Effects of Vagotomy on Cardiac Function in Rats during Postnatal Ontogeny

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We studied age-related peculiarities of changes in stroke volume, heart rate, and parameters of variational pulsogram after bilateral vagotomy in rats. Positive responses of stroke volume and heart rate to vagotomy appeared on postnatal week 4.

Key words: *vagus nerve*; *rat*; *stroke volume*; *heart rate variability, ontogeny*

Vagus nerve (VN) normally exerts a pronounced tonic inhibitory effect on the heart, which is confirmed by heart rate (HR) acceleration after bilateral vagotomy [1,4,7]. The degree of this vagotomy-induced tachycardia greatly varies in different animal species [7], while the existence of vagal tone in rats is disputable [4]. Some authors reported tonic effect of VN on rat heart at rest [1,3].

Postnatal development of sympathetic and parasympathetic innervation plays an important role in age-related peculiarities of cardiac function [9]. It is accepted that parasympathetic innervation of the heart develops earlier than sympathetic innervation during both phylogeny and ontogeny [12]. Age-related changes in cardiac functions are determined by strengthening of the parasympathetic and weakening of sympathetic influences [5].

Our aim was to study age-dependent changes in stroke volume (SV), HR and heart rate variability after bilateral vagotomy in rats at various stages of postnatal ontogeny.

MATERIALS AND METHODS

Experiments were carried out on 54 random-bred albino rats aged 2, 3, 4, 6, and 8 weeks and 120 days (adults). The rats were intraperitoneally narcotized with urethane (800 mg/kg,) and tied to the operation table. Both VN were separated and cut simultaneously. ECG and differential impedance cardiogram were continuously recorded for 60 min. Parameters of cardiac function were analyzed using $Conan_m$-2.0 complex electrophysiological laboratory software.

Variational pulsogram was analyzed according to Baevskii [2]. SV was calculated as described previously [10] with some modification [6].

RESULTS

In 2-week-old rats, bilateral vagotomy reduced HR. This decrease became significant after 5 min, while changes in SV remained negligible (Fig. 1, *b*, *d*). By min 60, HR continued to decrease ($p<0.001$), while SV slightly increased.

The third week of postnatal development in rats is characterized by an increase in motion activity and transition to mixed diet. After bilateral vagotomy HR in these animals gradually decreased ($p<0.001$) against the background of contemporary SV increase ($p<0.05$, Fig. 1, *b*, *d*). This increase in SV can be due to reflex excitation of the sympathetic nervous system resulting from partial deafferentation of the heart after vagotomy [11]. However, experiments with stimulation of the stellate ganglion showed that SV is not modulated by the sympathetic system at this age [1]. Most likely this

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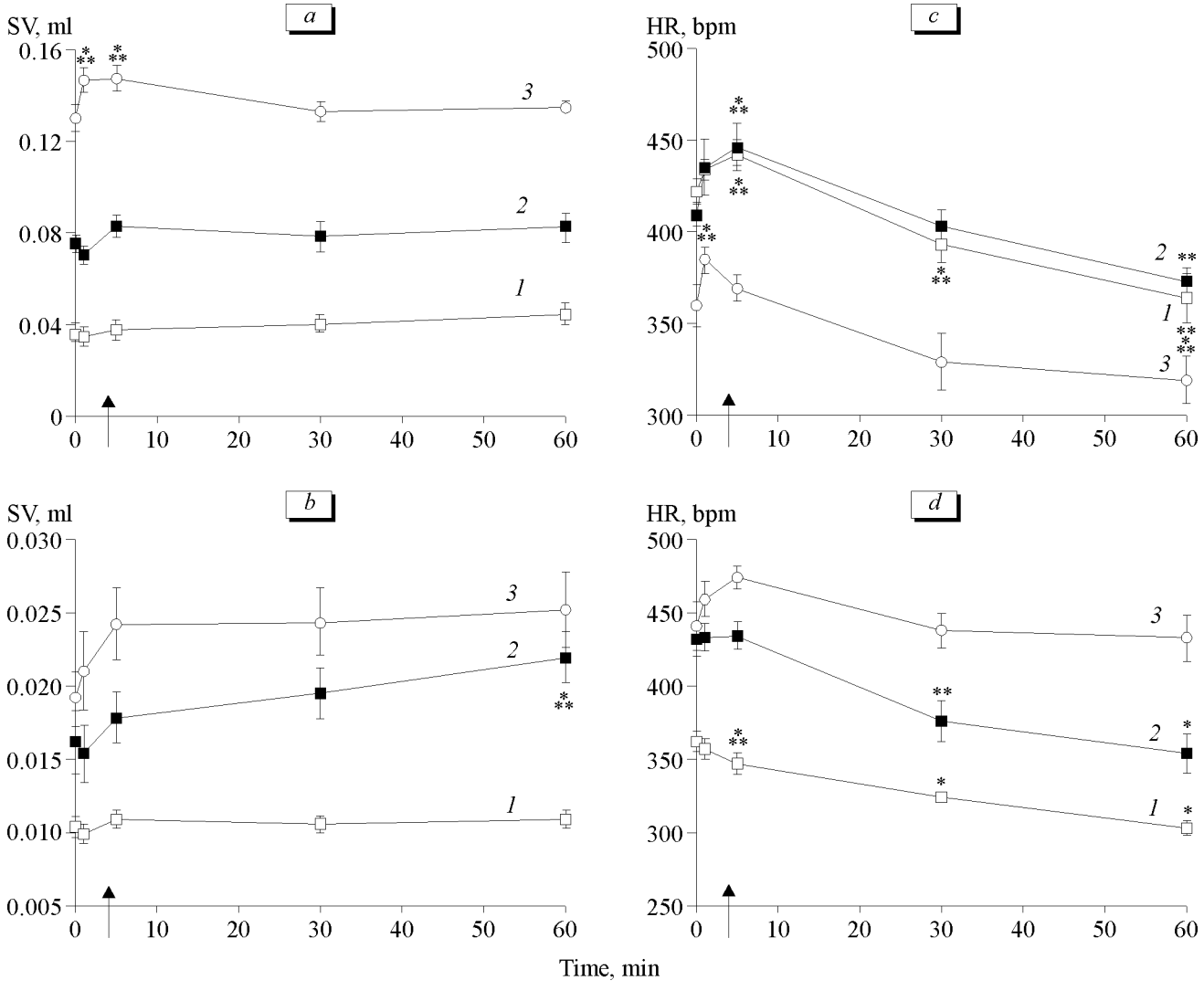

Fig. 1. Changes in stroke volume (SV, *a*, *b*) and heart rate (HR, *c*, *d*) induced by bilateral vagotomy in rats. Arrows show the moment of vagotomy. Age of rats (*a*, *c*): 7 weeks (*1*), 8 weeks (*2*), and 120 days (*3*); *b*, *d*): 2 weeks (*1*), 3 weeks (*2*), and 4 weeks (*3*); *p<0.001, **p<0.01, ***p<0.05 compared to the initial values.

increase in SV is a compensatory response to HR deceleration.

On week 4, bilateral vagotomy induced a slight increase in both SV and HR (Fig. 1, *b*, *d*). HR recovered after few minutes, while SV remained elevated (by 31.2%). This vagotomy-induced response in 4-week-old rats indicates that maturation of the autonomic innervation of the heart is completed at this age [12]. In 6-week-old rats, vagotomy significantly increased HR after 5 min (p<0.05), without significant changes in SV (Fig 1, *a*, *c*). By min 60, HR significantly decreased (p<0.01), while SV slightly increased (by 31.3%).

In 8-week-old rats both HR (p<0.05) and SV (by 9.95%) increased after vagotomy (Fig 1, *a*, *c*). Significant changes in the amplitude of variational pulsogram mode and its variation attested to strengthening of sympathetic and weakening of parasympathetic influences. By 60 min, HR decreased (p<0.05), while SV compensatory increased.

In adults, both HR and SV significantly increased 1 min after vagotomy (p<0.05). On min 5, HR returned to the initial value and then gradually decreased until the end of the observation period (p<0.05, Fig 1, *a*, *c*). SV remained above the initial value. This transient HR increase after bilateral vagotomy can result from blockade of preganglionic parasympathetic input [7] or sympathetic activation in response to cardiac afferent outflow impairment after vagotomy [8]. Cholinoreceptor blockade with atropine increases both HR and SV [6], hence vagotomy affects only tonic vagal influences on the heart. Subsequent recovery and decrease in HR (p<0.05) are compensated by increased SV, which

confirms that the inotropic and chronotropic effects are mediated by different mechanisms involved in homeostasis regulation [1,6].

Thus, in suckling rats (2-3 weeks), bilateral vagotomy induce a slight increase in SV and gradual decrease in HR. Postvagotomy bradycardia at this age is probably determined by sympathetic deficiency.

Parallel rise of HR and SV in response to bilateral vagotomy was first observed on postnatal week 4. This was associated with activation of the sympathetic nervous system and appearance of tonic vagal influences.

Pronounced positive shifts in SV and HR in response to vagotomy were typical of the prepubertal and pubertal periods. These responses probably result from enhanced endocrine function during puberty [11] or the formation of the cardiac sympathetic innervation at this age [9]. It is likely that maturity of cardiac adrenergic innervation is the major factor responsible for the observed peculiarities of cardiovascular response to vagotomy in adult rats.

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