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AFFERENTATION OF THE HEART IN SOME MYOCARDIOPATHIES

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Judging by the relative paucity of data in the literature [2-4, 6, 10], the role of the spinal afferent system of the heart is extremely important, for it is through it that information about the most important changes in functional state of the heart muscle must reach the regulating systems of the CNS both during formal activity and when various pathogenic agents act on the myocardium. In a previous investigation [1] the writers studied the representation of the spinal afferent system of the heart in the cerebral cortex and certain deep brain structures.

In the present investigation, which is a continuation of previous studies, changes in the information capacity of the spinal afferent system of the heart were examined under normal conditions and during the development of certain pathological states of the myocardium (reversible ischemia, necrosis).

EXPERIMENTAL METHOD

Several series of acute experiments were carried out on 18 mature cats under chloralose and with muscle relaxation. The principal electrophysiological method of investigation was the evoked potentials (EP) method; EP were recorded in the rostral zones of the cortex. Stimulation (square pulses, 0.3 msec, 5-10 mA, frequency not more than 0.3 Hz) was applied to the zone of the sinus node (SN) of the heart. The design of the bipolar stimulating electrodes also enabled solutions of the corresponding substances to be applied directly to the region of stimulation. Recording, averaging, and statistical analysis (by Student's test) of the basic parameters of EP were carried out on a coherent averager (Neuroaverager, from OTE-Biomedica) and an Iskra-1256 computer system. The level of significance of differences between means was taken to be $P \leqslant 0.05$. As a rule, at the end of the experiments, pieces of tissue from the region of the sinus node were taken from the animal's heart, after treatment by the standard method, ultrathin sections were cut from them for examination in the electron microscope.

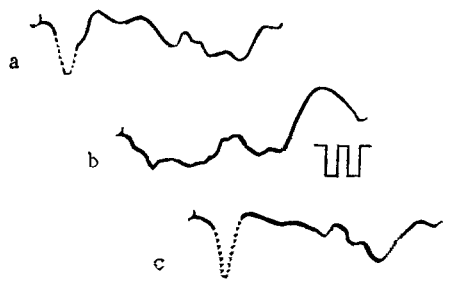

Fig. 1. Changes in cortical EP recorded during stimulation of SN in the normal heart (a), 2 min after injection of 0.1 ml of a 10% solution of neutral formalin into the myocardium (b), and 70 min after injection of formalin (c). Coherent averaging method was used (n = 20). Calibration: 60 μV, 20 msec.

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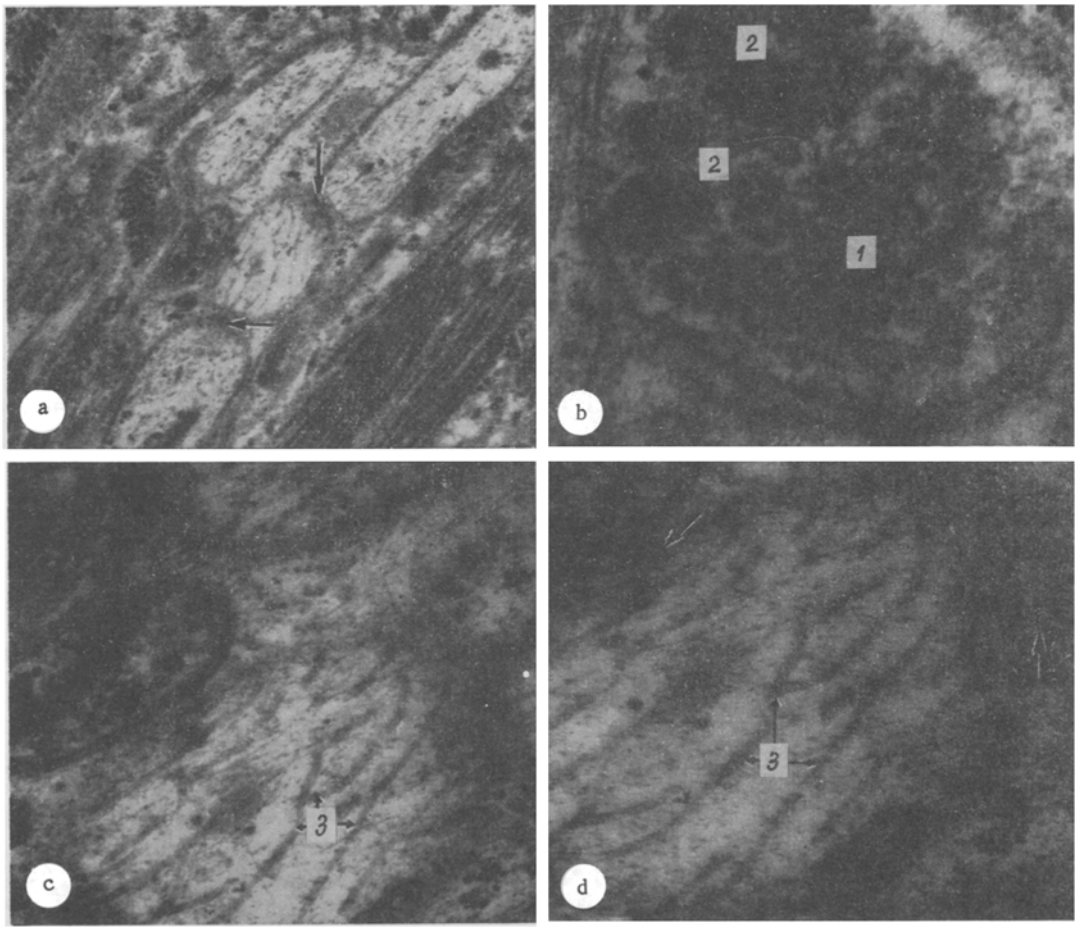

Fig. 2. Ultrastructure of sinus node region of the cat heart: a) transverse sections through axons in region of sinus node (intraaxonal junctions indicated by arrows). 9,000 ×; b) transverse section through axon in region of SN: axonal vesicles (1) and mitochondria (2) within an axon. 52,000 ×; c) axo-axonal synapse (arrows); fusion of membranes of two axons, microtubules in axon (3). 30,000 ×; d) region of axo-axonal synapse: condensed and fused membranes of two axons indistinctly outlined, intra-axonal microtubules (3), 40,000 ×.

EXPERIMENTAL RESULTS

Conductance of the afferent channel from SN to the cerebral cortex showed considerable changes during the development of certain pathological states of the myocardium. For instance, reversible short-term myocardial ischemia caused by compression of the coronary vessles of the second order (the system of the right of left coronary arteries) led to a marked and significant decrease in amplitude of the first positive phase of EP — to 34.3 ± 8.9 μV (the initial amplitude of this phase was 9.15 ± 8.0 μV) at the end of the first 5-min period of ischemia, and to 31.2 ± 6.7 μV at the end of the second period of ischemia. Focal necrosis of the right ventricle, caused by intracardiac injection of 0.1 ml of a 10% solution of neutral formalin led to the virtually complete disappearance of EP by the second minute after injection (Fig. 1a). Recovery of EP was observed not earlier than 50-70 min after injection of formalin (Fig. 1c). These changes in EP cannot be explained by changes in the hemodynamics and by worsening of the functional state of the CNS, because control stimulation of the sciatic nerve and of areas of skin topically close to the heart, before, after, and during ischemia or experimental necrosis evoked potentials identical in shape and latent period with the "cardial EP."

The phenomenon of blocking of the spinal cardiac afferentation may be the result of development of inhibition at different levels of the CNS. Meanwhile data in the literature [2, 3] and our own observations suggest that partial or complete blocking of the spinal afferent system of the heart may take place also at the level of the organ itself, on account

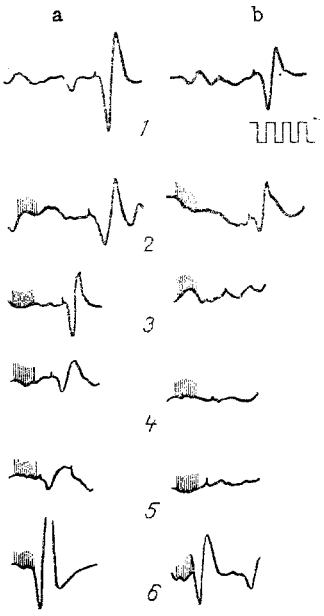

Fig. 3. Changes in cortical EP arising in response to stimulation of SN (12 mA, 0.3 msec) under the influence of preliminary stimulation of the peripheral end of the divided right vagus nerve (burst of pulses; each pulse 0.12 mA, 0.3 msec, following frequency in burst 1000 Hz). 1) EP without previous stimulation of vagus nerve; 2) interval between stimuli 220 msec; 3) 150 msec; 4) 120 msec; 5) 70 msec; 6) 20 msec. Calibration: 40 μV, 20 msec.

of neuronal mechanisms of the intracardial nervous system. Let us examine the argument in support of this view in more detail.

Electron-microscopic investigation of the region of SN (Fig. 2) revealed, in some sections, many round and oval formations 0.4-0.7 μ in diameter (Fig. 2a), surrounded by a double membrane. Inside these formations there were vesicles of mitochondria and also structures resembling microtubules (Fig. 2: b, c, d). Because of the structure of these formations they could be identified as transverse sections through axons. Between them there were junctions (marked by arrows on the electron micrographs) which, under high power (Fig. 2: c, d) appeared as two condensed and fused membranes, which had lost their clear outlines. All these observations suggest that in this case the structures were axo-axonal synapses.

The existence of axo-axonal synapses suggests that presymaptic inhibition may take place actually in the neuronal network of the intracardial nervous system. The electrophysiological phenomena recorded, which are characteristic of presynaptic inhibition, definitely confirm the results of the morphological investigation. In particular, efferent influences of the vagus nerves on conduction in spinal afferent pathways were studied in one series of experiments. In the experiments of this series a method of combined stimulation was used, when the conditioning stimulus (a "burst" of pulses — each pulse 0.3 msec, 0.12 mA; following frequency in the burst 1000 Hz) was applied to the peripheral end of the divided right vagus nerve, while the testing stimulus was applied, after intervals of 200-240, 140-150, 100-120, 60-80, and 10-20 msec to SN. There were two modifications of these experiments: during reversible myocardial ischemia for 5 min and on the intact heart. The character of the change in EP during interaction between stimuli on the substrate of the normal and ischemic heart was similar, but the "depth" of the changes in EP of the ischemic heart was undoubtedly greater. The traces illustrated in Fig. 3 show that a decrease in amplitude of the first phases of EP was observed when the interval between stimuli was 200-240 msec, and reached a maximum when the interval was 60-80 msec. If the interval was 10-20 msec, the EP was restored to a little above the original level. Excitation of efferent fibers of the vagus nerve thus has a prolonged (up to 240 msec) inhibitory influence on conduction of afferentation from the intact and injured heart to CNS structures along spinal pathways. Prolonged inhibitory influences of this kind are characteristic of presynaptic inhibition, and the nature of the technique used indicates that the site of this inhibition was evidently the nervous apparatus of the heart itself.

Investigations [5, 7] have shown that the mediator of presynaptic inhibition is gamma-aminobutyric acid (GABA). The results of a series of experiments in which a 0.5% solution of GABA was applied in a volume of 0.2-0.4 ml to SN actually in the region of application of the stimulating pulses. During the first minute after application of the GABA solution the amplitude of the first two phases of EP fell to 131.2 ± 19.0 μV, and by the 3rd minute to 21.9 ± 3.8 μV (initial sum of amplitudes 241.4 ± 25.8 μV). Recovery of EP was observed approximately 30 min after application. The rapidity of onset of the effect, and also the fact that GABA was applied in very small doses, indicate strongly that the point of its ap-

plication is the nervous apparatus of the heart itself. Further evidence in support of this view is given by the absence of change in shape or amplitude of EP arising in the same area of the cortex in response to stimulation of the sciatic nerve and of an area of skin topically close to the heart before, during, and after application of GABA.

Spinal cardiac afferentiation thus undergoes several changes that are the direct consequence of the stages of development of the pathological process in the myocardium. Complete or partial blockage of the spinal afferent system may be the result of presynaptic inhibition of afferent terminals at the level of the heart itself.

Limitation of conductance of the spinal afferent channel of the heart may evidently take place at the level of the heart itself as a result of local depolarization of spinal afferents, through the activity of inhibitory interneurons that are components of the intracardial nervous system. Under these circumstances interneurons may be triggered both "from above" — through the reflex arc of the vagus nerve, and "from below" — through afferent neurons of the intracardial nervous system.

However, when this hypothesis is submitted, the question of the biological significance of the phenomenon must be considered. We are inclined to the view that the phenomenon of blocking of spinal afferentiation is based on nothing more than a protective-adaptive reaction of the heart to the pathogenic agent. In fact, investigations [8, 9, 11] have shown that stimulation of cardiac sympathetic afferents against the background of ischemia aggravates that ischemia, whereas sympathetic denervation of the heart in acute myocardial ischemia considerably reduces the number of disturbances of the cardiac rhythm. Reduction of the afferent spinal flow may thus indirectly affect the intensity of sympathetic efferent volleys, and at a certain stage of the pathological process that is advantageous for the myocardium.

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