

# Mechanisms of Heart Pump Function Regulation among Immature Animals

B. I. Vakhitov<sup>1</sup>, I. Kh. Vakhitov<sup>1</sup>, A. H. Volkov<sup>2</sup>, S. S. Chinkin<sup>2</sup>

<sup>1</sup>Department of Veterinary Medicine, Kazan State Academy of Veterinary Medicine Named after N.E. Bauman, Kazan Federal University, Kazan, 420008, Russia, <sup>2</sup>Department of Veterinary and Sanitary Examination, Kazan State Academy of Veterinary Medicine Named after N.E. Bauman, Kazan, Sibirskiy Trakt 35, 420074, Russia

## Abstract

**Objective:** Studies were carried out to study the peculiarities of the pumping function of the heart of immature rats subjected to various regimes of motor activity at earlier stages of individual development. **Methodology:** White mongrel laboratory rats were used in the experiments, which were conditionally divided into two experimental test subgroups, and were subjected to forced muscle training-swimming and normal vivarium conditions, and parameters of the heart pumping function were recorded at 14, 42, and 70 days. **Results and Discussion:** The carried out studies allow to draw the conclusion that the heart rate (HR) and the shock volume of blood (SVB) among the animals kept in the regime of free motor activity (FrMA) from 14 to 70 days of age will largely change from 42 to 70 days of life. With a systematic muscular training, organized at earlier stages of postnatal development of rats, the pumping function of the heart and the mechanisms of its regulation undergo significant changes at the initial stage, i.e., from 14 to 42 days. **Conclusions:** The HR, the SVB, and the mechanisms of their regulation of small laboratory animals kept in the regime of FrMA will change to a greater extent in the age range from 42 to 70 days of life, and among the rats, susceptible to systematic muscle training, the parameters of heart pumping function and the mechanisms of its regulation undergo significant changes from 14 to 42 days of animals life.

**Key words:** Heart rate, muscle training, pumping function of the heart, rats, shock blood volume

## INTRODUCTION

The studies of a number of authors are devoted to the study of motor activity various regime influence regularities on the heart functions and the mechanisms of its regulation in postnatal ontogenesis.<sup>[1-6]</sup> However, a significant number of studies was carried out to study the features of heart chronotropic function, whereas the changes in the shock volume of blood (SVB) have not been studied sufficiently among immature animals. In KFU laboratory, a number of researchers conducted the experiments on the study of the SVB and the mechanisms of its regulation among immature animals subjected to various regimes of motor activity.<sup>[7-12]</sup> At that, the majority of the researchers started systematic muscular training of rats from the age of 21 days. At the same time, the features of changes in the parameters of the heart pump function and the mechanisms of its regulation are poorly studied among immature animals prone to muscle training at earlier stages of postnatal development. In this regard, for the 1<sup>st</sup> time, we conducted the

studies of heart pumping function and the mechanisms of its regulation among rats prone to muscle training from the age of 14 days.

## METHODOLOGY

White mongrel laboratory rats were used in the experiments, which were conditionally divided into two subgroups. The animals of the first experimental group, from 14 days of age to 70 days of age, were subjected to forced muscle training-swimming. The rats of the second experimental group, from 14 to 70 days of age, were kept under normal

**Address for correspondence:** B. I. Vakhitov, Department of Veterinary Medicine, Kazan State Academy of Veterinary Medicine Named after N.E. Bauman, Kazan Federal University, 18 Kremlevskaya Street, Kazan 420008, Russia.  
E-mail: Bulat.vakhitov.1989@mail.ru

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vivarium conditions - 6–8 animals per each (free motor activity – [FrMA]). The parameters of the heart pumping function were recorded at 14, 42, and 70 days of age.

To determine the SVB, tetrapolar thoracic rheography was used.<sup>[6]</sup> The differentiated rheogram was recorded with RPG-204 device among anesthetized rats with sodium ethaminal (40 mg/kg) and natural respiration. To study the sympathetic effects on the heart pumping function of rats, 0.1% solution was injected into the jugular vein through a catheter at the dose of 0.8 ml/100 g and promazine at the concentration of 0.17 mg/100 g of weight body. To block the parasympathetic effects in the jugular vein, a 0.1% solution of sulfuric acid atropine was injected through the catheter, at the dose of 0.3 mg/100 g of body weight. The severity of sympathetic and parasympathetic influences on rat heart pumping function was judged by the shifts of heart rate (HR) and SVB after the pharmacological blockade of the corresponding receptors.

The administration of obsidian blocks  $\beta$ -adrenoreceptors, and the introduction of promazine blocks  $\alpha$ -adrenoreceptors and chrono- and ino-tropic function of the heart decreases. The introduction of atropine, as is known, relieves the inhibitory effects of vagus nerves, and thus, there is the increase of HR and SVB due to the binding of post-synaptic M-choline receptors.

## RESEARCH RESULTS AND THEIR DISCUSSION

The HR of 14-day-old rats made  $380.3 \pm 7.7$  beats/min [Table 1]. During the process of rat keeping in the regime of FrMA, the HR decreased to  $428.3 \pm 9.5$  bpm by the 42<sup>nd</sup> day. This value was 58.0 beats/min higher than the initial data ( $P < 0.05$ ). By the 70<sup>th</sup> day of life, the HR decreased slightly (11.1 beats/min) and amounted to  $427.2 \pm 8.0$  beats/min ( $P < 0.05$ ) among the animals of FrMA group. Consequently, the HR increased among the rats from 14 to 42 days of age kept in the regime of FrMA, and some decrease is observed by the age of 70 days.

The HR has not undergone significant changes to the 42-day age among the rats subjected to systematic muscular training starting from the 14<sup>th</sup> day of age as compared with the baseline data, remaining at the level of 377–380 beats/min. During the subsequent muscle training of these same rats from 42 to 70 days of age, their HR decreased by 18.9 beats/min ( $P < 0.05$ ). Therefore, in the process of muscle training, organized from the 14<sup>th</sup> day of age, the HR does not undergo significant changes by the 42<sup>nd</sup> day of animal life, whereas the animals kept in the regime of FrMA experienced a significant increase of HR. Thus, systematic muscular training, organized from the age of 14 days, largely inhibits the natural increase of heartbeat rate [Table 2].

We also analyzed the changes in the SVB among the animals subjected to various regimes of motor activity

[Table 1]. The rats kept in the regime of FrMA from 14 to 42 days of age, the SVB increased from  $0.042 \pm 0.003$  to  $0.109 \pm 0.012$  ml. The increase in the SVB among the rats during 28 days of FrMA was 0.067 ml ( $P < 0.05$ ). In the process of the subsequent maintenance of these same rats within the regime of FrMA from 42 to 70 days of age, the SVB increased from 0.109 to 0.234 ml, i.e., by 0.125 ml ( $P < 0.05$ ). Consequently, in the course of next 28 days of life, the SBV of rats undergoes more significant changes than during the previous stage of life and the difference makes 0.058 ml ( $P < 0.05$ ). Thus, the rats kept in the regime of unlimited motor activity have a more expressed SBV increase in the range from 42 to 70 days of age than at the age from 14 to 42 days [Table 3].

Muscular training of rats contributes to a significant increase in the SVB. However, the rates of SBV growth are different among the rats at the first and second stage of muscle training. As our studies showed, in the process of swimming training,

**Table 1: Heart rate (beats/min) among the rats that were in different regimes of motor activity**

Terms of heart parameter indicator study	FrMA	MT
14 days	380.3±7.71	
42 days	438.3*±9.58	377.4±7.72
70 days	427.2±8.04	358.5±5.38

\*The difference is reliable in comparison with the values of the previous group ( $P < 0.05$ ). MT: Muscle training, FrMA: Free motor activity

**Table 2: Stroke volume of blood (ml) among the rats subjected to different regimes of motor activity**

Age	Amount of rats	FrMA	MT
14 days	20	0.042±0.003	
42 days	19	0.109*±0.012	0.238*±0.018
70 days	55	0.234*±0.011	0.327*±0.0014

\*The difference is reliable in comparison with the values of the previous group ( $P < 0.05$ ). FrMA: Free motor activity, MT: Muscle training

**Table 3: The reaction of heart rate (%) among the rats subjected to different regimes of motor activity with the blockade of adreno and choline-receptors**

Age	Motor activity modes	Heart rate response (%)		
		Obsidan	Prozazine	Atropine
14 days	FrMA	33.8±2.3	16.0±2.4	6.5±1.8
42 days	FrMA	29.1±2.6*	14.6±2.3	12.1±2.2*
	MT	22.1±2.5*	14.0±2.5	22.7±1.7*
70 days	FrMA	26.3±1.3*	13.8±3.8	21.6±1.6*
	MT	21.1±2.4*	10.6±2.3	29.2±1.8*

\*The difference is reliable in comparison with the values of the previous group ( $P < 0.05$ )

**Table 4:** The reaction of the shock volume of blood (%) among the rats subjected to different regimes of motor activity with the blockade of adreno and choline receptors

Age	Motor activity modes	Stroke volume of blood response (%)		
		Obsidan	Prozazine	Atropine
14 days	FrMA	18.5±3.3	26.6±4.8	35.8±3.4*
42 days	FrMA	17.2±2.9*	21.6±4.4	23.5±2.1*
	MT	22.3±3.1*	24.5±3.3	18.8±3.3*
70 days	FrMA	13.6±207*	17.3±4.8	18.6±2.4*
	MT	16.6±108*	18.5±6.7	15.8±2.1*

\*The difference is reliable in comparison with the values of the previous group ( $P < 0.05$ ). FrMA: Free motor activity, MT: Muscle training

the SVB increased from 0.042 to 0.238 ml from 14 to 42 days of age, i.e., by 0.196 ml ( $P < 0.05$ ). In the course of the subsequent muscle training of the same animals from 42 to 70 days of age, the SVB increased only by 0.089 ml ( $P < 0.05$ ). Consequently, during muscular training of rats at the age from 14 to 70 days, the rate of SVB increase during the first stage, i.e., from 14 to 42 days is more pronounced than in the subsequent stage, i.e., from 42 to 70 days of life [Table 4].

To study the sympathetic and parasympathetic influences on the pumping function of rat heart, obsidian, promazine, and atropine were introduced into the jugular vein through the catheter.

The introduction of obsidian and promazine for rats exposed to muscular training from 14 to 42 days of age caused the decrease of HR in comparison with the initial data by 83.7 beats/min (22.1%) and 39.3 beats/min (14.0%) ( $P < 0.05$ ). When atropine was administered, the HR among these rats increased by 87.7 beats/min (22.7%) ( $P < 0.05$ ). The subsequent muscular training of these rats from 42 to 70 days of age led to the decrease of HR response after the administration of adrenergic blockers. Thus, with the introduction of obsidian and promazine, the decrease of HR by 76 (21.1%) and 30.2 beats/min (10.6%), respectively ( $P < 0.05$ ), took place among 70-day-old rats. With the introduction of atropine, the HR of 70-day-old trained rats increased by 105.8 beats/min (29.2%). This response to HR after the administration of  $\alpha$ ,  $\beta$ -adreno and M-choline blockers was significantly lower in comparison with the response of HR recorded at 42 days of age. Consequently, in the process of systematic muscular training of rats at the age from 14 to 70 days, the decrease of HR is associated with the increase of vague nerve activity at a simultaneous decrease of sympathetic influences in the regulation of the chronotropic heart function. At that, it should be noted that the sympathetic influence in HR regulation is more pronounced during muscular training in the range from 14 to 42 days of age. Thus, if the sympathetic influence in the regulation of HR decreases by 11.7% among the trained rats in the age range from 14 to 42 days, then at the age from 42 to 70 days, this decrease was only 1.0% ( $P < 0.05$ ).

The reaction of SVB to the administration of obsidian and atropine was 18.5% and 35.8%, respectively, among 14-day-old rats. As a result of muscle training, the response of SVB to the administration of obsidian increased to 22.3% by the age of 42 days and decreased to 18.8% after the introduction of atropine. In the course of the subsequent muscular training of these same rats before 70-day-old age, the reaction of SVB to the administration of obsidian and atropine decreased slightly and amounted to 16.6 and 15.8%. However, this decrease of SVB reaction to the administration of obsidian and atropine is less pronounced than in the age of 42 days. Consequently, the rats prone to muscle training at earlier stages of postnatal development experience significant changes in the regulation of blood stroke volume at the initial stage of swim training.

## SUMMARY

The carried out studies allow us to draw the conclusion that the HR and the SVB among the animals kept in the regime of FrMA from 14 to 70 days of age will largely change from 42 to 70 days of life. With a systematic muscular training, organized at earlier stages of postnatal development of rats, the pumping function of the heart and the mechanisms of its regulation undergo significant changes at the initial stage, i.e., from 14 to 42 days. In our opinion, this fact is explained by the following. Against the background of the natural processes occurring in the developing body of a rat, muscle training causes significant changes in heart and the mechanisms of its regulation at earlier stages of postnatal development. First, myocardium hypertrophy develops at a significant rate. Probably, at the first stage of muscle training, this happens to a greater extent due to the acceleration of cardiomyocyte division processes. However, in the future, as the body grows and develops, muscle training does not significantly affect the processes of cell division and their population does not change significantly. In our view, the development of myocardial hypertrophy during the second stage of training is largely conditioned by the increase of cardiomyocyte weight. However, this process requires more time. Perhaps, due to this, the changes in the pumping function of the rat heart are less pronounced during the second stage of muscle training. Second, muscle training, organized at earlier stages of

postnatal development, significantly changes the sympathetic and parasympathetic influences, as well as their correlation in the regulation of heart pumping function. Muscle trainings also contribute to faster maturation of intracardiac regulatory mechanisms.

## CONCLUSIONS

1. The HR, the SVB, and the mechanisms of their regulation of small laboratory animals kept in the regime of FrMA will change to a greater extent in the age range from 42 to 70 days of life.
2. Among the rats, susceptible to systematic muscle training, the parameters of heart pumping function and the mechanisms of its regulation undergo significant changes from 14 to 42 days of animal life.

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