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SPIKE ACTIVITY OF BULBAR RESPIRATORY NEURONS IN CATS WITH MYOCARDIAL ISCHEMIA: MICROELECTRODE STUDY

S. D. Mikhailova, T. M. Semushkina,
P. Kohl, and G. I. Kositskii

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Clinical data are evidence of changes in respiratory function when the coronary blood flow is disturbed [9, 14]. It has been shown experimentally that changes in activity of some types of respiratory neurons of the ganglion nodosum and neurons of the respiratory center take place in response to compression of the coronary vessel [4, 6]. It can be tentatively suggested that the cause of the respiratory disturbances in these patients may be the modified character of afferent signals reaching the CNS in acute myocardial ischemia.

In this investigation the spike discharge of different types of respiratory neurons in the medulla was studied at different stages of myocardial ischemia.

EXPERIMENTAL METHODS

Experiments were carried out on 45 cats weighing 2.5-4 kg under pentobarbital anesthesia (30-40 mg/kg, intraperitoneally) with artificial respiration. Electrical activity of the respiratory neurons was recorded extracellularly with the aid of glass microelectrodes, filled with 2.5 M KCl. The neurons were identified by stereotaxic coordinates: 2-4 mm laterally and 3 mm rostrally and caudally to the level of the obex [7]. Myocardial ischemia was induced by compression of the circumflex branch of the left coronary artery by means of an adjustable loop for a period of not more than 15 min. In all experiments neuronal activity, the ECG in standard lead I or II, the blood pressure by the direct method in the coronary artery, using an EMT-35 electromanometer (Elema, Sweden), and the pneumogram by means of an EMT-32C transducer (Elema) were recorded continuously. The recorded signals were amplified on a M-42 four-channel myograph (Medicor, Hungary) and recorded on a four-channel SDR-41 tape recorder (Nihon Kohden, Japan) and on 70 mm RF-3 film by means of a four-channel MR-4 photographic recorder (Medicor). Spontaneous neuronal activity was processed manually and by ES 1020 or Iskra 226 computer, using a specially written program for statistical analysis. The character of activity of the respiratory neurons during the experimental procedure was determined over six respiratory cycles, with respect to the following parameters: number of spikes per burst (N), duration of the burst (T), and average spike frequency in the burst (F). The pH and gas composition of the arterial blood were measured before and after ligation of the coronary vessel, in the early (measurement of the ST interval on the ECG) and late (deformation of the QRS complex on the ECG) stage of myocardial ischemia. Values of pH, pO_2, and pCO_2 were determined by means of the micro-Astrup MBS 3Mk2 system (Radiometer, Denmark). The data were subjected to statistical analysis by Student's t test and the chi-square test.

EXPERIMENTAL RESULTS

Activity of 57 bulbar respiratory neurons was recorded: 27 inspiratory, 18 inspiratory-expiratory, 3 expiratory, and 9 expiratory-inspiratory. Activity of the respiratory neurons was analyzed with respect to ECG changes in the early and late stages of myocardial ischemia, when the cardiac rhythm was disturbed.

It will be clear from Fig. 1 (stage 1) that the inspiratory neurons changed their firing pattern after compression of the coronary vessel, even before the development of ischemic

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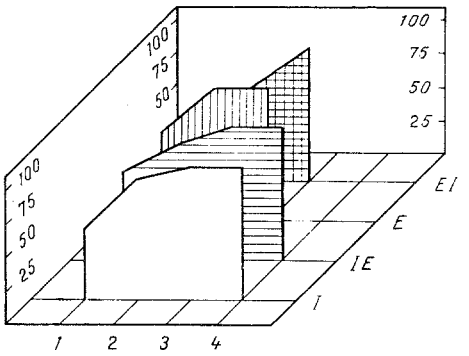

Fig. 1. Number of inspiratory (I), inspiratory-expiratory (IE), expiratory (E), and expiratory-inspiratory (EI) neurons changing their activity at different stages of myocardial ischemia; 1) first six respiratory bursts after compression of coronary vessel, 2) changes in ST interval on ECG. 3) deformation of QRS complex on ECG, 4) disturbance of cardiac rhythm; ordinate) number of reaction neurons (in %).

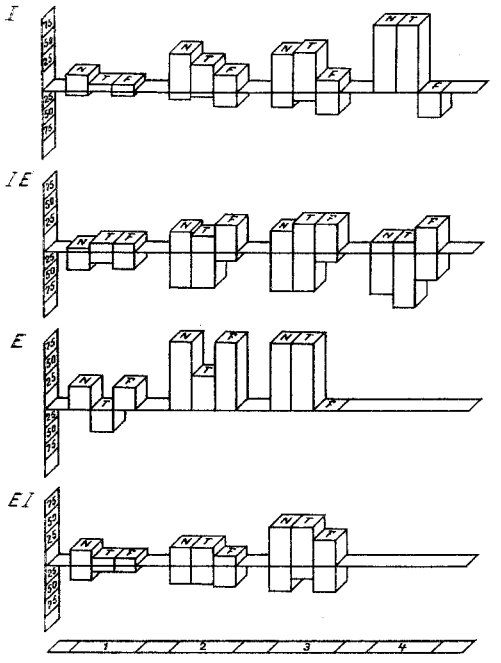

Fig. 2. Changes in activity of inspiratory (I), inspiratory-expiratory (IE), expiratory (E), and expiratory-inspiratory (EI) neurons in different stages of myocardial ischemia. Abscissa) stages of myocardial ischemia: 1, 2, 3, 4 (see Fig. 1). Ordinate) changes (in %) in number of spikes per burst (N), its duration (T), and frequency of spikes in burst (F).

changes on the ECG. The discharge of three late inspiratory neurons changed in response to actual compression of the coronary vessel. With the growth of myocardial ischemia the number of neurons involved in the response increased, to reach 100% in the late stage (Fig. 1, stages 2 and 3). Inspiratory neurons responded with an increase in the number of spikes in the burst ($p < 0.01$) and an increase in its duration ($p < 0.01$; Fig. 2). When the cardiac rhythm was disturbed, the number of spikes in the burst and its duration were increased in 100% on cases (Fig. 2).

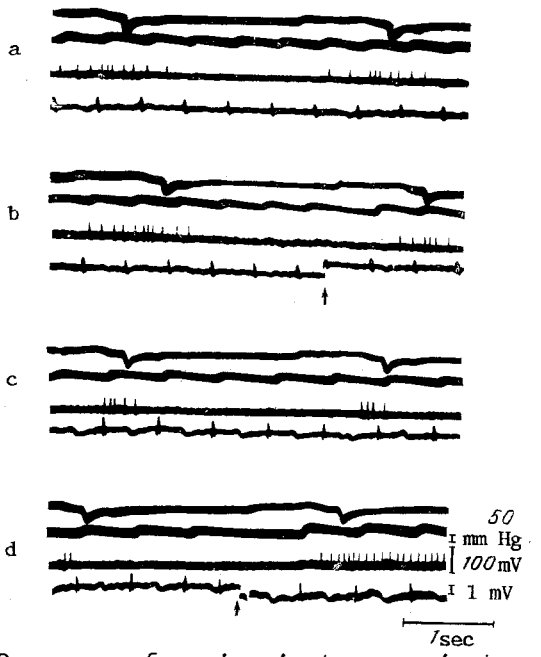

Fig. 3. Response of an inspiratory-expiratory neuron to the development of myocardial ischemia. a) Spontaneous activity of neuron, b) compression of coronary vessel (arrow), c) changes in ST segment on ECG, d) removal of loop from coronary vessel (arrow). From top to bottom: pneumogram, BP, spike discharge, ECG (displacement of isoelectric line corresponds to duration of compression).

The spike discharge of the inspiratory-expiratory neurons also changed after compression of the coronary vessel and before changes in the ECG (Fig. 1, stage 1); three neurons changed their firing pattern under these circumstances in response to actual compression of the coronary vessel (Fig. 3b) whereas two neurons did so in response to removal of the loop from the coronary artery (Fig. 3d). In the late stage of myocardial ischemia activity of all inspiratory-expiratory neurons changed (Fig. 1, stage 3). A decrease in the number and frequency of spikes in the volley was observed twice as often as an increase (Fig. 2). However, this trend of the response was not significant. Of three expiratory neurons recorded, two changed their firing pattern before ischemic changes appeared in the ECG. On the appearance of ischemic changes a response was observed in all expiratory neurons; a tendency was noted for the number of spikes in the volley, its duration, and the firing rate all to increase (Fig. 2).

Of nine expiratory-inspiratory neurons, six changed their firing pattern before the appearance of ECG changes (Fig. 1, stage 1). As the myocardial ischemia progressed, a response was observed in 100% of cases (Fig. 1, stages 2 and 3). It was characterized by uniformity of changes in all the parameters at different stages of myocardial ischemia (Fig. 2).

The results are evidence that after compression of the coronary artery and before changes typical of myocardial ischemia appear on the ECG, all groups of respiratory neurons recorded changed the character of their spike discharge. On the appearance of ischemic deformations of the ventricular complex of the ECG the number of responding neurons increased. With a further increase in myocardial ischemia, respiratory neurons without exception changed their firing pattern; inspiratory neurons increased the duration of the burst and the number of spikes in it in this case.

Bulbar respiratory neurons are known to be highly sensitive to changes in the pH, pO_2, and pCO_2 of the blood [1, 7, 12, 13, 15]. Accordingly, in the present investigation the time course of changes in pH, pCO_2, and pO_2 in arterial blood was studied at different stages of myocardial ischemia. Experiments were carried out on eight cats. Changes in pH and the blood gas composition observed in these experiments are in agreement with data obtained by other workers [2, 15]: in the early stage of development of myocardial ischemia a decrease in pCO_2 ($p < 0.01$) and an increase in pH ($p < 0.01$) of the blood were observed, whereas at the late stage these parameters returned to normal (Table 1). Hypocapnia is known to induce shortening of the burst, and the average frequency and number of spikes in it, in inspiratory and

TABLE 1. Changes in pH, pO_2, and pCO_2 of Arterial Blood of Cats in Early (I) and Late (II) Stages of Myocardial Ischemia (in % of background level)

Serial No.	Background			Stage of ischemia					
				I			II		
	pH	pO_2	pCO_2	pH	pO_2	pCO_2	pH	pO_2	pCO_2
1	7,42	64,8	26	—	—	—	—0,14	—0,31	+3,85
2	7,43	89,3	25	—	—	—	+0,27	—4,37	—12,0
3	7,43	85,5	25	+0,40	+2,11	—12,0	+0,13	—1,79	—3,45
4	7,44	83,8	23	+0,40	—2,15	—4,35	—0,27	—7,64	±0,0
5	7,43	86,5	24	+0,40	—3,70	—12,5	—	—	—
6	7,47	79,5	20	+0,54	—3,65	—15,0	—0,27	—1,01	—5,0
7	7,42	78,7	28	—0,13	—2,54	—3,57	—0,81	—18,17	±0,0
8	7,45	76,7	26	+0,67	+0,78	—7,69	—	—	—
			$\bar{x}$	+0,38	—1,52	—9,18	—0,18	—5,55	—2,77
p (by t test)				<0,01	>0,05	<0,01	>0,05	>0,05	>0,05

inspiratory-expiratory neurons [5, 12]. In the present experiments, on the other hand, a significant increase in spike activity of the cats' inspiratory neurons was observed against the background of a raised pH and lowered CO_2 concentration in the arterial blood. No consistent changes in spike activity were found among other types of bulbar respiratory neurons. This suggests that changes in the blood gas composition are not decisive for changes in activity of the types of neurons studied during myocardial ischemia. This conclusion is supported by the fact that with intensification of ischemic changes in the myocardium against the background of normalization of the blood gas composition the number of neurons changing their firing pattern increased.

Changes in activity of respiratory neurons could also take place under the influence of a change in blood pressure (BP). Lowering of BP is known to depress spike activity of inspiratory neurons [8, 11]. In the present investigations, on the other hand, against the background of myocardial ischemia, which as a rule is accompanied by a fall of BP, spike activity of the inspiratory neurons of the bulbar respiratory center of the cat was increased.

It can be tentatively suggested that the observed response of the bulbar respiratory neurons to myocardial ischemia cannot be explained purely by changes in pH, pO_2, pCO_2, and BP. It is probably determined also by other factors accompanying myocardial ischemia. With the development of the ischemic process in the myocardium changes take place in the firing pattern of neurons of the bulbar cardiovascular center [3]. Considering the closeness of morphological and functional connections between bulbar cardiovascular and respiratory neurons [10, 15], it can be postulated that changes in activity of the respiratory neurons during myocardial ischemia may arise under the influence of impulsation reaching them through the cardiovascular center. Meanwhile, the direct action of afferent impulsation from the heart on neurons of the bulbar respiratory center can also be postulated, for changes in the firing pattern both of respiratory neurons of the ganglion nodosum [4] and of bulbar respiratory neurons [6] take place in response to compression of the coronary vessel itself.

The afferent flow arising in response to compression of the coronary artery thus leads to changes in the firing pattern of neurons not only of the bulbar cardiovascular center, but also of the respiratory center.

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DIMINISHED CHEMOSENSITIVITY OF SENSOMOTOR CORTICAL NEURONS DURING ADAPTATION TO STRESS AND ITS ROLE IN THE PREVENTION OF FIBRILLATION IN ACUTE MYOCARDIAL ISCHEMIA

F. Z. Meerson, R. I. Kruglikov, S. S. Dyusenov, M. Yu. Markarova, and O. Kh. Koshtoyants

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Under the influence of acute ischemia, arrhythmias and fibrillation of the heart, often terminating in death, arise regularly in conscious animals of various species [4-6]. A definite role in the mechanism of these arrhythmias is played by overexcitation of the frontal cortex, induced by acute ischemia; it irradiates to certain hypothalamic centers and, from them, to the adrenergic centers of the brain stem, and so exerts a powerful adrenergic influence on the heart [6]. It has also been found that intracerebral injection of inderal (propanolol), which blocks this mechanism [6], or adaptation to stress, limiting the stress reaction [2], regularly limits fibrillation of the heart and death of conscious animals from acute ischemia. Observations in recent years have shown that this kind of protective effect is due to activation of stress-limiting systems, i.e., opioidergic, GABA-ergic, and serotoninergic systems, during adaptation; the mediators of these systems may limit excitation of the brain centers, and thus play a definite role in the pathogenesis of arrhythmias [1-3]. It may accordingly be postulated that adaptation with the aid of activation of stress-limiting inhibitory systems or in other ways may depress excitability of neurons of the sensomotor and, in particular, the frontal cortex, and thus limit excitation of the whole system of centers involved in the onset of fibrillation of the heart [2].

The aim of this investigation was to compare the effect of adaptation to short-term immobilization stress on the chemosensitivity of sensomotor cortical neurons and on the resistance of the rat heart to arrhythmias arising in conscious animals during acute ischemia.

EXPERIMENTAL METHODS

Experiments were carried out on male Wistar rats weighing 180-200 g. The animals were adapted by daily fixation in the supine position; the first day for 15 min, the second for 30 min, and thereafter 10 times for 1 h each time. Next, in acute experiments on animals immobilized with α-tubocurarine, a miniature micromanipulator was secured to the skull, and by means of it a triple-barreled structured electrode was inserted to the level of layers IV-V of the sensomotor cortex. The electrodes were filled with 3 M NaCl solution (recording electrode), a 2 M solution of acetylcholine (ACh; pH 4.0), and a 0.2 M solution of noradrenaline (NA) bitartrate. Neurotransmitters were applied to the neurons by electrophoresis (30-40

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