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ROLE OF GANGLION NODOSUM NEURONS IN COMPENSATORY RESPIRATORY MECHANISMS IN ACUTE MYOCARDIAL ISCHEMIA

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In myocardial ischemia compensatory mechanisms not only of the cardiovascular, but also of the respiratory system are activated. The realization of these compensatory processes is usually linked with changes in the blood gas composition and hemodynamics and with stress reactions [4, 6-9]. However, it is not yet clear what role is played in these compensatory reactions by different components of the afferent apparatus of the cardiovascular and respiratory systems. It was shown previously under artificial respiration conditions that changes in spike discharges of the integrative neurons of the ganglion nodosum, receiving afferent information from the reflexogenic zones of the heart and lungs, arise immediately after restriction of the coronary blood flow [1].

The aim of this investigation was to study under natural breathing conditions the character of changes in spike activity of different kinds of ganglion nodosum neurons during the development of myocardial ischemia, complicated or not by ventricular fibrillation.

EXPERIMENTAL METHOD

Experiments were carried out on 74 male and female cats weighing 3-4 kg, anesthetized with pentobarbital (40 mg/kg, intraperitoneally). Myocardial ischemia was induced by the method in [2]. The animals were switched to natural breathing by airtight closure of the chest wall, with careful suturing of the pericardium to the thoracic muscles. Activity of ganglion nodosum neurons was recorded extracellularly with glass microelectrodes by the method described previously [10]. The spike discharge, the ECG in standard lead II, the blood pressure in the femoral artery, and the pneumogram were recorded on an M-42 myograph ("Medicor"). These parameters were recorded on magnetic tape by SDR-41 tape recorder ("Nihon Kohden") and in a parallel procedure, on RF-3 70-mm film with an MR-4 photographic recorder ("Medicor"). Activity of 44 ganglion nodosum neurons was analyzed: 31 integrative neurons (late inspiratory, continuous with respiratory modulation, cardio-pulmonary, and inspiratory-expiratory), five complete inspiratory and eight cardiovascular neurons. The numerical results were subjected to statistical analysis by Student's, chi-square, and signs tests.

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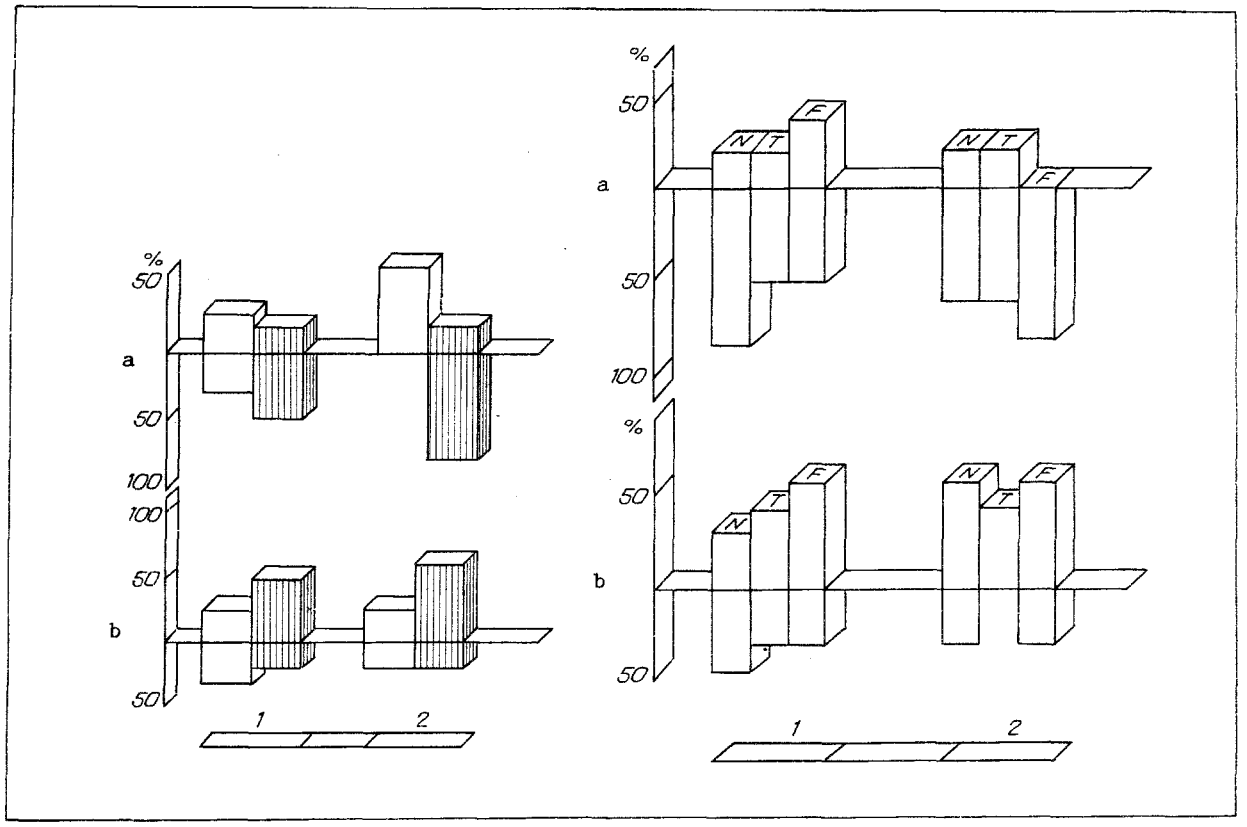

Fig. 1 Fig. 2

Fig. 1. Changes in parameters of external respiration in myocardial ischemia complicated (a) and not complicated (b) by ventricular fibrillation. Abscissa, stages of myocardial ischemia: 1) occlusion of coronary vessel, 2) deformation of QRS complex of ECG. Ordinate, number of experiments (in %) in which frequency (unshaded columns) and depth (shaded columns) of respiration were changed.

Fig. 2. Changes in activity of integrative ganglion nodosum neurons during development of myocardial ischemia, complicated (a) and not complicated (b) by ventricular fibrillation. Abscissa, stages of myocardial ischemia: 1) occlusion of coronary vessel, 2) deformation of QRS complex of ECG. Ordinate, number of neurons (in %) changing number of spikes in volley (*N*), its duration (*T*), and firing rate in volley (*F*).

EXPERIMENTAL RESULTS

In accordance with the program of the investigation, the frequency of development of cardiac arrhythmias following occlusion of the circumflex branch of the left coronary artery and against the background of natural breathing was investigated initially in 17 animals. The results of these experiments showed that in about half of the animals only single extrasystoles were observed, with grouped ventricular extrasystoles in 35% and ventricular tachycardia in 47% of animals; ventricular fibrillation, however, developed in only 17.6% of the experiments.

In the next series of experiments spike activity of different types of neurons of the ganglion nodosum was recorded in 57 animals. Activity of 44 neurons was analyzed at different stages of development of myocardial ischemia under natural breathing conditions. Neurons recorded in 13 experiments were not analyzed, for they either had low amplitude of activity or their activity disappeared before any change took place in the ECG. Depending on the outcome of the development of myocardial ischemia, all the animals were divided into two groups. Group 1 consisted of animals in which myocardial ischemia was complicated by the development of fibrillation. Group 2 consisted of animals in which myocardial ischemia was not complicated by the development of fibrillation. In both groups a comparative analysis was undertaken of changes in functional parameters reflecting cardiac and external respiratory activity, with spike activity of ganglion nodosum neurons.

In the animals of group 1 (10 experiments) immediately after disturbance of the coronary blood flow and before any change in the ECG or blood gas composition, changes took place in the parameters of external respiration. An increase and a decrease in the respiration rate were observed equally often, but so far as the depth of breathing is concerned, in these experiments it was most frequently reduced. In the late stages of development of ischemia in the myocardium (deformation of the QRS complex of the ECG) the number of experiments in which an increase in frequency and decrease in depth of respiration were observed itself increased (Fig. 1a). The development of myocardial ischemia was accompanied by changes in the firing pattern of the ganglion nodosum neurons. In response to the very first occlusion of the coronary vessel, spike activity of the integrative neurons was changed in 100% of experiments. Later, with an increase in the degree of ischemic disturbances of the myocardium changes were observed in the character of the firing pattern of these neurons. In response to occlusion of the coronary vessel opposite changes in spike activity of the integrative neurons were noted: the number of spikes in the volley was reduced in 83% of experiments and increased in 17%; the duration of the volley was reduced in 50% of experiments and increased in 17%; the firing rate was reduced in 15% of experiments but increased in 34%. In the late stages of development of myocardial ischemia (deformation of the QRS complex of the ECG) 80% of integrative neurons reduced the number of spikes in the volley, and indeed an increase in that number was not observed in any single experiment (Fig. 2a). The firing pattern of the late inspiratory neurons showed parallel changes with those in external respiration.

In the animals of group 2, in which myocardial ischemia was not complicated by fibrillation, in response to occlusion of the coronary vessel alone, in the absence of changes in the ECG and blood gas composition, a decrease in the frequency and an increase in the depth of respiration were observed in a higher percentage of experiments than in the animals of group 1. At the late stages of development of myocardial ischemia (deformation of the QRS complex of the ECG) there was an increase in the number of experiments in which an increase in the depth of respiration was noted (Fig. 1b). In the animals of this group different changes were observed in the firing pattern of the neurons than in the animals of group 1. For instance, in response to simple occlusion of the coronary vessel, the firing pattern of 85% of integrative neurons changed: a reduction of the number of spikes in the volley was observed in 42% of the experiments, and an increase in 29%; there was a decrease in the duration of the volley in 29% of experiments and an increase in 42%; a decrease in the firing rate was observed in only 29% of experiments, but an increase in 57% of experiments. In the late stages of development of myocardial ischemia, this trend of the response of the integrative neurons was preserved (Fig. 2b). The firing pattern of the complete inspiratory neurons changed parallel to the changes in external respiration.

During the development of myocardial ischemia under natural breathing conditions, in the animals of groups 1 and 2 the cardiovascular neurons of the ganglion nodosum did not respond to occlusion of the coronary vessel, except in those cases when occlusion was accompanied by extrasystoles. With an increase in the degree of ischemic changes in the myocardium the number of cardiovascular neurons changing their firing pattern increased. For instance, whereas before the ECG changes 12.5% of neurons responded, at the stage of a change in the ST interval 50% of neurons reacted, and on deformation of the QRS complex, the spike activity of all cardiovascular neurons of the ganglion nodosum now changed. A similar response of the cardiovascular neurons during the development of myocardial ischemia under artificial respiration conditions was observed by Kositskii et al. [2] and by Mikhailova et al. [5].

Comparison of changes in the parameters of external respiration with the spike activity of different types of ganglion nodosum neurons during the development of myocardial ischemia may lead to the conclusion that the respiratory reaction is combined with changes in activity of the integrative and complete inspiratory neurons. A special role under these circumstances is evidently played by integrative neurons of the ganglion nodosum, which are the first to modify their activity in response to coronary occlusion, whether under conditions of natural or artificial respiration. Considering that myocardial ischemia, whether complicated or uncomplicated in the future by ventricular fibrillation, is accompanied by different types of changes in external respiration, it can be tentatively suggested that the character of the change in respiration plays an important compensatory role in the development of ischemic cardiac arrhythmias. This is also shown by the fact that under conditions of natural breathing the frequency of onset of ventricular fibrillation during myocardial ischemia is significantly lower (17.6%) than under conditions of artificial respiration (55.5%) [3].

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EFFECT OF PROPRANOLOL ON METABOLIC PROCESSES IN BLOOD AND LYMPH IN ACUTE MYOCARDIAL INFARCTION

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Despite the widespread use of propranolol in clinical practice, including in acute myocardial infarction (AMI) [2, 4, 6], there is virtually no information about its effect on the biochemical parameters of the lymph. Yet the biochemical composition of the lymph reflects the most intimate processes of tissue metabolism and responses of the body to various exogenous factors [1, 3, 5]. The aim of this investigation was to study the action of propranolol on some parameters of carbohydrate and electrolyte metabolism and also on the acid-base balance (ABB) in the blood and lymph during development of AMI.

EXPERIMENTAL METHOD

Experiments were carried out on 30 mongrel dogs weighing 12-22 kg. A model of AMI was created by ligating the anterior interventricular artery under pentobarbital anesthesia (30 mg/kg, intravenously). Lymph was obtained from the drained thoracic duct (a parallel recording made of the rate of the lymph flow), and blood was obtained from the femoral artery. Parameters of ABB were determined on a Micro-Astrup apparatus (Denmark), Na, K, and Ca on a "Microlit" apparatus (Finland), by an ion-selective method. Lactate and glucose concentrations were studied spectrophotometrically on a "Labsystem-900" analyzer (Finland), using standard kits. Propranolol was injected immediately after ligation of the coronary artery and thereafter twice a day for 3 days in a dose of 0.1 mg/kg.

EXPERIMENTAL RESULTS

After creation of the model of AMI marked changes in metabolic processes were observed in both blood and lymph (Table 1, Fig. 1). Starting from 15 min of coronary arterial occlusion, an increase was observed in the lactate and glucose levels

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