EFFECT OF STIMULATION OF THE SENSOMOTOR CORTEX ON THE FIRING PATTERN OF BULBAR CARDIOVASCULAR NEURONS DURING MYOCARDIAL ISCHEMIA

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UDC 616.127-005.4-06:616.12-008.318-02:616.831.22-008.1-092.9

KEY WORDS: bulbar cardiovascular neurons; sensomotor cortex; myocardial ischemia; cardiac arrhythmias.

Stimulation of the sensomotor cortex during myocardial ischemia is accompanied by a significant increase in the frequency of development of idioventricular arrhythmias [3]. The participation of the sensomotor cortex in the regulation of cardiac activity is known to be realized through the cardiovascular center in the medulla [1, 2, 4]. It can be tentatively suggested that during myocardial ischemia descending influences from the sensomotor cortex take part in modification of unit activity in the bulbar cardiovascular center, which has been shown to precede the onset of severe disturbances of the cardiac rhythm [6]. Evidence in support of this possibility is given also by data showing that a conduction block along the path between the frontal cortex and brain stem prevents the development of ischemic ventricular fibrillation [7].

The aim of this investigation was to study the firing pattern of bulbar cardiovascular neurons during myocardial ischemia in response to stimulation of the sensomotor cortex.

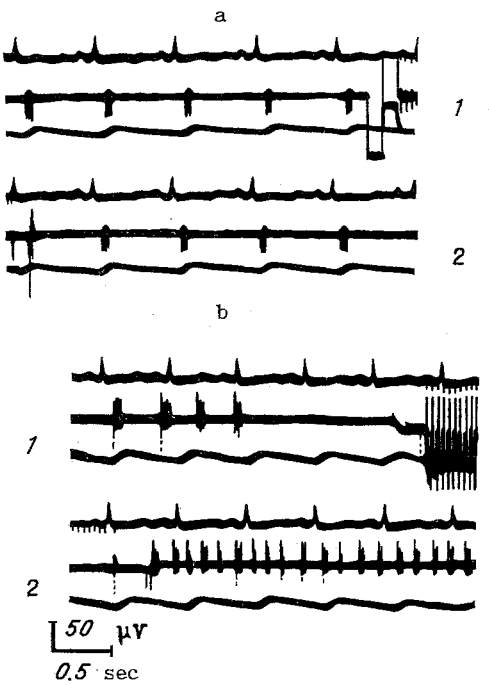

Fig. 1. Response of afferent neuron (a) and interneuron (b) of bulbar cardiovascular center to sensomotor cortical stimulation. 1) Initial firing pattern, 2) firing pattern after cortical stimulation. Here and in Fig. 2, from top to bottom: ECG, unit activity, blood pressure.

N. I. Pirogov Second Moscow Medical Institute. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 104, No. 9, pp. 263-265, September, 1987. Original article submitted June 20, 1986.

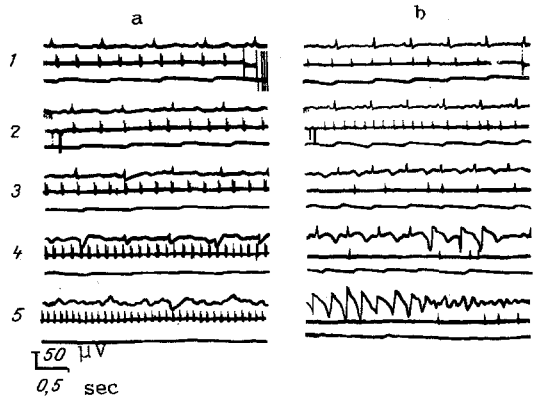

Fig. 2. Response of afferent neuron (a) and interneuron (b) of bulbar cardiovascular center to development of myocardial ischemia during stimulation of the sensomotor cortex. 1) Initial firing pattern, 2) 10 sec after compression of coronary artery, 3) elevation of ST segment, 4) onset of idioventricular arrhythmias, 5) ventricular fibrillation.

EXPERIMENTAL METHOD

In acute experiments on cats of both sexes weighing 3-4 kg, anesthetized with pentobarbital (30-40 mg/kg, intraperitoneally) and with artificial ventilation of the lungs, myocardial ischemia was induced by compressing the circumflex branch of the left coronary artery for up to 15 min. The cerebral cortex in the region of the anterior sigmoid gyrus was stimulated by the method described previously [3]. Cardiovascular neurons were identified in the region of the nucleus of the tractus solitarius [5]. Discharges of the neurons were recorded extracellularly by means of glass microelectrodes filled with 2.5 M KCl solution. Parallel recordings were made of the ECG in standard lead I or II and the blood pressure in the femoral artery. All parameters were recorded on an M-42 four-channel myograph (Medicor, Hungary). The functional group to which the neurons belonged was determined from the character of the original firing pattern, in accordance with previous investigations [6]. Unit activity was analyzed immediately after the end of cortical stimulation (10 sec after compression of the coronary artery), at different stages of myocardial ischemia (changes in the ST segment, deformation of the ventricular complex, respectively on the ECG) and immediately before the development of idioventricular arrhythmias. The significance of the responses was estimated by Student's test and the chi-square test.

EXPERIMENTAL RESULTS

Before tackling the main task of the investigation, it was necessary to study the responses of afferent and interneurons of the bulbar cardiovascular center to stimulation of the sensomotor cortex. For this purpose, the discharge pattern of 12 afferent neurons and 27 interneurons was analyzed in 32 experiments. The afferent neurons did not change their activity in response to stimulation ($p < 0.05$; Fig. 1a). The interneurons responded in 82% of cases to stimulation of the sensomotor cortex by a change in their discharge pattern (Fig. 1b). Their response under these circumstances varied in direction, with either an increase (41%) or decrease (23%) of their discharge frequency and changes in their regularity (50%). The discharge pattern of the interneurons returned to its initial type 60-90 sec after the end of stimulation. Thus the afferent neurons and interneurons of the bulbar cardiovascular center respond differently to stimulation of the sensomotor cortex.

In the next series of experiments activity of nine afferent neurons and 17 interneurons of the bulbar cardiovascular center was analyzed during myocardial ischemia and stimulation of the sensomotor cortex. The response of a neuron to isolated cortical stimulation was studied, then to a combination of cortical stimulation and compression of the coronary artery, and finally at different stages of myocardial ischemia.

In most cases (79%) the response of the same interneuron to isolated cortical stimulation and to combined cortical stimulation and compression of the coronary artery was qualitatively different, and often opposite in character ($p < 0.001$). This points to the possibility

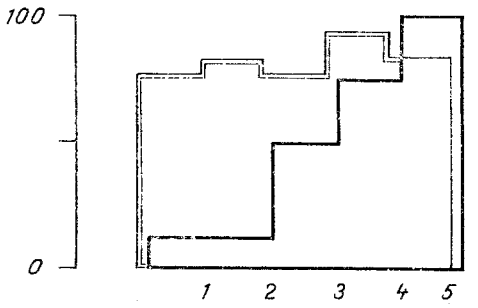

Fig. 3. Number of afferent neurons (single line) and interneurons (double line) of the bulbar cardiovascular center changing their firing pattern at different stages of myocardial ischemia and during stimulation of the sensomotor cortex. 1) Isolated cortical stimulation, 2) 10-15 sec after compression of the coronary artery against the background of cortical stimulation, 3) changes in the ST segment, 4) deformation of the QRS complex, 5) before the development of idioventricular arrhythmias.

of interaction between the discharge arising from myocardial receptors and from the sensomotor cortex, at the interneuron level in the bulbar cardiovascular center. The afferent neurons in most cases did not change their discharge pattern 10-15 sec after compression of the coronary artery accompanied by cortical stimulation. Their response was observed only on the appearance of ischemic changes on the ECG. The number of afferent neurons involved in the response increased during the development of ischemia in the myocardium ($r = 0.975$, $p < 0.05$), and all the neurons changed their activity immediately before the onset of arrhythmias (Fig. 2A). Meanwhile the majority of interneurons changed the character of their discharges during the first 10-15 sec after compression of the coronary artery. With the growth of ischemic changes on the ECG the firing pattern of the interneurons underwent further changes (Fig. 2b). Analysis of the discharges of the afferent neurons and interneurons at different stages of myocardial ischemia revealed a low degree of interaction in their response to the development of myocardial ischemia (Fig. 3, $r = 0.525$, $p > 0.05$). Under these conditions ischemia of the heart muscles was accompanied in 100% of cases by the development of severe idioventricular arrhythmias.

The character of activity of the bulbar cardiovascular neurons is particularly interesting in myocardial ischemia complicated by the development of ventricular fibrillation (70% of the experiments). During stimulation of the sensomotor cortex the predominant slowing of the firing rate of neurons in the bulbar cardiovascular cortex, which we observed previously preceding the development of ischemic ventricular fibrillation [6], was not found. In addition, the degree of disparity between the response of the afferent neurons and interneurons at the different stages of ischemia was more marked ($r = -0.05$). Meanwhile, when myocardial ischemia during stimulation of the sensomotor cortex did not lead to the onset of ventricular fibrillation, a high degree of correlation was observed between the responses of the afferent neurons and interneurons to the development of ischemia ($r = 0.995$). However, in this case also the response of the bulbar cardiovascular neurons also varied in direction.

During stimulation of the sensomotor cortex, modification of the activity of the bulbar cardiovascular center, preceding the development of severe ischemic disturbances of the cardiac rhythm, is thus manifested both as absence of correlation between the activity of afferent neurons and interneurons and as differences in the direction of changes in the firing pattern of both interneurons and afferent neurons of the center. Stimulation of the sensomotor cortex, changing activity primarily of the interneurons of the bulbar cardiovascular center, enhances the degree of disintegration of unit activity in the center during myocardial ischemia. This last mechanism evidently lies at the basis of the increase in the frequency of development of ischemic arrhythmias, including ventricular fibrillation, observed during stimulation of the sensomotor cortex.

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

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UDC 612.178.1.014.424

KEY WORDS: monkeys; vagus nerve; burst stimulation; frequency of stimulation; heart rate; synchronization of rhythms.

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

Red Army Kuban Medical Institute, Krasnodar. Research Institute of Experimental Pathology and Therapy, Academy of Medical Sciences of the USSR, Sukhumi. (Presented by Academician of the Academy of Medical Sciences of the USSR B. A. Lapin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 104, No. 9, pp. 266-267, September, 1987. Original article submitted July 3, 1986.

 0007-4888/87/0009-1180$12.50