Effect of Electrical Stimulation of Vagus Nerves on Cardiac Activity in Sympathectomized Rats during Postnatal Ontogeny

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In intact rats vagal stimulation reduced heart rate, but had no effect on stroke volume. In sympathectomized animals this treatment decreased both the heart rate and stroke volume. Sympathectomized rats displayed higher sensitivity to vagal nerve stimulation compared to intact animals of the same age (except for rats aging 21 and 56 days).

Key Words: *vagus nerve; rat; stroke volume; sympathectomy; stimulation; ontogeny*

There are ambiguous data on the effect of vagal nerve (VN) stimulation that can increase or decrease the heart rate (HR) [9]. There are various hypotheses on the mechanisms of HR acceleration during VN stimulation, *e.g.* quantitative principle of regulatory influences on the heart [10]. Moreover, in some animal species VN includes numerous sympathetic fibers [3]. Therefore, the increase in HR during VN stimulation can result from activation of the sympathetic fibers. Experiments with complete or partial blockade of the sympathetic or parasympathetic systems are of considerable interest. Central parasympathetic influences on the heart can be blocked by VN transection. However, surgical approach to the blockade of sympathetic influences is difficult and does not produce the desirable effect [5,12]. Pharmacological sympathectomy prevents adrenergic modulation of cardiac activity [7]. Most studies were denoted to the effect of sympathectomy on HR [4,8]. Little is known about the effect of sympathectomy on stroke volume (SV) and HR during postnatal ontogeny [1].

Here we studied age-related differences in changes of SV and HR in intact and sympathectomized rats produced by simultaneous bilateral stimulation of VN during postnatal ontogeny.

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MATERIALS AND METHODS

Experiments were performed on 197 male and female outbred rats. The animals were divided into control (n=88) and experimental groups (n=109). We examined rats of 7 age groups (14, 21, 28, 42, 56, 70, and 120 days). Sympathectomy was produced by daily administration of warm (38°C) guanethidine sulfate in a dose of 10 ml/kg for 28 days after birth [7]. Guanethidine sulfate was dissolved in physiological saline containing isobarin in a concentration of 2.5 mg/ml. The control group included animals of the same age kept under similar conditions. The rats were narcotized with 25% urethane (1.2 g/kg) and fixed on an operating table. VN were prepared under a MBS-1 binocular microscope. VN were stimulated via platinum electrodes using an ESL-2 stimulator. Frequency of the stimulating current producing significant decrease in HR was selected individually for each rat. The amplitude, frequency, and duration of stimuli were 0.5-5 V, 1-12 Hz, and 5 msec, respectively. ECG and differential rheogram were recorded for 15 min after each treatment to assay cardiac activity. The data were processed by the method of R. M. Baevskii [2]. SV

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was calculated as described previously [11] with modifications [6].

The results were analyzed by Student's *t* test and pairwise test (Microsoft Excel software).

RESULTS

Simultaneous bilateral stimulation of VN in intact and sympathectomized rats of various ages significantly reduced HR (Table 1). It should be emphasized that in sympathectomized animals HR drop was achieved at or lower power of electric current than in intact rats.

Simultaneous bilateral VN stimulation decreased HR in 14-day-old intact and sympathectomized rats ($p<0.001$). SV slightly increased in intact rats, but then decreased and rapidly returned to normal (30th second) in sympathectomized animals.

In 21-day-old intact rats SV remained unchanged during bilateral stimulation of VN, but slightly increased and rapidly returned to normal 30 sec after treatment. In sympathectomized animals SV slightly decreased during VN stimulation, increased by 7.4% by the 30th second, and returned to normal 15 min after treatment.

Simultaneous stimulation of VN produced a short-term decrease in SV in 28-day-old intact rats (by 4.2%, Table 1). In sympathectomized animals SV decreased by 6.4% during VN stimulation, progressively increased by the 15th minute, and surpassed the baseline level by 5.9%.

In 42-day-old rats of both groups simultaneous stimulation of VN was accompanied by a short-term decrease in SV. In intact rats SV decreased more significantly than in sympathectomized animals (Table 1).

In 56-day-old intact rats SV did not change during bilateral stimulation of VN, increased by 5.4% 30 sec after treatment, and then remained above the baseline level. In sympathectomized animals SV decreased by 7.1% during bilateral stimulation of VN, but 30 sec after treatment it increased to 0.117±0.005 ml and surpassed the baseline level by 4.5%.

Simultaneous stimulation of VN had no effect on SV in 70-day old intact rats. In sympathectomized

TABLE 1. HR (bpm) and SV (ml) in Intact and Sympathectomized Rats of Various Ages during Simultaneous Bilateral Stimulation of VN (*M*±*m*)

Age, days	HR (bpm)		SV (ml)	
	baseline level	stimulation	baseline level	stimulation
14-day-old				
intact (*n*=10)	372.0±4.2	348.0±4.4*	0.023±0.001	0.024±0.001
sympathectomized (*n*=19)	378.0±7.5	354.0±6.2*	0.027±0.001	0.026±0.001
21-day-old				
intact (*n*=12)	392.0±7.8	357.0±9.1*	0.056±0.006	0.056±0.006
sympathectomized (*n*=12)	429.0±4.8	400.0±4.8*	0.059±0.005	0.056±0.005
28-day-old				
intact (*n*=11)	386.0±9.1	351.0±9.2*	0.082±0.003	0.079±0.004
sympathectomized (*n*=18)	435.0±2.7	402.0±2.9*	0.072±0.003	0.067±0.003
42-day-old				
intact (*n*=12)	382.0±11.8	354.0±11.5*	0.121±0.008	0.109±0.006
sympathectomized (*n*=17)	395.0±6.4	367.0±6.8*	0.090±0.003	0.087±0.004
56-day-old				
intact (*n*=12)	387.0±10.3	354.0±8.9*	0.136±0.006	0.138±0.008
sympathectomized (*n*=17)	391.0±10.3	362.0±10.3**	0.112±0.005	0.104±0.005
70-day-old				
intact (*n*=12)	372.0±8.6	345.0±6.7*	0.149±0.008	0.151±0.008
sympathectomized (*n*=13)	389.0±2.6	360.0±2.8*	0.114±0.002	0.101±0.003*
120-day-old				
intact (*n*=19)	345.0±4.2	321.0±3.9*	0.195±0.006	0.193±0.009
sympathectomized (*n*=13)	362.0±6.1	334.0±5.1*	0.198±0.004	0.175±0.004*

Note. *$p<0.001$ and **$p<0.01$ compared to baseline.

animals SV decreased by 11.3% ($p<0.001$), but increased by the 5th minute after treatment (Table 1).

SV remained unchanged during simultaneous stimulation of VN in intact adult rats. In sympathectomized animals SV decreased from 0.198±0.004 to 0.175±0.004 ml ($p<0.001$), but returned to normal 30 sec after treatment (Table 1).

Our results show that simultaneous stimulation of both VN decreased SV in sympathectomized sucking and prepubertal rats (days 14-42 of life). The decease in SV was statistically significant in 70-day-old rat pups and most pronounced in adult animals. In intact rats this treatment had no effect on SV. Probably, this reaction of the heart to VN stimulation in sympathectomized animals is related to destruction of the sympathetic nervous system. Activation of the sympathetic nervous system during VN stimulation in intact rats (especially in adult animals) maintained the circulation volume at a level necessary for vital activity.

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