Parasympathetic Cardiac Effects in Sympathectomized Rats

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In adult sympathectomized rats the right and left vagus nerves exhibited asymmetric effects on heart rate and strength of cardiac contractions. After vagotomy, the heart rate and stroke volume remained high in sympathectomized rats, but returned to normal in intact animals. The sympathetic nervous system plays a role in postvagotomic tachycardia. Sympathectomized rats were characterized by higher reactivity of cardiac β-adrenoceptors to propranolol compared to intact animals.

Key Words: *vagus nerve; heart; stroke volume; sympathectomy; stimulation*

Normal function and adaptation of the organism to environmental changes can be attained under conditions of a certain ratio between sympathetic and parasympathetic influences on the heart. Adrenergic and cholinergic regulation of the heart rate (HR) and strength of cardiac contractions are studied separately. In these experiments, one of the compartments of the autonomic nervous system is blocked or damaged. Rats sympathectomized with guanethidine in the early period of life served as the model to study functional activity of the sympathetic nervous system. Most studies were devoted to estimate the effect of sympathectomy on HR [3,4]. Little is known about the response of HR and stroke volume (SV) in sympathectomized animals to various factors [1,9,10].

Here we studied changes in SV and HR in intact (IR) and sympathectomized rats (SR) during consecutive and simultaneous bilateral stimulation of the vagus nerves before or after vagotomy and propranolol administration.

MATERIALS AND METHODS

Experiments were performed on 32 adult male and female rats aging 120 days. The animals were divided into control (n=19) and treatment groups (n=13). Sympathectomy was induced by administration of warm (38°C) guanethidine sulfate in a daily dose of 10 ml/kg (2.5 mg/ml Isobarin in physiological saline) for 28 days after birth. Control animals of the same age were kept under similar conditions.

The rats were narcotized with 25% urethane in a dose of 1.2 g/kg and fixed on an operation table. The vagus nerves were prepared under a MBS-1 binocular microscope. The nerves were stimulated via platinum electrodes using an ESL-2 stimulator. The frequency of electric current producing significant HR decrease was selected individually for each rat. The amplitude, frequency, and duration of stimulation were 0.5-5 V, 1-12 Hz, and 5 msec, respectively.

β-Adrenoceptor antagonist propranolol (0.8 mg/kg) was injected into the femoral vein. ECG and differential rheogram were recorded for 15 min after each treatment to study cardiac activity. The data were processed on a complex electrophysiological device based on the method of R. M. Baevskii of computer processing of ECG [2]. Differential rheogram was recorded to calculate SV by the equation [12] with modifications [1,8].

The results were analyzed by Student's t test and pairwise Wilcoxon test.

RESULTS

Pharmacological sympathectomy with guanethidine sulfate had a strong effect on cardiac activity. SV

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TABLE 1. HR in IR and SR during Stimulation of Vagus Nerves before and after Vagotomy and Propranolol Administration (bpm, $M \pm m$)

Treatment	Group	Basal values	During stimulation	Recovery period			
				30 sec	5 min	10 min	15 min
Right-sided stimulation	IR	341.0±4.7	316.0±4.7***	339.0±4.7	339.0±5.0	340.0±5.1	338.0±5.4
	SR	372.0±6.4	339.0±6.4***	376.0±6.2	369.0±6.7	367.0±6.5	367.0±6.7
Left-sided stimulation	IR	341.0±6.1	317.0±6.1***	338.0±6.5	339.0±5.9	339.0±5.9	340.0±5.9
	SR	368.0±6.4	336.0±5.7***	362.0±6.0	360.0±6.8	359.0±6.9	358.0±6.7
Bilateral stimulation	IR	345.0±4.2	321.0±3.9***	341.0±4.2	345.0±4.6	347.0±4.7	348.0±4.6
	SR	362.0±6.1	334.0±5.1***	364.0±6.2	360.0±6.1	360.0±6.0	360.0±5.7
Vagotomy	IR	347.0±5.4	—	359.0±3.9*	361.0±3.2**	353.0±3.8	349.0±4.0
	SR	360.0±5.9	—	380.0±7.1**	391.0±7.8**	382.0±6.4**	383.0±6.3**
Bilateral stimulation after vagotomy	IR	348.0±6.0	324.0±5.5***	346.0±6.1	346.0±6.3	346.0±6.4	348.0±6.8
	SR	393.0±6.2	352.0±6.0***	392.0±6.5	388.0±6.9	389.0±7.7	389.0±7.9
Propranolol administration	IR	349.0±6.2	—	310.0±5.7***	283.0±6.1***	277.0±6.2***	275.0±6.0***
	SR	395.0±7.2	—	360.0±5.8***	318.0±4.0***	314.0±4.4***	313.0±4.6***
Bilateral stimulation after vagotomy and propranolol administration	IR	275.0±6.0	257.0±5.6**	275.0±5.9	273.0±6.4	273.0±6.4	273.0±6.7
	SR	313.0±4.5	285.0±5.2***	314.0±4.2	310.0±3.8	309.0±4.2	309.0±4.2

Note. Here and in Table 2: *$p<0.05$, **$p<0.01$, and ***$p<0.001$ compared to the basal value.

TABLE 2. SV in IR and SR during Stimulation of Vagus Nerves before and after Vagotomy and Propranolol Administration (ml, *M*±*m*)

Treatment	Group	Basal values	During stimulation	Recovery period			
				30 sec	5 min	10 min	15 min
Right-sided stimulation	IR	0.183±0.007	0.183±0.008	0.191±0.009	0.188±0.008	0.187±0.008	0.193±0.008
	SR	0.177±0.005	0.176±0.007	0.176±0.004	0.181±0.006	0.196±0.005	0.188±0.004
Left-sided stimulation	IR	0.195±0.008	0.176±0.010**	0.180±0.010	0.190±0.009	0.197±0.009	0.196±0.008
	SR	0.181±0.005	0.162±0.005***	0.174±0.006	0.180±0.005	0.190±0.006	0.191±0.005
Bilateral stimulation	IR	0.195±0.006	0.193±0.009	0.195±0.008	0.194±0.007	0.196±0.006	0.201±0.007
	SR	0.198±0.004	0.175±0.004***	0.194±0.004	0.203±0.002	0.204±0.004	0.198±0.006
Vagotomy	IR	0.199±0.010	—	0.186±0.011	0.194±0.010	0.197±0.010	0.204±0.010
	SR	0.199±0.004	—	0.204±0.004	0.193±0.003	0.200±0.005	0.211±0.005*
Bilateral stimulation after vagotomy	IR	0.207±0.015	0.204±0.015	0.206±0.015	0.204±0.014	0.204±0.014	0.205±0.013
	SR	0.219±0.003	0.224±0.006	0.217±0.002	0.220±0.003	0.212±0.002	0.206±0.002*
Propranolol administration	IR	0.197±0.008	—	0.193±0.007	0.219±0.011*	0.213±0.013	0.202±0.011
	SR	0.208±0.002	—	0.217±0.005	0.257±0.001***	0.241±0.004***	0.240±0.004***
Bilateral stimulation after vagotomy and propranolol administration	IR	0.214±0.005	0.199±0.004**	0.214±0.006	0.186±0.010**	0.187±0.010**	0.195±0.004
	SR	0.238±0.004	0.191±0.009***	0.217±0.008*	0.225±0.007	0.235±0.006	0.213±0.009**

decreased, while HR increased in SR compared to IR (Table 1).

Stimulation of the right vagus nerve with threshold current decreased HR in IR and SR, but it returned to normal by the 30th second. SV in animals of both groups remained unchanged during stimulation of the right vagus nerve, but slightly increased by the 15th minute (Table 2).

In IR stimulation of the left vagus nerve with threshold current decreased HR and SV, but these parameters returned to normal after 30 sec and 15 min, respectively. In SR, this treatment was followed by a short-term decrease in HR and SV. HR in SR returned to normal by the 30th second and remained practically unchanged in the follow-up period. SV in SR progressively increased and exceeded the basal level by 5.5% after 15 min.

As differentiated from stimulation of the right vagus nerve, stimulation of the left vagus nerve in adult IR and SR was accompanied by a significant decrease in HR and SV. These data reflect asymmetry in the effects of the vagus nerve on HR and strength of cardiac contractions in SR. Therefore, the strength of cardiac contractions is primarily regulated by the left vagus nerve. Similar results were obtained on intact animals under various experimental conditions [6,7,10].

Simultaneous bilateral stimulation of the left and right vagus nerves in IR and SR with threshold current was followed by a short-term decrease in HR. SV decreased slightly in IR, but significantly in SR (by 11.6%, $p<0.001$). Parameters of cardiac activity in animals of both groups returned to normal by the 30th second. The observed peculiarities in the reaction of HR and SV in SR induced by vagal nerve stimulation are probably determined by destruction of the sympathetic nervous system. Compensatory excitation of the sympathetic nervous system during nerve stimulation in IR probably maintains cardiac output at an optimal level.

Simultaneous bilateral vagotomy in adult IR was followed by a significant increase in HR and slight decrease in SV. These parameters returned to normal in the follow-up period. HR and SV in SR significantly increased after bilateral vagotomy and remained high by the end of the study (Table 1, 2).

Simultaneous electrostimulation of distal ends of the vagus nerves was performed to evaluate the role of efferent nerve fibers in the vagus nerves and to exclude reflex influences during stimulation of intact vagus nerves.

Bilateral stimulation of the distal ends of the vagus nerves in adult IR and SR with threshold current produced a short-term decrease in HR ($p<0.001$), but had little effect on SV. The strength of electric current to produce a negative chronotropic effect was much higher compared to that observed during stimulation of intact vagus nerves. These data indicate that afferent fibers in the vagus nerve play a role in the reflex decrease in HR during stimulation. The decrease in HR may be also related to activation of the sympathetic nervous system, which activates intracardiac postganglionic parasympathetic neurons [5,13].

Propranolol administration to 120-day-old IR and SR after bilateral vagotomy was followed by a progressive decrease in HR (by the 15th minute, $p<0.001$). SV significantly increased after 5 min, but slightly decreased by the end of study. Most significant changes in HR and SV were observed in SR.

Stimulation of distal ends in the vagus nerves in IR and SR after blockade of β-adrenoceptors with propranolol was followed by a significant short-term decrease in HR. SV decreased under these conditions, returned to normal in the follow-up period, and decreased again by the 15th minute. As distinct from bilateral stimulation of intact vagus nerves and distal nerve segments, stimulation of distal segments in the vagus nerves of IR and SR after β-adrenoceptor blockade was followed by a significant decrease in HR and SV. The peculiar changes in the parameters of cardiac activity in response to propranolol indicate that β-adrenoceptors are involved in the regulation of cardiac activity not only in IR, but also in SR.

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