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ACCURATE CONTROL OF THE HEART RATE IN MONKEYS BY BURST STIMULATION OF THE VAGUS NERVE

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Evidence of a definite role of the method of vagus nerve stimulation in the realization of its cardiochronotropic effect has been obtained [9-12]. In particular, it has been shown that the heart of the frog [4], rat [3], guinea pig [11], rabbit [1], cat [1, 2, 6], and dog [1] can synchronize their contractions with the rhythm of burst stimulation of the vagus nerve within a frequency band from moderate bradycardia to the level of pacemaker activity of the atrioventricular node. The facts evidently indicate that there exists a hitherto unknown mechanism of central regulation of the heart rate, based on discrete control of the length of each individual cardiac cycle. At the same time it is evidence that to postulate a general biological significance of the phenomenon under discussion, it must be shown to exist in a broader spectrum of species, including primates and man.

The aim of this investigation was to study vagal control of the heart rate in one of the higher animals, *Macaca rhesus*.

EXPERIMENTAL METHOD

Experiments were carried out on five adult male rhesus monkeys weighing 9.4 ± 0.9 kg, anesthetized with chloralose and pentobarbital (60 and 12 mg/kg respectively, intravenously). In all cases the right vagus nerve (VN) was isolated and divided at the level of the larynx and its peripheral end was stimulated by an ÉSU-2 stimulator with bursts of pulses (2 msec, 6 thresholds, 1-16 stimuli, 40 Hz, in a burst). The ECG was recorded on an ÉLKAR-6 electrocardiograph by means of a bipolar platinum probe introduced into the right atrium through the external jugular vein. An IM-789 oscilloscope was used to monitor the events visually. Fuller details of the technique were described previously [1, 6].

EXPERIMENTAL RESULTS

The initial heart rate (HR) varied from 150 to 187.5 beats/min (mean 155.3 ± 15.4 beats/min). During periodic stimulation of VN by single pulses synchronization of the rhythms occurred within the frequency range from 131.4 ± 11.3 to 126.0 ± 13.0 beats/min (Fig. 1). Any

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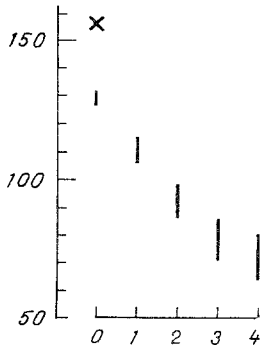

Fig. 1. Ranges of synchronization of rhythms during burst stimulation of VN. Abscissa, logarithm to base 2 of number of pulses in burst; ordinate, frequency of rhythm synchronization (beats/min). X) Initial HR.

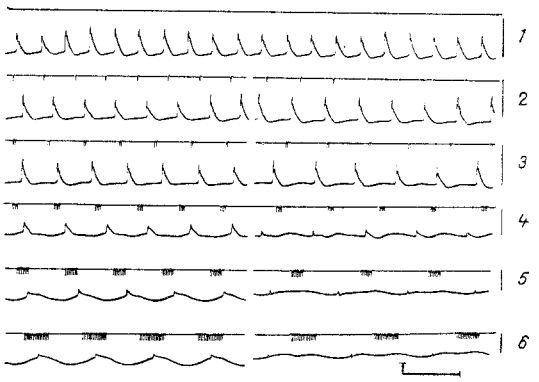

Fig. 2. Ranges of synchronization of rhythms during burst stimulation of vagus nerve. 1) Initial ECG: 2-6) ECG during stimulation of VN by bursts consisting of 1, 2, 4, 8, and 16 pulses respectively. Left half of each fragment (2-6) represents upper limit of range of synchronization of rhythms; right half — lower limit. Top trace of each fragment is marker of stimulation of VN, bottom trace — intra-atrial ECG (highest amplitude is P wave). Calibration: 5 mV, 1 sec.

change in the frequency of stimulation of VN within the limits of this frequency range led to precisely such a shift of HR (Fig. 2) as, from the point of view of the traditional assessment of the intensity of the chronotropic effect of VN, would be distinctly paradoxical in character [9, 10]. An increase in the number of pulses in the burst increased the width of the range of synchronization and, at the same time, shifted it down the frequency scale Figs. 1 and 2). In particular, if there were 2, 4, 8, and 16 pulses in a burst range of of synchronization of rhythms were 115 ± 9.6 — 105.1 ± 10.2, 98.4 ± 7.2 — 85.6 ± 8.8, 85.5 ± 5.9 — 69.2 ± 8.4 and 79.9 ± 6.4 — 62.6 ± 7.7 beats/min (Fig. 1). Thus, the combined range of control of the heart rate was 84.6-40.3%, or 44.1% of the initial heart rate. The lower limit of the combined range of control of heart rate, just as in other animals [1-3, 5], corresponded to the level of activation of the atrioventricular node, whose automaticity could not be controlled by burst stimulation of VN.

A characteristic feature of all ranges of synchronization was the strict regularity of the arrangement of artefacts of VN stimulation during recording of the ECG. For instance, during rhythm synchronization at the upper limit of each range the stimulation artefact was always located on the left of the P wave on the ECG, whereas in the case of synchronization at the lower limit of the range, it was invariably shifted to the right of the P wave (Fig. 2).

This last circumstance indicates that the discrete character of control of the heart rate is based on variation of sensitivity of the sinoatrial node in the course of the cardiac cycle to the chronotropic influence of bursts of vagal excitation [5, 8, 10, 12]. Confirmation of this fact is given by the electrocardiographic picture during stimulation of VN with a frequency above or below the corresponding limits of the given synchronization range. Interference between myogenic and neurogenic rhythms observed under these circumstances leads to the result that each stimulation of VN takes place in a new phase of the cardiac cycle, so that it induces a correspondingly different chronotropic effect, which as a whole, is perceived as marked sinus arrhythmia [6]. Meanwhile both in arrhythmia and in rhythm synchronization, the minimal duration of the cardiac cycle was always much greater than its initial value (Fig. 2), and in our view this is evidence of the existence of two components of the negative chronotropic effect of VN stimulation. The first component is tonic, and its magnitude is independent of the phase of the cardiac cycle and determines the level of stable bradycardia against the background of which rhythm synchronization develops (Figs. 1 and 2). The second component is also synchronizing; its amplitude is closely linked with the phase of the cardiac cycle in which VN is stimulated, but the duration of the effect is brief, commensurate with the duration of one cardiac cycle [5]. The hypothesis expressed above is in good agreement with experimental data indicating [7] the existence of two types of efferent cardiac fibers of VN, which differ sharply from each other in the duration of the chronotropic effect observed when they are stimulated separately. Under conditions of natural regulation of the heart rate, the manifestation of these components of the chronotropic effect of VN is evidently isolated in character or variably combined, thus allowing a wider combined range of control of HR than is possible experimentally. On the whole, however, the facts obtained with burst stimulation of VN in monkeys correlate with data obtained on other species of animals [1-4], so that the existence of a fundamental mechanism of central regulation of the cardiac rhythm, based on discrete control of the duration of each cardiac cycle, can be postulated with a high degree of confidence.

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