ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

The Reaction of Blood Stroke Volume of Sympathectomized Rats to The Stimulation of Vagus Nerves.

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ABSTRACT

We have studied the reaction of blood stroke volume to unilateral stimulation of the right or left vagus nerve as well as to the instantaneous reciprocal stimulation of vagus nerves in the postnatal ontogenesis of intact sympathectomized rats. We have found age related peculiarities of how the heart of sympathectomized species reacts to electrical stimulation of the vagus nerve. We have established age properties of the heart's reaction of rats to electrical stimulation of vagus nerves in the conditions of pharmacological sympathectomy. Sympathectomized rats of the ages under consideration, excluding only 14-day old species, show lesser levels of blood stroke volume than intact rats, which is probably compensated by higher levels of their cardiac rate. The obtained data concerning the influence of blood stroke volume changes on unilateral right-sided or left-sided stimulation confirm asymmetry of the vagus nerves' influence on heart activity. The main claim is that regulation of the heart inotropic function is conducted to a larger extent by the left vagus nerve. The results of our research of intact and sympathectomized rats reveal the active role of the sympathetic section of the vegetative nervous system in the regulation of blood stroke volume in the course of activation of the parasympathetic channel of heart regulation. Compensating increase in the influence of the parasympathetic section of the vegetative nervous system alongside growing activity of the sympathetic channel is probably the mechanism of protecting heart from overpressure.

Keywords: heart, blood stroke volume, vagus nerve, sympathetic nerve, ontogenesis, sympathectomy.

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INTRODUCTION

There are several points of view regarding the interrelation between the influence of sympathetic and parasympathetic nerves on the heart such as antagonism, synergism, intercompensation and accentuated antagonism [[1],[2]]. Single electrical stimulation of these nerves can give the opposite results, which can be attributed to a laboratory phenomenon [[3],[4],[5]].

Some researchers explain the obtained divergent results by the number of fibers involved in the implementation of regulatory influences on the heart [[6], [7]]. In some species of animals, the vagus nerves (VN) contain a large number of sympathetic fibers [[8]], therefore the acceleration of the heart rate during VN stimulation may be associated with excitation of the sympathetic conductors.

Thus, the research with stimulation [[9],[10],[11]], exclusion or blockage of one of the divisions of the autonomic nervous system in animals is an experimental model [[2],[12],[13]], which helps to find answers to many questions [[14],[15],[16]]. To study the role of the central nervous parasympathetic influences on the heart we applied the stimulation, transection of the VN, and administration of blockers [[3],[17]], and the exclusion of the sympathetic influences can be effectively achieved through the pharmacological sympathectomy of animals [[18],[19],[20]]. Most of the researches are devoted to the investigation of the effect of sympathectomy on the chronotropic heart function [[3]], and the data on the effect of sympathectomy on stroke volume (SV) in postnatal ontogenesis are rare [[17],[21]], which has determined the relevance of our research.

Objective of the research was to study the age-specific characteristics of SV changes in intact and sympathectomized rats with right-handed, left-handed, as well as simultaneous bilateral stimulation of the VN in postnatal ontogenesis.

RESEARCH METHODS

The experiments were conducted on intact and sympathectomized laboratory rats aged 14, 21, 28, 42, 70, 56, 70 and 120 days. Sympathectomy was carried out by daily administration of guanethidine sulfate solution heated to 38ºC based on 10 ml/kg of body weight for 28 days after birth. Guanethidine sulfate solution was prepared in saline at a concentration of 2.5 mg/ml. The control group consisted of animals of similar age, kept under identical conditions. The rats were anesthetized with 25% urethane solution based on 1.2 g/kg of body weight and fixed on the operating table, where the VN was dissected with the use of binocular microscope MBS-1. Vagus nerves were stimulated with platinum electrodes on the stimulator ЕСЛ-2. The frequency of the stimulation current, which caused a significant slowing of the heart rate, was adjusted individually for each rat. The amplitude of the irritating pulses was 0.5-5, frequency – 1.12 Hz, and duration – 5 ms. To analyze the cardiac activity, we recorded ECG and differentiated rheogram for 15 minutes after each experimental intervention. We processed the results in an integrated electrophysiology laboratory, which is based on the method of ECG processing by R.M. Baevskii, with the option to process the differentiated rheogram for calculating stroke volume (SV) by the Kubicek formula modified as [[21]].

Statistical processing of findings was performed by Student t-test and a paired test using Microsoft Excel.

RESULTS AND DISCUSSION

In order to identify the level of interaction and the degree of relation of extra-cardiac nerves in the regulation of cardiac activity, define the role of the sympathetic nerves in the cardiac adaptive reactions upon activation of a parasympathetic regulation channel we conducted a study on rats of different age groups after their pharmacological sympathectomy.

According to information received from the sympathectomized rats, the stroke volume is less (Table 1) than in intact rats, which is compensated by higher indices of heart rate, perhaps, in order to maintain the required minute volume of blood flow.

ISSN: 0975-8585

To determine the role of the right and left vagus nerves in the regulation of inotropic cardiac function of the sympathectomized animals we conducted a series of experiments with single right-sided, left-sided and bilateral simultaneous stimulation of both vagus nerves with the threshold current in postnatal ontogenesis.

During right-sided stimulation of vagus nerves with the threshold current in the sympathectomized preweaning rats in contrast to the intact rats (14- and 21-day-old) during stimulation the stroke volume decreases, which, apparently, is a consequence of possible impairments of compensatory reactions after sympathectomy. The negative inotropic response to stimulation is manifested in the 28-and 42-day-old sympathectomized animals, but this decline is less pronounced than that in rats aged 14 and 21 days (Table 1). 56-day-old sympathectomized rats, as well as the intact rats, in response to stimulation of the right vagus nerve show positive inotropic response, but this increase is weakly pronounced. Perhaps, this reaction of SV to stimulation of vagus nerve in 56-day-old rats is associated with activation of the endocrine system during puberty, which is also confirmed by literature data.

Table 1: Changing stroke volume (ml) in rats of different age during stimulation of vagus nerves (M±m)

Age (days)		n	Right-side stimulation		Left-side stimulation		Bilateral stimulation	
			init.	with stimul.	init.	with stimul.	init.	with stimul.
14	intact	10	0.024± 0.001	0.024± 0.001	0.023± 0.0001	0.024± 0.001	0.023± 0.001	0.024± 0.001
	sympathect.	19	0.026± 0.001	0.024± 0.001	0.026± 0.001	0.026± 0.001	0.027± 0.001	0.026± 0.001
21	intact	12	0.062± 0.007	0.062± 0.005	0.059± 0.005	0.059± 0.005	0.056± 0.006	0.056± 0.006
	sympathect.	12	0.057± 0.003	0.052± 0.002	0.056± 0.004	0.055± 0.004	0.059± 0.005	0.056± 0.005
28	intact	11	0.084± 0.004	0.078± 0.005	0.085± 0.004	0.081± 0.003	0.082± 0.003	0.079± 0.004
	sympathect.	18	0.071± 0.003	0.069± 0.004	0.069± 0.004	0.071± 0.003	0.072± 0.003	0.067± 0.003
42	intact	12	0.112± 0.004	0.106± 0.005	0.114± 0.007	0.116± 0.005	0.121± 0.008	0.109± 0.006
	sympathect.	17	0.090± 0.005	0.087± 0.006	0.090± 0.006	0.091± 0.006	0.090± 0.003	0.087± 0.004
56	intact	12	0.130± 0.005	0.138± 0.006	0.133± 0.007	0.131± 0.008	0.136± 0.006	0.138± 0.008
	sympathect.	17	0.103± 0.004	0.105± 0.003	0.109± 0.005	0.107± 0.006	0.112± 0.005	0.104± 0.005
70	intact	12	0.135± 0.004	0.131± 0.004	0.150± 0.007	0.139± 0.004	0.149± 0.008	0.151± 0.008
	sympathect.	13	0.109± 0.004	0.108± 0.004	0.107± 0.003	0.108± 0.003	0.114± 0.002	0.101± 0.003***
120	intact	19	0.183± 0.007	0.183± 0.008	0.195± 0.008	0.176± 0.010**	0.195± 0.006	0.193± 0.009
	sympathect.	13	0.177± 0.005	0.176± 0.007	0.181± 0.005	0.162± 0.005***	0.198± 0.004	0.175± 0.004***

Note: the significance of differences as compared with initial values before stimulation * p<0.05; ** p<0.01; *** p<0.001

Both 70-day-old and adult 120-day-old sympathectomized animals, as well as the control rats of the same age, showed no significant changes in the SV at stimulation point of the right vagus nerve (Table 1).

A pronounced negative inotropic response to stimulation of the left vagus nerve was observed in the studied groups of rats with their aging. Both intact and sympathectomized preweaning and prepubertal rats had virtually no changes in SV during the stimulation of the left vagus nerve, while in 70-day-old and adult rats the stroke volume reduced. At the same time, this reduction of stroke volume in adult rats during stimulation of the left vagus nerve is significant (p <0.001).

Thus, this fact confirms once again the asymmetric influences of vagus nerves on cardiac activity, indicating that the regulation of the inotropic function of the heart is to a greater extent performed by the left vagus nerve, and the asymmetry starts to manifest itself in the pubertal period [[18]].

Simultaneous bilateral stimulation of vagus nerves in intact 14-day-old rats causes some positive inotropic response (4.4%). 28- and 42-day-old rats show decline in SV, which confirms the turning age of late preweaning and prepubertal periods of the development of cardiac regulation. Both intact pubertal rats (day 56), mature rats (70-day-old) and adult animals at the time of stimulation have no significant changes in stroke volume observed.

The single-moment bilateral stimulation of vagus nerves in sympathectomized animals causes reduction in stroke volume. At the same time, during growth and development, the severity of the negative reaction of stroke volume increases. For example, reduction in stroke volume in the preweaning and prepubertal rats (14- to 42-day-old) at the point of stimulation is 5-7%, while 70-day-old and adult rats show more pronounced reduction (8-12%) that is significant ($p<.001$).

Probably, these cardiac reactions of sympathectomized rats to stimulation of vagus nerves are associated with the destruction of the sympathetic nervous system. At the same time, the excitation of the sympathetic nervous system at the point of vagus nerve stimulation in intact animals, especially in adults, allows to maintain the desired level of cardiac output.

Significant changes in the parameters of variation pulsogram, reflecting the state of parasympathetic (ΔH) and sympathetic (CMO) nervous system, are observed during stimulation of the vagus nerves, which indicates the strengthening of parasympathetic and weakening of sympathetic nerve influences at the point of stimulation. Further, they quickly recover to 30 s and subsequently remain virtually unchanged.

SUMMARY

Analysis of cardiac activity in the groups of studied animals has shown that the sympathectomized rats have less volume of cardiac output than the intact, which is compensated by higher heart rate values.

During stimulation of the right vagus nerve in intact and sympathectomized rats, the stroke volume does not change significantly, and these fluctuations are not significant. Stimulation of the left vagus nerve, unlike the right, in adult intact and sympathectomized rats, on the background of significant reduction in heart rate, causes a significant decrease in the stroke volume. Left-sided stimulation of vagus nerve in the growing intact and sympathectomized rats and on the background of the expressed slowing of the heart rate does not cause changes in stroke volume. The findings confirm the asymmetric influence of vagus nerves on the cardiac activity, indicating that the regulation of inotropic function of the heart is to a greater extent performed by the left vagus nerve.

Simultaneous bilateral stimulation of the vagus nerves in intact animals of all ages causes no significant changes in stroke volume. Simultaneous stimulation of both vagus nerves in the sympathectomized animals causes increase in severity of negative inotropic effect with aging. For example, the preweaning and prepubertal rats showed some reduction in stroke volume, which in 70- and 120-day-old sympathectomized rats achieves significant changes as compared with the initial values.

CONCLUSION

Thus, the results of studies conducted in intact and sympathectomized rats indicate the prevailing impact of the sympathetic division of the autonomic nervous system in the regulation of the stroke volume as compared with the heart rate upon activation of parasympathetic channel of cardiac regulation.

Conflict of Interests

The author declares that the provided information has no conflicts of interest.

ISSN: 0975-8585

ACKNOWLEDGEMENTS

The work is performed according to the Russian Government Program of Competitive Growth of Kazan Federal University

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