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Indicators Of Pumping Heart Function In Immature Rats Subjected To Muscle Training At Different Stages Of Postnatal Development.

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ABSTRACT

This paper deals with the features of changes in the indicators of cardiac pump function of rats and their regulation mechanisms during systematic muscle training organized at an earlier stage of their development, i.e., since 14th day of birth. It was found for the first time ever that the indicators of pumping cardiac function in rats subjected to systematic muscle training from day 21 to 70 of birth undergo more substantial changes in the age range of 42 to 70 days. Whereas, the indicators of pumping cardiac function in animals subjected to muscle training from day 14 to 70 of birth changed largely in the age range of 14 to 42 days. Moreover, muscle training of rats started on day 14 of birth result in more pronounced changes in the regulation of pumping cardiac function than the muscle training started on day 21 of birth.
Keywords: immature rats, muscle training, heart rate, stroke volume, cardiac output, regulation of pumping cardiac function.

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INTRODUCTION

A number of authors have devoted their studies to the investigation of the laws of influence of various modes of physical activity on heart functions and its regulation mechanisms in postnatal ontogenesis [1,3,6,9,12,13]. At the same time, a considerable amount of works deals with the study of the characteristics of the chronotropic cardiac function of a developing organism. While the mechanisms of stroke volume regulation in immature animals are not well understood, and mainly performed in the laboratory of physiology of exercise of Kazan Pedagogical University [1,2,4,5,8,11,12,13,14,15]. However, the features of changes in the indicators of the pumping cardiac function and its regulation mechanisms in the developing organism subjected to muscle training in the earlier stages of postnatal development have been insufficiently studied. In this context, we have carried out a study of the indicators of pumping cardiac function and its regulation mechanisms in rats subjected to muscle training from day 14 of their birth.

Objective of the research was to study the indicators of the pumping cardiac function and its regulation mechanisms during muscle training started from day 14 of birth.

Research tasks

- To analyze the features of changes in heart rate (HR), stroke volume (SV) and cardiac output (CO) in the rats subjected to muscle training at earlier stages of their development
- To study the regulation mechanisms of HR, SV and CO during muscle training organized at earlier stages of postnatal development

METHODS

The experiments were conducted on outbred laboratory albino rats aged 14, 42 and 70 days.

To simulate various modes of physical activity, the rats were divided into two experimental groups starting from day 14 of birth. Rats of the first group were kept in standard vivarium conditions, in 6-8 animals (unlimited physical activity - UPA). Animals of the second experimental group were subjected to muscle training starting from day 14 to 70 of birth, i.e. an enhanced physical activity mode was simulated. Stroke volume was determined by tetrapolar chest rheography (W.I. Kubicek et al., 1966) [16]. A differentiated rheogram was recorded in rats anesthetized with aethaminalum-natrium (40 mg/kg) at natural respiration using RPG-204 device. To study the sympathetic influence on the pumping cardiac function in rats, 0.1% Obsidan solution was introduced to the jugular vein through the catheter at a dose of 0.8 ml/100 g, and Prazosin at a concentration of $1 \cdot 10^{-7}$mol/L at a dose of 0.17 mg/100 g of body weight. Parasympathetic influences were blocked by injecting 0.1% solution of sulfuric acidic atropine. The severity of both sympathetic and parasympathetic influences on the cardiac pumping function of rats was assessed by shifts in HR, SV and CO after pharmacological blockade of the relevant receptors.

Introduction of Obsidan blocks β-AR, and the introduction of Prosasin blocks α-AR, resulting in reduction in chrono- and inotropic function of the heart. Introduction of atropine, as is known, removes an inhibitory effect of the vagus nerves and, consequently, contributes to an increase in SV and HR, by binding the postsynaptic M-choline receptors.

RESULTS AND DISCUSSION

The heart rate in 14-day-old rats was 380.3 bpm. Keeping the rats under unlimited physical activity mode resulted in the increased heart rate up to 438.3 bpm by day 42. This value was 58 bpm greater as compared with the original data (P<0.05). The heart rate in rats subjected to systematic muscle training starting from day 14 of birth did not change significantly by day 42 in comparison with the original data, and remained at a level of 377-380 bpm. During subsequent muscles training, there were no significant changes in heart rate of young rats under 70 days old recorded. Therefore, the heart rate undergoes no significant changes in the process of muscle training started from day 14 of birth until day 42, while the animals being kept under unrestricted physical activity mode showed a significant acceleration of their heart rate. Consequently, systematic muscle training started from day 14 of birth inhibit largely the natural age-related acceleration of heart rate.

Stroke volume in rats contained under unrestricted physical activity regime increased during 14-42-day-period from 0.042 to 0.109 ml, i.e. by 0.067 ml (P<0.05). During the subsequent maintenance of the same rats under unrestricted physical activity from day 42 to 70, their SV increased by 0.125 ml (P<0.05). Consequently, the rats kept under unrestricted physical activity showed a more pronounced increase in SV during the period of 42 to 70 days, than during 14-42 days.

Muscle training contribute to significant increase in stroke volume in rats. However, the growth rates of SV in rats during muscle training from day 14 to 70 of birth are not equally pronounced. Systematic swimming exercises done in the age range of 14 to 42 days resulted in stroke volume growth by 0.196 ml (P<0.05). However, during the subsequent muscle training, stroke volume of the same animals in the period of 42-70 days increased by only 0.089 ml (P <0.05). Consequently, the rats subjected to muscle training at the earlier stages of ontogenesis show more pronounced growth rate of stroke volume during the period of 14-42 days, than during 42-70 days.

The analysis of the growth rate of stroke volume in rats subjected to muscle training starting from day 21 and 14 of birth found a certain difference. According to the employees of the laboratory of exercise physiology [1,12], muscle training of rats started from day 21 of birth leads to increase in the systolic ejection by day 42 of animals' life by 0.096 ml (P<0.05). During the subsequent muscle training, stroke volume of the same rats during 42-70 days increased by 0.190 ml (P<0.05). Therefore, both the rats subjected to muscle training from day 21 of birth, and the rats kept under unrestricted physical activity have shown a significant increase in stroke volume observed in the age range of 42 to 70 days. According to our records, the muscle training of rats started from day 14 of birth, leads to an increase in SV by 0.196 ml (P<0.05) by day 42 of rats' life. This value was twice higher than the stroke volume in rats subjected to muscle training from day 21 of birth. However, during the subsequent muscle training, stroke volume of the same rats increased by only 0.089 ml (P<0.05) during 42-70 days. Consequently, the rats subjected to muscle training from day 14 of their birth had more pronounced growth rate of stroke volume in the age range of 14 to 42 days. Therefore, it can be noted that if the rats subjected to muscle training from day 14 of birth have more pronounced increase in stroke volume up to day 42, then the animals subjected to muscular training from day 21 of birth have increase in their stroke volume during 42-70 days. It should be noted that we found no significant difference in stroke volume indicators at the age of 70 days in the rats subjected to muscle training from day 14 of birth and those subjected to training from day 21.

We have also conducted the analysis of the weekly gain in stroke volume in rats subjected to muscle training from day 14 and 21 of their birth. The weekly gain in stroke volume in animals subjected to muscle training from day 21 was approximately 0.032 ml by day 42. The weekly gain in stroke volume in rats subjected to muscle training from day 14 of birth was 0.049 ml by day 42, which is 0.017 ml higher than that of animals subjected to muscle training from day 21 (P<0.05). However, in the age range of 42 to 70 days, the weekly gain in stroke volume in rats subjected to muscle training from day 21 of birth increased up to 0.047 ml. While the weekly gain in stroke volume in rats subjected to muscle training from day 14 of birth was only 0.022 ml in the age range of 42 to 70 days. Consequently, the weekly gain rate of stroke volume in rats subjected to muscle training from day 14 of birth is significantly higher at the initial stages of muscle training than in the following periods. The weekly gain rate of stroke volume in rats subjected to muscle training from day 21 of birth are more uniform in the period of 21 to 42 days and 42 to 70 days.

The analysis of the growth rate of cardiac output in rats subjected to muscle training from day 21 and 14 of birth also found a certain difference. According to the researches [1,12], muscle training of rats started from day 21 of birth leads to an increase in cardiac output by 40.0 ml/min (P<0.05) by day 42. According to our information, muscle training started from day 14 of birth contribute to the increase in CO by 73.7 ml/min (P<0.05) by day 42 of rats' life. This value was 1.8 times higher as compared with CO indicators of rats subjected to muscle training from day 21 of birth. Consequently, muscle training of rats started from day 14 of birth cause significant changes in cardiac output during the initial stages of training. However, during the subsequent muscle training the growth rate of cardiac output in the same animals IOC slows down considerably.

The analysis of the weekly growth rate of cardiac output revealed that the weekly gain in cardiac output in rats subjected to muscle training from day 21 of birth was 13.3 ml/min during the period of 42-70 days. The weekly gain in cardiac output in the age range of 42 to 70 days increased significantly and was 17.2

ml/min [1,12]. The weekly gain in cardiac output in rats subjected to muscle training from day 14 of birth was high - 18.4 ml/min during the period of up to 42 days. However, the weekly gain in cardiac output in the age range of 42 to 70 days decreased significantly and was only 6.8 ml/min. Therefore, the muscle training organized at the earlier stages of rats ontogenesis provides for more pronounced weekly increase significantly in CO at the initial stage of training, which subsequently slows down considerably. The rats subjected to muscle training from day 21 have not high growth rate of cardiac output at the initial stage of training, which, however, significantly increases later.

Thus, we can conclude subject to the above stated that the indicators of pumping cardiac function in rats subjected to systematic muscle training from day 14 to 70 of birth undergo more substantial changes in the age range of 14 to 42 days, while the indicators of pumping cardiac function in rats subjected to systematic muscle training from day 21 to 70 of birth show significant changes in the age range of 42 to 70 days.

To study both sympathetic and parasympathetic influence on the cardiac pumping function in rats, the animals received Obsidan, Prazosin and atropine through the catheter into the jugular vein.

Administration of Obsidan and Prazosin to rats subjected to muscle training from day 14 to 42 of birth has led to decreased heart rate as compared with the original data, respectively by 83.7 bpm (22.1%) and 39.3 bpm (14.0%) ($P<0.05$). Administration of atropine to the same trained rats caused heartbeat acceleration by 87.7 bpm (22.7%) ($P<0.05$). The subsequent muscle training by swimming of the same rats from day 42 to 70 resulted in lower heart rate response to the introduction of Obsidan and Prazosin. The administration of Obsidan and Prazosin to trained rats on day 70 of birth caused a decrease in heart rate, respectively by 76.0 bpm (21.1%) and 30.2 bpm (10.6%) ($P<0.05$). The administration of atropine to 70-day-old rats subjected to muscle training caused increase in heart rate by 105.8 bpm (29.2%) ($P<0.05$). This heart rate response to the introduction of α, β-AR and M-CR blockers was significantly lower as compared with the response in heart rate recorded at the age of 42 days. Therefore, a decrease in heart rate in the process of systematic muscle training of rats from day 14 to 70 is associated with an increased activity of the vagus nerve at simultaneous reduction in the activity of the sympathetic influence in the regulation of chronotropic heart function. We should also note that both sympathetic and parasympathetic influences in the regulation of heart rate undergo different changes in the process of muscle training of rats. For example, if the sympathetic influence in the regulation of heart rate decreases by 12.7% by day 70 of birth as compared with initial values, then the parasympathetic influence increases by 22.7% ($P<0.05$). These changes in the regulation of heart rate in trained rats are more pronounced as compared with the changes in the regulation of chronotropic heart function of rats kept under unlimited physical activity. It should also be noted that the trained rats in contrast to rats kept under unlimited physical activity had more pronounced changes in the sympathetic influence in the regulation of heart rate during muscle training in the period of 14 to 42 days. For example, if the sympathetic influence in regulation of heart rate decreases by 11.7% in the rained rats in the age range of 14 to 42 days, then in the period of 42 to 70 days its reduction will be only 1.0% ($P<0.05$).

According to the employees of the laboratory of exercise physiology [1,12], the rats subjected to muscle training from day 21 of birth have their heart rate response to the administration of Obsidan and atropine at the age of 70 days equal to 31.2% and 21.6%, respectively ($P<0.05$). According to our data, the 70-day-old rats being subjected to muscle training from day 14 of birth have their heart rate response to the administration of Obsidan and atropine equal to 21.1% and 29.2%, respectively. Consequently, we can conclude that muscle training of rats organized at earlier stages of the animals' ontogenesis leads to a greater reduction in sympathetic effects in the regulation of heart rate.

The rats subjected to muscle training from day 14 of birth have their stroke volume response to the administration of β and α-adrenergic blockers at the age of 42 days equal to 0.051 ml (22.3%) and 0.046 ml (24.5%), respectively ($P<0.05$). Stroke volume response to the administration of M-cholinergic blocker was 0.044 ml (18.8%) ($P<0.05$). Consequently, an insignificant reduction in the sympathetic influence in the regulation of stroke volume occurs during muscle training of rats from day 14 to 42, as compared with the original data. The subsequent muscle training of the same rats from day 42 to 70 days promoted a decrease in stroke volume response to the introduction of Obsidan and atropine. For example, the rained 70-day-old rats have their stroke volume response to the administration of Obsidan and Prazosin equal to 0.056 ml (16.6%) and 0.052 ml (18.5%), respectively ($P<0.05$). The introduction of atropine to the same rats resulted in increased stroke volume by 0.053 ml (15.8%) ($P<0.05$), as compared with the original data. Consequently, a reduction in the sympathetic and parasympathetic influence in the regulation of stroke volume occurs during the subsequent muscle training of rats from day 42 to 70. Thus, the sympathetic influence in the SV regulation in rats subjected to muscle training from day 14 to 42 of birth does not change significantly, as compared with the original data. However, a reduction in the sympathetic and parasympathetic influence in the regulation of stroke volume occurs during the subsequent muscle training of the same rats until day 70 of birth. We should also note that the sympathetic influence in the SV regulation in trained 70-day-old rats was higher than in rats kept under unrestricted physical activity.

According to other researches [1,12], the rats subjected to muscle training from day 21 of birth have their stroke volume response to the administration of Obsidan and atropine at the age of 70 days equal to 29.8% and 18.0%, respectively. According to our data, the 70-day-old rats being subjected to muscle training from day 14 of birth have their stroke volume response to the administration of Obsidan and atropine equal to 16.6% and 15.8%, respectively. Consequently, we can conclude that muscle training of rats organized at earlier stages of the animals' ontogenesis leads to a greater reduction in both sympathetic and parasympathetic effects on stroke volume.

Heart rate (bpm) of rats subjected to various physical activity

Age	Animals quantity	Unrestricted physical activity	Muscle training	Muscle training - UPA
14 days	20	380.3 ± 7.71		
42 days	19	438.3* ± 9.58	377.4±7.72	
70 days	55	427.2 ± 8.04	358.5±5.38	
210 days	44	405.7*± 8.87		364.5±7.78

* - significant difference, as compared with the values of the previous group (P< 0.05).

Stroke volume (ml) of rats subjected to various physical activity

Age	Animals quantity	Unrestricted physical activity	Muscle training	Muscle training - UPA
14 days	19	0.042 ± 0.003		
42 days	18	0.109* ± 0.012	0.238* ± 0.018	
70 days	54	0.234*± 0.011	0.327*±0.0014	
210 days	35	0.317* ± 0.011		0.397*±0.014

* - significant difference, as compared with the values of the previous group (P< 0.05).

Cardiac output (l/min) of rats subjected to various physical activity

Age	Animals quantity	Unrestricted physical activity	Muscle training	Muscle training - UPA
14 days	20	15.9 ± 2.85		
42 days	19	47.7 *± 4.92	89.7 *± 3.97	
70 days	105	99.9*±4.19	117.0*± 6.11	
210 days	44	128.1*± 8.62		145.71*± 9.46

* - significant difference, as compared with the values of the previous group (P< 0.05).

Heart rate response (%) of rats subjected to various physical activity with the blocked adrenergic and cholinergic receptors

Age	Physical activity regimen	Heart rate response (%)		
		With Obsidan	With Prazosin	With atropine
2 weeks	UPA	33.8±2.3	16.0±2.4	6.5±1.8

6 weeks	UPA TR	29.1±2.6* 22.1±2.5*	14.6±2.3 14.0±2.5	12.1±2.2* 22.7±1.7*
10 weeks	UPA TR	26.3±1.3* 21.1±2.4*	13.8±3.8 10.6±2.3	21.6±1.6* 29.2±1.8*
30 weeks	UPA TR-UPA	29.0±1.7* 24.0±1.4*	10.9±3.3 11.8±4.2	23.6±2.1* 23.7±1.7*

Note * - significant difference, as compared with the values of the previous group (P< 0.05).

Stroke volume response (%) of rats subjected to various physical activity with the blocked adrenergic and cholinergic receptors

Age	Physical activity regimen	Stroke volume response (%)		
		With Obsidan	With Prazosin	With atropine
2 weeks	UPA	18.5±3.3	26.6±4.8	35.8±3.4*
6 weeks	UPA TR	17.2±2.9* 22.3±3.1*	21.6±4.4 24.5±3.3	23.5±2.1* 18.8±3.3*
10 weeks	UPA TR	13.6±207* 16.6±108*	17.3±4.8 18.5±6.7	18.6±2.4* 15.8±2.1*
30 weeks	UPA TR-UPA	12.3 ±2.7* 14.9±1.8*	16.1±4.8 16.7±6.5	23.2±3.4* 16.4±2.1*

Note * - significant difference, as compared with the values of the previous group (P< 0.05).

SUMMARY

- Regular muscle training organized at the early stages of rats' postnatal development causes significant changes in the indicators of cardiac pumping function in the age range of 14 to 42 days, whereas the indicators of cardiac pumping function in animals subjected to unlimited physical activity undergo more pronounced changes during the period of 42-70 days.
- Regular muscle training started at the early stages of rats' postnatal development has a significant impact on the mechanisms of extracardiac regulation of the cardiac pumping function.

CONCLUSION

Based on the results of our studies we may conclude that the indicators of pumping cardiac function in rats subjected to systematic muscle training from day 21 to 70 of birth undergo more substantial changes in the age range of 42 to 70 days. Whereas, the indicators of pumping cardiac function in animals subjected to muscle training from day 14 to 70 of birth changed largely in the age range of 14 to 42 days. Moreover, muscle training of rats started on day 14 of birth result in more pronounced changes in the regulation of pumping cardiac function than the muscle training started on day 21 of birth. Consequently, the indicators of the cardiac pumping function and the regulation mechanisms change largely during muscle training of rats started at the earlier stages of their postnatal development.

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