HEART RATE CONTROL BY BURST STIMULATION OF THE VAGUS NERVE IN RATS

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KEY WORDS: vagus nerve; burst stimulation; heart rate; heart rate control.

Several workers have shown in recent years that during burst stimulation of the vagus nerve (VN) synchronization of the frequency of the stimulating bursts with the heart rate can be obtained [6, 7]. Slowing or quickening of the frequency of the bursts within certain limits leads to slowing or quickening of the heart rate (HR). It was later shown that by varying the number of pulses in the burst a successive series of ranges of control, which overlap one another partially, can be obtained. This ultimately enables HR to be controlled over a wide range of values in cats [1-3], rabbits, dogs [1, 3], and frogs [4, 5].

However, the range of control has not been studied in the case of so widely used an experimental animal as the albino rat. This was accordingly the aim of the investigation to be described here.

EXPERIMENTAL METHOD

Experiments were carried out on 13 rats of both sexes weighing 250-350 g, under general anesthesia (75 mg **chloralose** + 15 mg pentobarbital sodium/kg body weight) with artificial ventilation of the lungs and maintenance of a constant body temperature. The peripheral end of the divided right VN in the cervical region was placed on platinum bipolar electrodes with an interelectrode distance of 2 mm. VN was stimulated with bursts of square pulses from an ESU-2 stimulator. The frequency, duration, and amplitude of pulses in the burst were 80 Hz, 1 msec, and 2-6 V, respectively. The control phenomenon was studied by the use of 1, 2, 4, 8, and 16 pulses per burst. HR was determined from the ECG, recorded on an N-338 automatic writer. The IM-789 indicator served for visual monitoring. Atropine (0.2-0.3 mg/kg, intravenously) was used for pharmacologic analysis.

EXPERIMENTAL RESULTS

To obtain the control phenomenon, bursts of pulses were applied periodically to the nerve. Synchronization of HR with the rhythm of stimulation of VN occurred 3-4 cycles after the beginning of stimulation with bursts of a definite frequency. This phenomenon went beyond the simple coincidence of rhythms and was stable in character within a particular frequency range, when a change in the following frequency of the bursts regularly gave rise to precisely the same change in HR, i.e., there was a clear tendency toward control, in the direction of both slowing and quickening of the rate (Fig. 1).

TABLE 1. Ranges of Control of Heart Rate in Rats (M ± m)

Number of pulses in burst	Upper limit of rhythm binding	% of original	Lower limit of rhythm binding	% of original	Width of range of control	% of original
1	234,7±8,5	72,1	217,1±9,4	66,7	17,6±3,2	5,4
2	189,6±8,7	58,4	157,7±11,4	48,6	31,9±2,9	9,8
4	146,2±8,7	45,6	114,0±10,8	35,5	32,2±1,3	10,1
8	117,0±11,6	37,0	98,6±10,7	31,2	18,4±2,5	5,8
16	97,0±10,8	30,4	79,6±10,4	25,0	17,4±3,3	5,4

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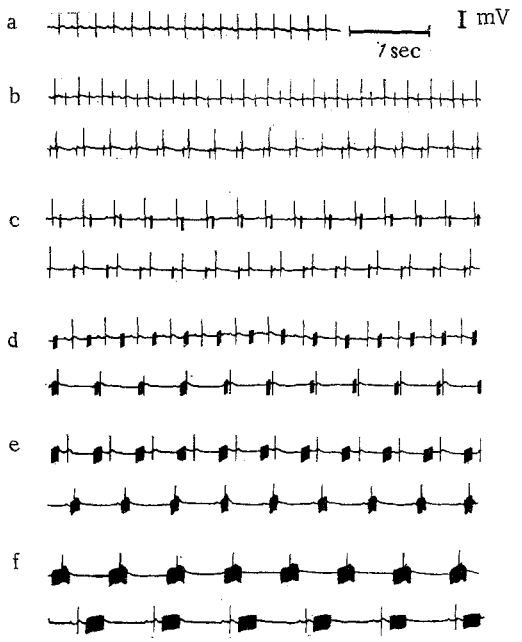

Fig. 1

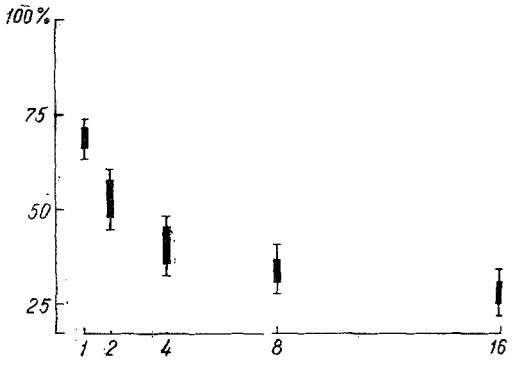

Fig. 2

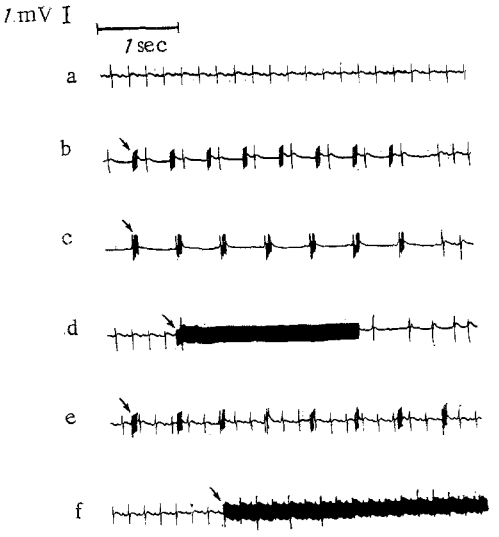

Fig. 3

Fig. 1. Control of heart rate by burst stimulation of vagus nerve in a rat. a) Initial ECG; b-f) ranges of control during stimulation of nerve by bursts consisting of 1, 2, 4, 8, and 16 pulses, respectively. Top trace in each fragment corresponds to upper limit of range of control, bottom trace to lower limit. Stimulating bursts recorded as artifacts on ECG.

Fig. 2. Limits of ranges of control during vagus nerve stimulation by bursts of pulses in rats. Bold lines show ranges of control, thin lines ±m. Abscissa, number of pulses in burst; ordinate, changes (in %).

Fig. 3. Effect of atropine on heart rate control phenomenon. ECG of rat: a) original HR; b, c) upper and lower limits of range of control with four pulses per burst; d) vagus arrest during periodic stimulation of VN; e,f) burst and periodic stimulation of VN after intravenous injection of atropine in a dose of 0.2 mg/kg body weight. Stimulation recorded as artifact on ECG.

The limits and position of the range of control were determined primarily by the number of pulses in the burst. As Table 1 shows, the greatest width of the range corresponded to four pulses per burst (10.1% of the original rate).

Dependence of the position of the ranges of control relative to the initial rate, taken as 100%, on the number of pulses in the burst is illustrated in Fig. 2. Its exponential character will be noted. The total range of controlled bradycardia (from the upper limit with one pulse per burst to the lower limit with sixteen pulses) in rats was 47.1% (Fig. 3).

To study the nature of controlled bradycardia in rats atropine was injected intravenously. This abolished both the control effect and the effect of periodic stimulation of VN, evidence that muscarinic cholinergic structures are concerned in the mechanism of the control phenomenon.

Comparison of these results with those of previous experiments on cats, dogs, and rabbits [1, 3] indicates that controlled bradycardia is common in its nature. Meanwhile, in rats, the position of the ranges of control along the HR scale was lower than for the other animals mentioned above, for the same number of pulses per volley. For instance, in the present experiments the upper limit of the range of control with one pulse per burst was 72.1% of the original rate, whereas in the other animals it varied from 83.6 to 77.5%, whereas the lower limit with 16 pulses per burst was 25.0% in rats, but varied from 43.4 to 30.7% in cats, rabbits, and dogs. At the same time, the width of the total range, which was 47.1% in rats, agreed closely with that obtained in dogs (46.9%), intermediate in position between the width for rabbits (61.9%) and cats (34.1%). These differences probably reflect as yet unstudied species differences in regulation of the heart and, in particular, relations between the influences of the sympathetic and parasympathetic divisions of the autonomic nervous system, and also representation of their efferent fibers in the cervical portion of VN. The absence of overlapping of most adjacent limits of the range of control in the present experiments indicates simply that, under natural conditions, there is a finer gradation of burst discharges in parasympathetic efferent fibers of VN, whereas the presence of a control phenomenon during burst stimulation of VN in different animals is further conclusive evidence of the general biological character of the phenomenon.

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