EFFECT OF HYPERACTIVITY OF PREGANGLIONIC SPINAL NEURONS ON RHYTHM OF THE HEALTHY AND INJURED HEART

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Hyperactivation of the dorsal noradrenergic pathway, evoked by electrical stimulation of the locus coeruleus (LC) or by creating a generator of pathologically enhanced excitation (GPEE) in it, has been shown to be accompanied by an increase in the rate of contraction of the healthy heart and by various disturbances of the rhythm of the injured heart. It has also been shown that preganglionic sympathetic neurons (PN) of the spinal cord, which are under the influence of supraspinal noradrenergic structures, play to some degree an independent role in the coordinated activity of heart and blood vessels [1, 2, 5].

It was accordingly decided to study the effect of hyperactivation of PN on the cardiac rhythm. The investigation was undertaken in connection with a study of the role of hyperactive determinant structures in the pathogenesis of diseases of regulation [3].

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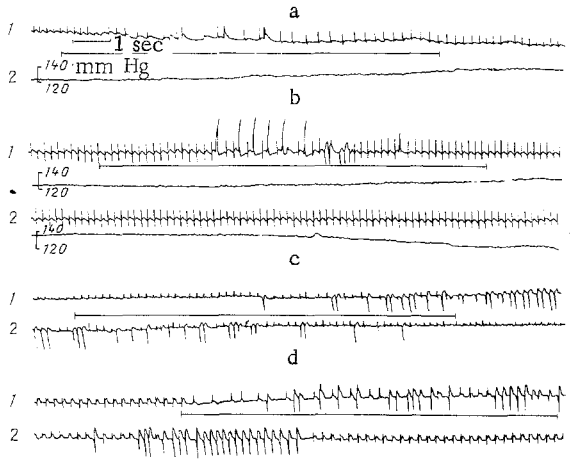

Fig. 1. Effect of electrical stimulation of PN of spinal cord on cardiac rhythm. a) Intact spinal cord, intact heart; b) intact spinal cord, intact heart after subcutaneous injection of atropine; c) divided spinal cord, intact heart; d) intact spinal cord, acute myocardial ischemia. a, b: 1) ECG (lead II), 2) BP in carotid artery; c, d: 1) ECG during electrical stimulation, 2) ECG after stimulation. Horizontal line indicates time of electrical stimulation.

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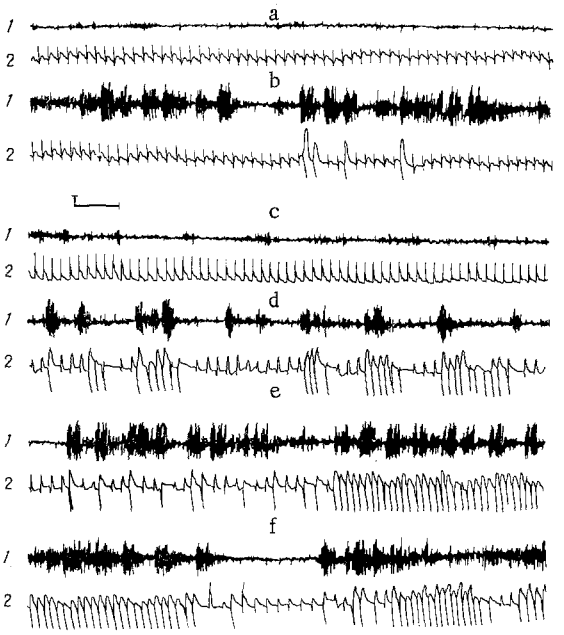

Fig. 2. Character of cardiac contractions after injection of TT into intermediate zone of spinal cord (T3). Healthy heart: a) immediately after injection of TT; b) 40 min after injection of TT. Ischemic heart: c) immediately after injection of TT; d) 15 min, e, f) 40 min after injection of TT. 1) EA of intermediate zone of spinal cord, 2) ECG (lead II). Calibration: 50 μV, 1 sec.

EXPERIMENTAL METHODS

Experiments were carried out on 52 noninbred male albino rats weighing 180-200 g. In the experiments of series I the responses of the healthy heart to electrical stimulation of PN at the level T2-T4 were studied in animals with an intact (11 experiments) and divided (11 experiments) spinal cord and also with acute myocardial ischemia and an uninjured spinal cord (11 experiments). In series II, the animals received an injection of tetanus toxin (TT, 0.1 μl, 200 MLD) [3] into the spinal cord in the region of Rexed's lamina VII (T3), where representation of the sympathetic neurons is maximal [6], to create a GPEE. The character of the change in rhythm of the healthy (seven experiments) and ischemic heart (seven experiments) was studied under these circumstances. In the control group of animals inactivated TT was injected into the same region (five experiments). Preparations for the experiment (tracheotomy, isolation of the carotid artery, exposure of the spinal cord and its division) were made under ether anesthesia. In experiments with division of the spinal cord, it was divided 24 h before the experiment at the level C8-T1. Electrical stimulation of PN (Rexed's lamina VII) was carried out with an ÉSL-2 apparatus with a frequency of 200 Hz, pulse duration 0.6 msec, and amplitude 5-10 V for 10 sec, using glass electrodes filled with 4 M NaCl (diameter of tip 10-15 μ). In animals receiving injections of TT, global electrical activity (EA) of the segment "poisoned" with TT was recorded by means of glass electrodes (4 M NaCl, 10-15 μ) and a UBP2-03 amplifier. In some experiments, during electrical stimulation of PN, the blood pressure (BP) in the carotid artery was recorded by means of an electromanometer. Acute myocardial ischemia was induced by ligation of the anterior coronary artery in its lower third. The ECG (in three standard leads), EA of segmental structures of the spinal cord, and BP were recorded on an Elkar-6 electrocardiograph. To determine the location of the electrodes and the region of injection of TT, the region of the spinal cord chosen for study was examined histologically.

EXPERIMENTAL RESULTS

The healthy heart, in animals with an intact spinal cord, responded to electrical stimulation of PN by single and grouped polytopic extrasystoles. The development of extrasystoles

was preceded by the appearance of sinus bradycardia (Fig. 1a). Subcutaneous injection of atropine (2 mg/kg) prevented the appearance of bradycardia but did not affect the structure of the arrhythmias (Fig. 1b, 1). A change of rhythm was observed as a rule 3-4 sec after electrical stimulation and it ended 1-2 sec before the end of stimulation (Fig. 1a). A rise of BP usually took place at the 6th or 7th second of electrical stimulation and reached a maximum after stimulation (Fig. 1a, c, 1, 2).

During electrical stimulation of PN in animals with a divided spinal cord the latent period of onset of the arrhythmias was increased to 5-6 sec; arrhythmias occurred throughout the period of stimulation and often did not disappear until 15-30 sec after the end of stimulation. The character of the arrhythmia showed no significant change compared with that in intact animals (Fig. 1c, 1, 2).

A different picture was observed during electrical stimulation of PN in an animal with acute myocardial infarction. The latent period of onset of arrhythmias was sharply reduced or was practically absent. Grouped extrasystoles, which appeared at the beginning of stimulation, changed into an idioventricular rhythm. In three experiments ventricular tachycardia ended in death. Normalization of the rhythm took place 10-40 sec after stimulation ceased (Fig. 1d, 1, 2). The appearance of a GPEE in the intermediate zone of the spinal cord after microinjection of TT into Rexed's lamina VII also disturbed the cardiac rhythm. In animals with a normal heart ventricular extrasystoles were observed as a rule in association with powerful seizure discharges of the generator toward 30-40 min after injection of TT (Fig. 2b, 1, 2). In animals with acute myocardial ischemia, however, single and grouped ventricular extrasystoles appeared in the initial period of GPEE (5-15 min after injection of TT); disturbances of the cardiac rhythm, moreover, correlated with discharges of the generator (Fig. 2d, 1, 2). At the height of development of GPEE (40-50 min) the periodic seizures induced the appearance of a ventricular rhythm (Fig. 2e, 1, 2). In the period between seizures the rhythm usually was restored (Fig. 2f, 1, 2). In most experiments the ideoventricular rhythm changed into ventricular tachysystole and the animals died.

It can accordingly be concluded that the formation of hyperactive structures in the intermediate zone of the upper thoracic segment of the spinal cord can disturb the cardiac rhythm. The results showed that if the spinal cord is intact and the heart undamaged, disturbances of its rhythm associated with hyperactivation of PN are short in duration and do not depend on the response of BP to electrical stimulation. Rapid abolition of the arrhythmias is evidence that inhibitory control of supraspinal structures is sufficiently effective, on the one hand, and that the adaptive mechanisms of the myocardium itself are effective, on the other hand. If the heart is damaged its autonomic control mechanisms are disturbed and hyperactivation of the sympathetic apparatus of the spinal cord begins to act as the initial factor in the onset of arrhythmias, the character and course of which are determined by reactivity of the heart muscle.

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