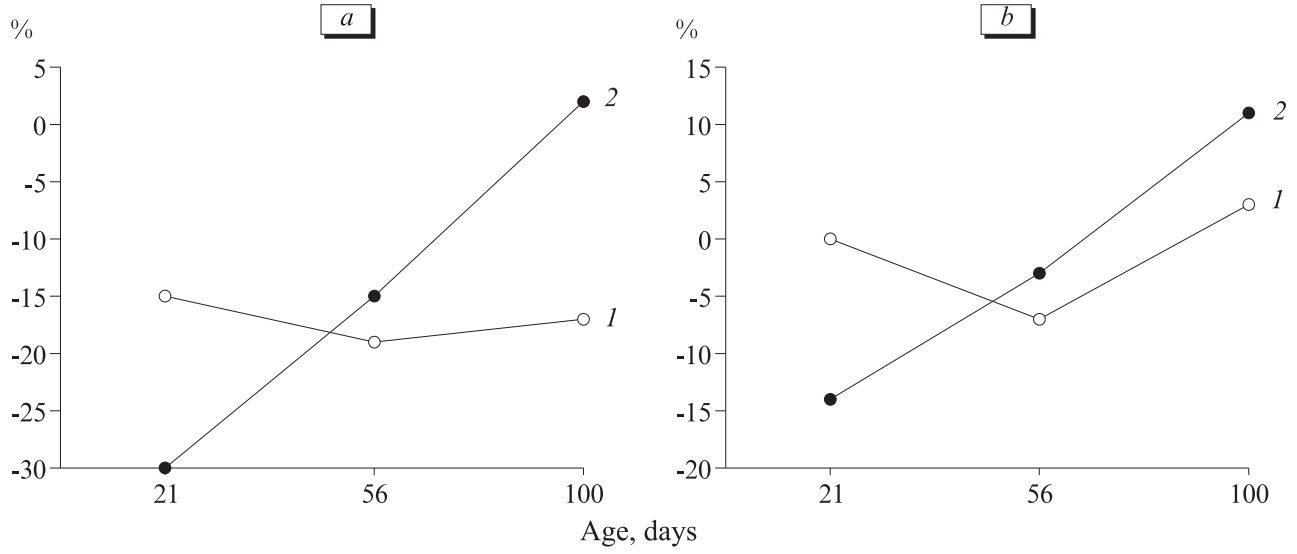

Fig. 1. Stroke volume (*a*) and cardiac output (*b*) in rats of different ages after suprathreshold stimulation of the stellate ganglion under control conditions (*1*) and during β-adrenoceptor blockade (*2*).

TABLE 1. Cardiac Activity in Rats Receiving Propranolol during Postnatal Ontogeny (*M*±*m*)

Age		SV, ml	CO, ml/min	Mode amplitude, %
21-day-old	baseline level	0.0143±0.0010	4.81±0.32	41.74±0.32
	after 15 min	0.0208±0.0010*	5.32±0.42	37.71±3.04
56-day-old	baseline level	0.0315±0.0030	10.37±1.37	32.74±4.29
	after 15 min	0.0416±0.0080**	11.79±2.67	43.84±3.54**
100-day-old	baseline level	0.0698±0.0060	18.48±1.53	41.21±4.67
	after 15 min	0.0731±0.009	16.93±2.35	34.81±3.94

Note. *$p<0.01$ and **$p<0.05$ compared to the baseline level.

day-old rats increased in response to stimulation of the stellate ganglion (Fig. 1, *a*). CO decreased in animals aging 21 and 56 days (by 14 and 4%, respectively) and did not return to normal even by the 10th minute after stimulation. However, CO increased by 11% in adult rats and returned to normal 7 min after stimulation. In animals aging 21 and 56 days we revealed a decrease in the amplitude of rheogram by 9 ($p<0.01$) and 5%, respectively, and Tu by 13 ($p<0.05$) and 7%, respectively. Ad and Tu in 56-day-old rats returned to the baseline level 3 and 10 min after stimulation, respectively. These parameters underwent insignificant variations in 21-day-old animals, but remained practically unchanged in adult rats.

Our results show that stimulation of the sympathetic ganglion produces different changes in SV in rats of different age groups under control conditions and during β-adrenoceptor blockade. Sympathetic stimulation was followed by a decrease in SV in control animals. Similar changes were revealed in rats aging 21 and 56 days and receiving propranolol. The data indicate that β-adrenoceptors play a major role in the realization of sympathetic influences on SV in these animals. During early postnatal ontogeny, nerve elements of the heart develop much more rapidly than muscle tissue. Muscle and connective tissue are morphologically immature in this period, which contributes to low inotropic activity of the heart. Electrical stimulation had no effect on SV in adult rats under control conditions and during β-adrenoceptor blockade. CO in these animals tended to increase, which maintained the optimal level of circulation.

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