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REGULATION OF THE HEART AFTER ISCHEMIC DAMAGE TO THE VENTRICULAR MYOCARDIUM

D. P. Bilibin and O. A. Shevelev

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KEY WORDS: sinus node of the heart; afferentation; cerebral cortex; ischemia.

The characteristics of responses of the afferent systems of the heart during ischemia and changes in the functional state of the organ accompanying potentiation of descending influences [4, 5, 7, 8] has been inadequately studied.

Previously [1, 2] it was shown that impulsation from certain formations of the myocardium to the cerebral cortex (CC) is conducted mainly along spinal afferent systems.

The aim of this investigation was to study the conduction of afferent impulsation from the zone of the sinus node of the heart (ZSN), one of the myocardial formations of the greatest importance from the point of view of regulation, to CC during ischemia of the right and left ventricles of varied duration. In addition, a model of disturbed coronary blood flow was used to study responses of the heart during potentiation of efferent influences of the vagus nerve.

EXPERIMENTAL METHOD

Altogether four series of experiments were carried out on 19 cats and 14 rabbits. In the first three series, experiments were carried out on cats weighing 2.5-3 kg, anesthetized with chloralose (40-50 mg/kg) and curarized. In these experiments bipolar stimulating electrodes were fixed to ZSN and the heart was subjected to square pulses 0.3 msec in duration, 10-15 mA in amplitude, and with a frequency of not more than 0.3 Hz. Evoked potentials (EP), recorded from the exposed surface of CC at the focus of maximal activity, were analyzed by the coherent cumulation method on a Neuroaverager (Biomedica, Italy), with 10-15 presentations of the discrete signal. The ECG also was recorded in standard lead II. In the experiments of series IV, potentiation of descending influences of the parasympathetic system was induced in rabbits weighing 2-2.5 kg, anesthetized with hexobarbital (0.01-0.02 g/kg), by electrical stimulation of the right vagus nerve at the level of the thyroid cartilage, by series of square pulses of current 1 msec in duration, with a frequency of 50 Hz, and the strength of 1-3 mA. In this series of experiments both the undivided vagus nerve and its peripheral end after bilateral vagotomy were stimulated. Stimulation of ZSN and of the nerve trunks was carried out by means of an ÉSU-2 stimulator. Disturbances of the coronary blood flow were induced by compressing the second-order arteries on the left or right side by means of a silk ligature, placed inside a rigid plastic tube, by means of which the development of myocardial ischemia could be induced for a varied period of time. In the experiments of series I triple reversible ischemia of the left ventricular myocardium was induced by the following scheme: the first period of ischemia lasted 5 min, the second 10 min, and the third 15 min; the interval between periods of ischemia was 10 min. In the experiments of series II reversible ischemia of the right ventricular myocardium was induced by the same scheme. In the experiments of series III the coronary blood flow in the territory of the right coronary artery was

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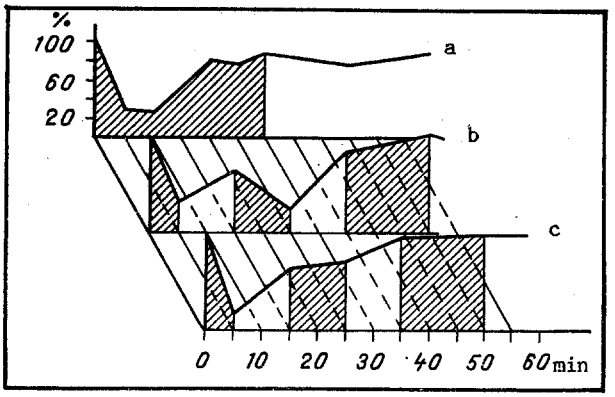

Fig. 1. Changes in combined amplitude (in percent of initial value) of first two phases of EP recorded in rostral zones of the cortex of the right hemisphere, as a result of stimulation of ZSN during experimental ischemia of the right and left ventricles. a) Continuous ischemia of the right ventricle; b, c) subsequent periods of ischemia, increasing successively in duration, of right and left ventricles, respectively. Periods of ischemia are distinctively shaded.

interrupted for 30 min. In the experiments of series IV the duration of left ventricular ischemia was 40 min. The processes were recorded every 5-10 min. To monitor the state of the animal's CNS in the course of the experiment EP were recorded during sciatic nerve stimulation. In the first three series of experiments the total amplitude of the first two phases of EP were subjected to statistical analysis. In series IV the heart rate (HR) was counted during the 5 sec before and after vagus nerve stimulation. The results were expressed in beats per minute. The usual statistical tests of significance were carried out.

EXPERIMENTAL RESULTS

During stimulation of ZSN, EP were recorded in all experiments in the form of a distinct positive-negative deflection of potential, the combined amplitude of the first two phases of which lay between 150 and 300 μV. Interruption of the coronary blood flow (in the first 3 series) led after only 5 min to a marked and statistically significant fall of amplitude of the first two phases of EP, despite no change in stimulus strength. For instance, during left ventricular ischemia the combined amplitude fell from 218 ± 37.9 to 36 ± 7.6 μV, or 16.5% of the initial value ($p < 0.1$), whereas during right ventricular ischemia it fell from 183 ± 21.5 to 46.3 ± 10.2 μV, i.e., to 25.2% ($p < 0.01$). Restoration of the coronary blood flow after ischemia for 5 min caused the amplitude of EP to rise during ischemia of the left ventricle to 65.2%, and of the right to 64.4%. During continuous ischemia, the rise of amplitude of EP was smaller, namely 51% of the initial value at the 15th minute. The pattern of these changes, expressed as percentages of the initial data, can be discerned in Fig. 1. The second and third periods of left ventricular ischemia, it will be noted, did not lead to a fall in the amplitudes of EP, and in this series of experiments a tendency was observed for their recovery independently of any subsequent disturbances of the coronary blood flow. Repeated right ventricular ischemia caused the amplitude of EP to fall again, but during the third period of ischemia the amplitude of the potentials was the same as initially (190 ± 18.4 μV). This pattern was characteristically repeated in all experiments of the first three series. The effects described are illustrated by the results of one experiment in Fig. 2. In all the experiments of these series EP were recorded to sciatic nerve stimulation: the amplitude at the beginning of the experiment was 242 ± 12 μV, at the 5th minute of ischemia 226 ± 20.4 μV, at the end of the 3rd period of ischemia 230 ± 10.9 μV, and after restoration of the coronary blood flow 210 ± 14.8 μV.

In the experiments of series IV, bradycardia developed in response to stimulation of the undivided right vagus nerve, with slowing of the heart rate by 59.6%: from 296.7 ± 13.3 to 120 ± 14.6 beats/min ($p < 0.01$). At the 5th minute of ischemia the response of the heart to vagus nerve stimulation was reduced by 1.8%: from 256.7 ± 8.3 to 252.2 ± 25.7 beats/min. During the next 25 min of ischemia the response of the heart to stimulation of the vagus nerves gradually was restored, and after 40 min had reached 45.3%: HR fell from 250 ± 5 to 136.7 ± 11.3

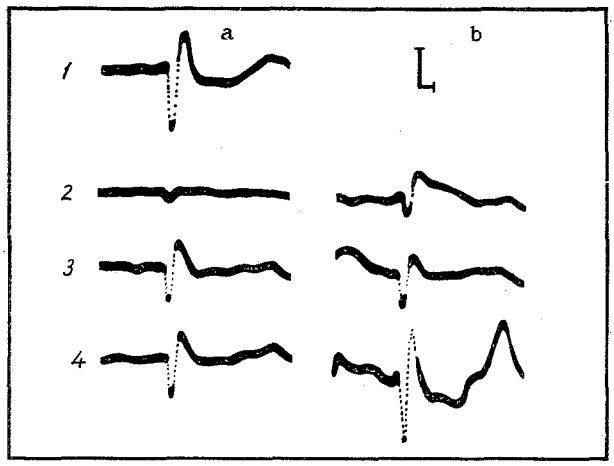

Fig. 2. Changes in EP recorded in rostral zones of cortex of right hemisphere as a result of stimulation of ZSN during experimental ischemia of the right ventricle. 1: a) EP before ischemia; 2: a) at end of 5th minute of first period of ischemia, b) at 10th minute of the first interischemic interval; 3: a) at 10th minute of second period of ischemia, b) at 10th minute of second interischemic interval; 4: a) at 15th minute of third period of ischemia, b) 10 min after termination of ischemia. Calibration: 20 msec, 60 μV.

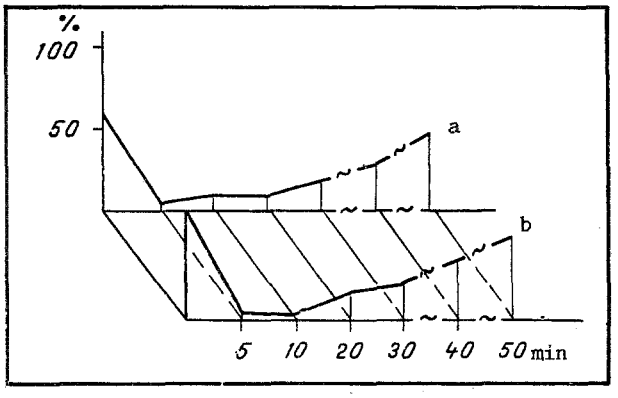

Fig. 3. Time course of changes in slowing of HR (in percent of initial value) during electrical stimulation of the intact right vagus nerve (a) and after bilateral trunk vagotomy (b), during continuous ischemia of the left ventricle.

beats/min ($p < 0.01$). After bilateral vagotomy, stimulation of the peripheral end of the right vagus nerves caused HR to fall by 64.5%: from 316.4 ± 14.4 to 112.3 ± 22.3 beats/min ($p < 0.01$). At the 5th minute of ischemia, stimulation of the same intensity lowered HR by only 2.1%: from 300.4 ± 16.8 to 294.2 ± 21.4 beats/min. The response was later restored, and reached 43.4% after 40 min: it fell from 286.8 ± 14.2 to 162.4 ± 14.4 beats/min (Fig. 3).

The data given above reveal most importantly of all the development of two regular responses of the control systems of the heart to ischemic damage of the ventricles: first, significant limitation of afferent flows, at least from ZSN to CC, and second, the development of a phenomenon of "slipping of the heart" from the control of the vagus nerves. Incidentally, both these responses developed in the earliest stages of ischemia and disappeared when damage to the myocardium became more severe. It can be tentatively suggested that at the time of development of an acute disturbance of the coronary circulation inhibitory processes develop in the intracardial nervous system and convert the heart to an autonomous mode of operation. Under these circumstances the other afferent channels do not undergo any significant changes (experiments with sciatic nerve stimulation). This hypothesis is confirmed by data in the literature [3]. Without dwelling on an analysis of the mechanisms of the responses thus recorded, their relatively rapid fatigue must be noted, which was expressed variously

depending on which part of the heart was subjected to ischemic damage, and for how long the coronary blood flow was disturbed. Prolonged ischemia, causing the development of irreversible damage to parts of the heart, evidently also damages the intracardial nervous system, which becomes unable to control the afferent flows. It is important to note that during the first minutes of ischemia the heart also "slips" from descending influences. It is stated in the literature that stimulation of the vagus nerve during myocardial ischemia does not lead to the development of bradycardia [6], but no analysis of the phenomenon observed is given. Comparison of the results of the first three series of experiments and those of series IV suggest a single biological explanation for these responses. Limitation of afferent flows from the damaged heart to the CNS may in fact facilitate defense of the body and of the heart itself against the development of cardiac pain and the appearance of pathological foci of excitation in CC and deep brain structures. In turn, the "slipping" of the heart from the control of central descending influences may prevent involvement of the myocardium in responses which, if hemodynamically sustained, may lead to aggravation of the pathology. All this suggests that the patterns of regulation of the heart described in this paper under conditions of ischemic damage to the ventricular myocardium are a manifestation of a defensive–adaptive response, which is one of a combination of responses of the body aimed at restoring function predominantly of the pathologically changed organ.

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INCREASE IN CARDIOPROTECTIVE ANTIOXIDANT ENZYME ACTIVITY DURING ADAPTATION OF RATS TO SHORT-TERM STRESS

T. G. Sazontova, Yu. V. Arkhipenko, and F. Z. Meerson

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KEY WORDS: protective antioxidant enzymes; stress; adaptation; rat heart.

Emotional–painful stress, which can itself activate lipid peroxidation (LPO) in the heart [3], lowers the resistance of the isolated atria to the action of LPO inducers [4]. Conversely, adaptation of animals to short-term stress significantly increases the resistance of the isolated atria to the arrhythmogenic action of H_2O_2 [2]. It has accordingly been suggested that the efficiency of antioxidant protection is enhanced during adaptation of the animal to stress situations and to other environmental factors [6].

The aim of this investigation was to study the effect of stress and of adaptation to short-term stress on the activity of enzymes of antioxidant protection: catalase (CT), superoxide dismutase (SOD), and glutathione peroxidase (GPO), and also on the α-tocopherol (TP) concentration in the myocardium.

Laboratory of Pathophysiology of the Heart, Research Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow.

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