Effect of Vagotomy on Heart Rate in Intact and Sympathectomized Rats of Different Ages

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A comparative analysis of temporal variations of the heart rate variability after cutting and stimulation of the vagus in sympathectomized and intact rats showed that changes in heart rate after bilateral vagotomy in sympathectomized rats are opposite to those in the controls. It is postulated that postganglionic fibers modulate sympathetic influence on intracardiac parasympathetic neurons.

Key Words: *rat; vagus; sympathectomy; heart; stimulation*

Cutting of the vagus nerve leads to a marked decrease in heart rate (HR) in animals and humans [5], although in small rodents the postvagotomy tachycardia is very mild [4], suggesting that acceleration of cardiac rhythm after vagotomy is due to excitation of the sympathoadrenal system in response to stimulation of afferent nerve fibers within the vagus [8], rather than being caused by interruption of parasympathetic tonic activity. It should be noted that 48% of nerve fibers in rat vagus are sympathetic fibers [2], while the content of afferent nerve fibers in the vagus is 14- to 15-fold higher than that of efferent fibers [10].

At the present time, there is controversy over the mechanisms of postvagotomy tachycardia. Some researchers believe that vagotomy leads to a faster HR by activating the sympathetic nervous system [3,8], while others claim that this system is not implicated in the development of postvagotomy tachycardia [7]. Previously, we showed that the initial transient rise of HR is followed by its normalization or even bradycardia. It is impossible to derive any unequivocal conclusion from studies in which the effect of vagotomy on HR in animals with interrupted sympathetic nerve supply after surgical or chemical sympathectomy was investigated [3,7].

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Based on the hypothesis that HR decreases during postnatal life as a result of reduced sympathetic and enhanced parasympathetic influences [1], we decided to examine the effect of vagotomy on HR in sympathectomized animals of various ages. In this study we compared HR variabilities in chemically sympathectomized and intact rats of different ages after vagotomy and vagal stimulation.

MATERIALS AND METHODS

Experiments were performed on 47 random-bred albino rats aged 4, 6, 8, and 20 weeks. The animals were sympathectomized by injecting guanethidine sulfate (25 mg/kg subcutaneously) for 28 days [6]. Intact age-matching rats (n=44) maintained under the same conditions served as the control. Right vagotomy was performed under Urethane anesthesia (25%, 800 mg/kg intraperitoneally). Electric stimuli were applied to the proximal right vagus nerve and of intact left nerve, after which left vagotomy was performed with subsequent stimulation of the distal end of the left vagus nerve using an ESL-2 stimulator with platinum electrodes. Stimulation parameters were selected individually: 5 V, 0.7-5 Hz, interstimulus interval 8-16 msec, and stimulus duration 0.8-1.6 msec. The ECG were recorded and processed using special software based on the method of R. M. Baevskii. The following parameters were compared:

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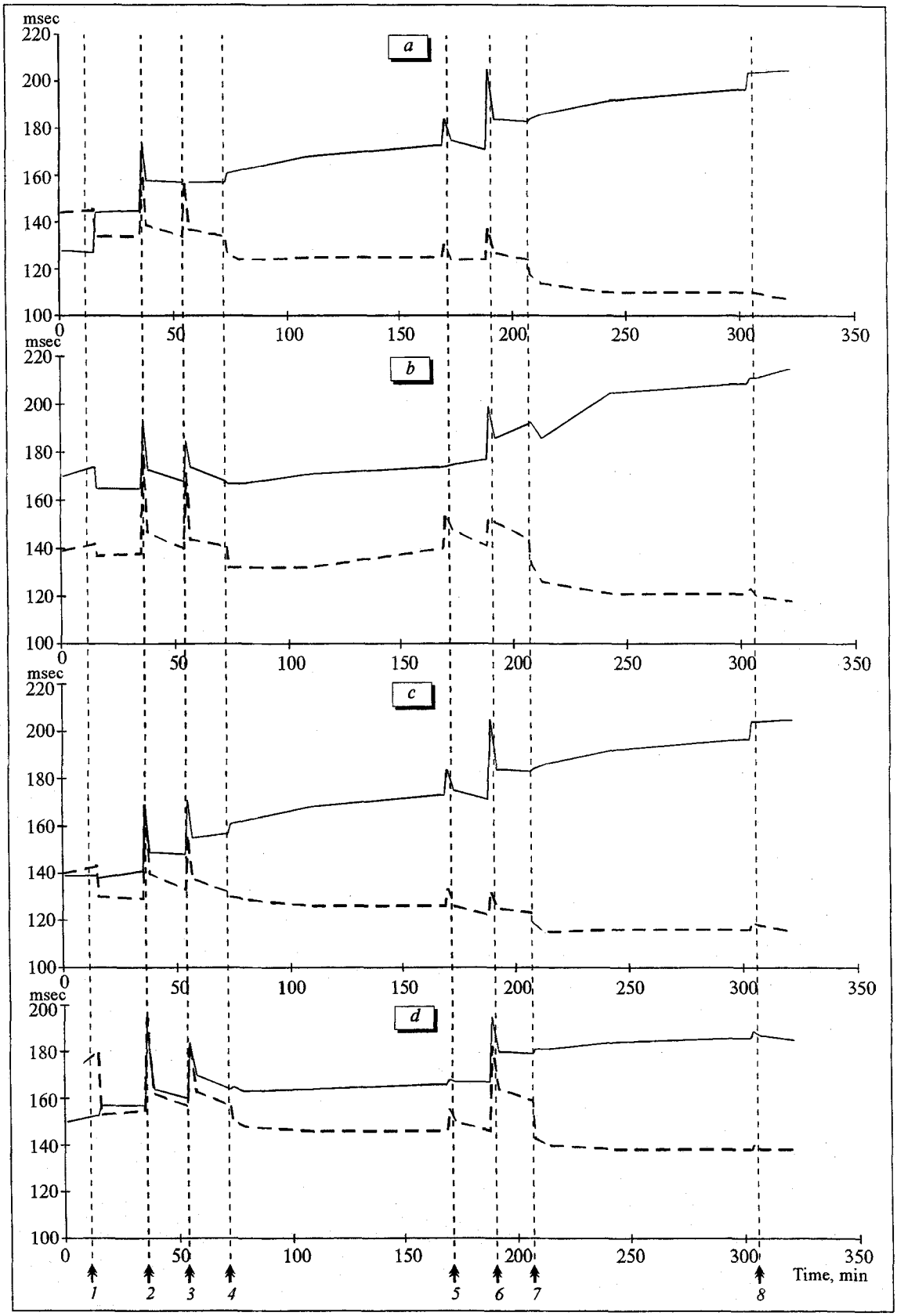

Fig. 1. Temporal variations of mean cardiointerval in rats aged 4 (*a*), 6 (*b*), 8 (*c*), and 20 (*d*) weeks. *1*) Bilateral vagotomy; *2*) stimulation of right vagus; *3*) stimulation of left vagus; *4*) right vagotomy; *5*) stimulation of proximal right vagus; *6*) stimulation of intact left vagus; *7*) left vagotomy; *8*) stimulation of distal left vagus. Solid line: intact rats (control); dashed line: sympathectomized rats.

mean cardiointerval, mode, amplitude of the mode, standard deviation, variation range, and tension index.

RESULTS

There were slight intergroup differences in baseline HR values (before vagotomy), which were lower in 4-week-old sympathectomized rats and higher in the other three age groups compared with intact controls.

Right vagotomy increased HR in all chemically sympathectomized rats and in intact (control) rats. In intact, but not sympathectomized rats, HR returned to normal by the 5th min after vagotomy.

Electrostimulation of the proximal segment of the cut right vagus decreased HR in all rats, although to various extent. Subsequent stimulation of intact left vagus also decreased HR, the decrease being the greatest in sympathectomized adult rats (25%, $p<0.001$) and the smallest in sympathectomized 6-week-old rats. In sympathectomized and then right-vagotomized rats aged 6, 4, and 8 weeks, stimulation of intact left vagus led to a smaller decreases in HR than in control animals of the same age after right vagotomy, while the HR decrease in test and control adult (20-week-old) rats was virtually the same. It should be noted that HR in sympathectomized rats of all age groups was significantly higher after right vagotomy than in intact controls. Left vagotomy performed 90 min after right vagotomy accelerated HR in sympathectomized rats of all age groups, the effect being the highest in 6- and 20-week-old animals (by 8% and 10%, respectively; $p<0.05$). It should be noted that HR did not normalize after the second vagotomy.

A comparison of HR variabilies after the second (left) vagotomy revealed much greater differences than after the first vagotomy. Heart rate increased in sympathectomized rats of all ages (particularly in 4-week-old rats) and decreased in control animals, although to different degrees in different age groups. As Fig. 1 shows, the differences between the mean cardiointervals after bilateral vagotomy tended to decrease with increasing age.

Stimulation of the distal end of the left vagus after bilateral vagotomy resulted in a transient fall of HR in sympathectomized rats aged 6, 8, and 20 weeks.

Comparative analysis of temporal variations of variation rate, mode amplitude, and tension index revealed a slight predominance of parasympathetic regulatory influences in sympathectomized rats compared with the control animals.

The following hypothesis may be helpful for understanding the mechanisms underlying the effects observed in this study. Sympathetic postganglionic fibers modulate parasympathetic intracardiac postganglionic neurons. A reduction in such an influence on the intracardiac cholinergic neurons in sympathectomized rats provides for the opposite effects of vagal cutting in intact and desympathetized rats. Presumably, chemical sympathectomy with guanethidine sulfate causes death of catecholamine-containing cardiac cells which act as intermediate neurons in intracardiac reflex arcs and keep maintain the activity of sinus node pacemakers at a constant level [9]. Our results suggest that vagal regulation of HR in rats is modulated by sympathetic influences.

REFERENCES

1. A. Adolf, *Development of Physiological Regulations* [Russian translation], Moscow (1971).
2. R. V. Belousov, "Variations with time in the morphology of the conducting system in the subdiaphragmatic portion of the vagus," Author's Synopsis of Dissertation [in Russian], Saransk (1994).
3. E. N. Goncharenko and M. G. Udel'nov, *Origin of Heart Rate Acceleration After Division of the Vagi* (*Proceeding of the Department of Physiology, Moscow State University*) [in Russian], Moscow (1953).
4. G. P. Konradi, in: *Physiology of the Circulation. Physiology of the Heart* [in Russian], Leningrad (1980), pp. 400-411.
5. I. P. Pavlov, *Centrifugal Nerves of the Heart*, in: *Collected Works* [in Russian], Vol. 1, Moscow - Leningrad (1951), pp. 374-393.
6. I. M. Rodionov, V. N. Yarygin, and A. A. Mukhammedov, *Immunological and Chemical Sympathectomy* [in Russian], Moscow (1988).
7. V. M. Smirnov, *Byull. Eksp. Biol. Med.*, **120**, No. 8, 125-128 (1995).
8. M. G. Udel'nov, *Neural Regulation of the Heart* [in Russian], Moscow (1961).
9. V. N. Shvalev, A. A. Sosunov, and G. Guski, *Morphological Basis of Cardiac Nerve Supply* [in Russian], Moscow (1992).
10. E. Agostony, Y. E. Chinnok, and B. N. Daly, *Physiologie*, **135**, No. 1, 182-205 (1957).