weeks postoperation, 22-26% thymus involution was observed in the animals with marked autotomy. Adrenal hypertrophy was found 2-6 weeks postoperation in the rats with severe autotomy, 7-8 weeks postoperation in the rats with severe and mild autotomies, and in the animals with repeated autotomies.

Thus, the model of DPS caused by transection of the sciatic nerve showed the onset of autotomies in all the operated rats by the 5th month postoperation. It was established that DPS is a constant process, the course of autotomy being wavelike or continuous. The microcirculatory disorders observed two weeks to six months after sciatic nerve transection were shown to be the result of the development of DPS. These disturbances were found in the animals with marked autotomies and did not depend upon whether these were primary or repeated. The healing of the self-mutilated extremities correlated with the normalization of the microcirculation. The microcirculatory disorders observed in the group of animals with continuous autotomy were comparable to those observed during the repeated autotomies; however, in the latter case the number of microvessels with stasis rose significantly and degranulation of the mast cells increased.

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Characteristics of Neurons of the Nodose Ganglion with Constant Spike Activity

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Key Words: *neurons of the nodose ganglion; myelinated and unmyelinated fibers; hemodynamic tests*

Information from the receptors of the cardiovascular system is conducted to the CNS along myelinated and unmyelinated fibers of the vagus nerves. Best studied is the impulse activity from the motor receptors of the atria, ventricles, and blood vessels, which is transmitted along myelinated fibers and is synchronized to the heart rhythm [2,5,8,10]. It has been shown that the nodose ganglion neurons discharging in the heart rhythm receive afferent information transmitted at the speed of excitation conductance (17-32 m/sec) along fibers of the vagus nerve [4]. A constant impulse from the heart receptors and not

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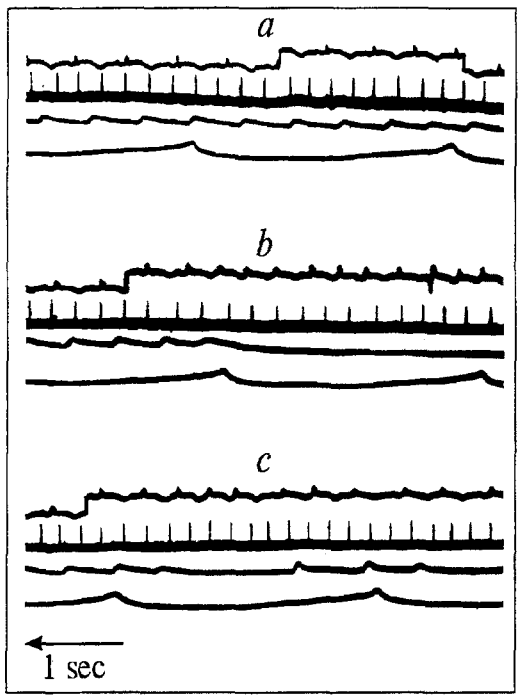

Fig. 1. Absence of reaction of constant regular neurons to hemodynamic tests. *a*) extension of right atrium; *b*) occlusion of aorta; *c*) occlusion of pulmonary artery. From top to bottom: ECG (shift of curve corresponds to period of influence), neurogram, AP in femoral artery, pneumogram.

synchronized to the electrocardiogram (ECG) is conducted along unmyelinated fibers [11]; synchronization of this impulse to the phases of the heart rhythm can be achieved, however, under a number of influences acting on the heart [5,6].

There are neurons with regular and irregular constant spike activity in the nodose ganglion. Taking this into account, we aimed to elucidate which type of neurons perceive afferent information from the receptors of the cardiovascular system and which type of fibers of the vagus nerve take part in the transmission of this information.

MATERIALS AND METHODS

The experiments were carried out on 27 nembutal-narcotized (40 mg/kg, intraperitoneally) cats of both sexes weighing 2.5-4 kg. The animals were placed on artificial respiration using a Vita-1 volume-frequency respirator. After thoracotomy was performed and the pericardium was opened, a ligature was passed beneath the aorta and pulmonary artery at the level of their origin from the ventricles. A thin doderon suture was passed beneath the left coronary artery. Polyethylene catheters were inserted into the left and right atrium. Then a ligature was passed beneath the descending part of the aorta, and vagotomy was performed above the diaphragm. The right vagus nerve on the neck was separated from the sympathetic nerve, and placed in a special device for nerve cooling, the temperature of the nerve being controlled by a mounted thermostat. The nerve was thoroughly isolated from the surrounding tissues; its temperature was regulated by changing the flow rate of the cooling fluid. The activity of nodose ganglion neurons was recorded on an M-42 myograph (Medikor) using extracellular glass electrodes filled with 2.5 M KCl. Records of the neuronal spike activity, ECG in the standard lead II, arterial pressure (AP) in the femoral artery, the pneumogram, and the nerve temperature were performed on an SRD-41 magnetograph (Nihon Kohden) using magnetic tape and on an MR-4 photorecorder (Medikor) using photographic film. The activity of 40 neurons of the nodose ganglion was analyzed. The significance of the results was assessed according to Student's *t* test.

RESULTS

The reactions of the two groups of neurons to the hemodynamic tests were studied in order to elucidate the functions of the constant spike activity neurons of the nodose ganglion. Group 1 comprised neurons with regular constant spike activity; group 2 comprised neurons with irregular constant activity. The following hemodynamic tests were used for cardiovascular system stimulation: a) left and right atrium extension induced by an injection of 5 ml Ringer solution; b) occlusion of the aorta at the site of its origin from the atrium; c) occlusion of the aorta above the diaphragm; d) occlusion of the pulmonary

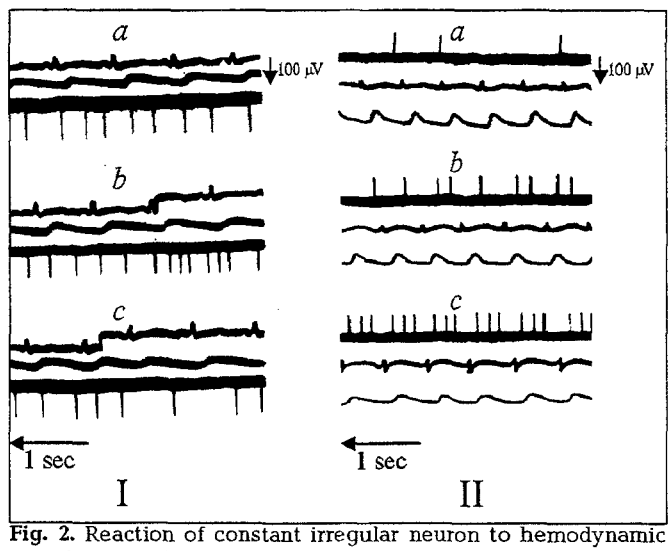

Fig. 2. Reaction of constant irregular neuron to hemodynamic tests (*I*) and ischemia development in myocardium (*II*). *I*: *a*) basic level of activity; *b*) occlusion of coronary artery, *c*) extension of right atrium; *II*: *a*) basic level of activity; *b*) 2nd minute of ischemia development in myocardium, *c*) 7th minute of ischemia development in myocardium. From top to bottom: *I*) ECG, AP in femoral artery, neurogram; *II*) neurogram, ECG, AP in femoral artery.

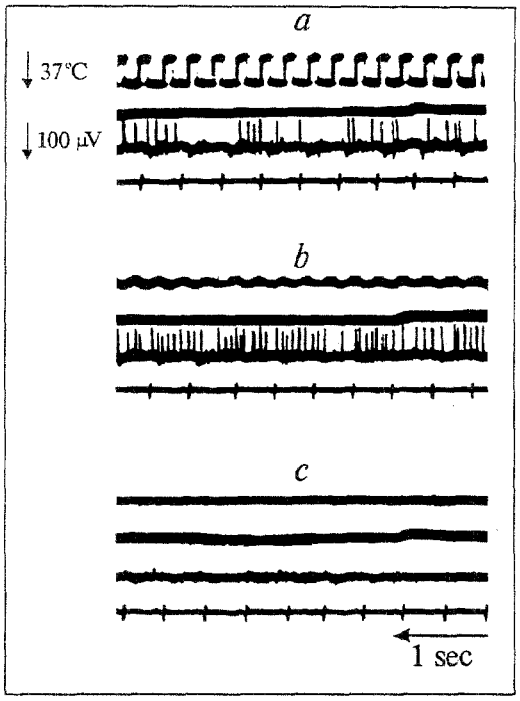

Fig. 3. Reaction of constant irregular neuron to vagus cooling. *a*) neuronal activity at vagus temperature of 37°C; *b*) increase of frequency of neuronal activity at vagus temperature of 6°C; *c*) absence of neuronal activity at vagus temperature of 0°C. From top to bottom: vagus temperature, pneumogram, neurogram, ECG.

artery at the site of its origin from the ventricle; e) occlusion of the left coronary artery. During these functional tests the neuronal reactions arising during the first second of the test were taken into account.

In most cases neurons with regular constant activity (10) discharged at a frequency of 5-16 imp/sec, while in one neuron only a frequency of 46 imp/sec was observed. The neurons of this group showed no reaction to the tests (Fig. 1). The absence of changes of spike activity in response to the hemodynamic tests attests to the fact that the investigated regular constant activity neurons of the nodose ganglion did not receive afferent information from the cardiovascular system.

Neurons with regular constant activity (19) showed a diverse basic level of impulse frequencies, varying in the range of 0-25 imp/sec in the same neuron. Extension of the right and left atrium induced changes in the constant spike activity of the "irregular" neurons in 33% and 67% of experiments, respectively. Neurons of this group (70%) reacted to the occlusion of the main vessels; occlusion of the coronary artery led to a change of the spike activity in 50% of these neurons (Fig. 2, *I*). At the same time, it should be mentioned that in a number of cases a synchronization of the activity of these neurons to the ECG phases was observed against the background of the development of ischemic processes in the myocardium (Fig. 2, *II*).

Thus, the basic level of activity of irregular neurons of the nodose ganglion changed in practically all hemodynamic tests (in contrast to that of "regular" neurons), this being evidence that they receive afferent information from the receptors of the cardiovascular system.

In the next series of experiments (8) the spike activity was studied in 11 irregular neurons of the nodose ganglion against the background of inhibited impulse transmission along myelinated and unmyelinated fibers of the vagus nerve. Cooling of the nerve to 6°C has been shown to block impulse transmission along the myelinated fibers [7]. Against such a background no changes of activity were observed in three neurons, the activity of three other neurons was reduced, and no activity was registered in two neurons. Cooling of the vagus to 0°C is reported to block impulse transmission also along the unmyelinated fibers [9]. Under these conditions no activity was observed in any of the investigated irregular neurons of the nodose ganglion (Fig. 3).

The absence of changes of spike activity in some neurons under conditions of blocked excitation conductance along myelinated fibers is probably evidence that information arrives at these neurons along unmyelinated fibers only. Since changes of spike activity were observed when the vagus nerve was cooled to 6°C, we assumed that these neurons received information conducted along both myelinated and unmyelinated fibers of the nerve, this information being transmitted by its own processes as well as via the synapses of other neurons. The presence of synaptic connections between neurons of the nodose ganglion has been verified with the aid of both morphological and electrophysiological methods [1,3,12].

Thus, the hemodynamic tests induce changes of the spike activity just in the irregular neurons of the nodose ganglion and produce no effect on neurons with regular constant spike activity. The latter observation indicates that afferent information, conducted from the receptors of the cardiovascular system along myelinated and unmyelinated fibers of the vagus nerve, can participate in the regulation of not only neurons synchronized to the pulse, but also constant irregular neurons of the nodose ganglion. The integrated activity of these types of cells obviously plays an important role in the rearrangement of cardiovascular activity under changing hemodynamics.

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Effect of Sodium Valproate, Phenobarbital, and Diazepam Administered in Combination on Convulsions Induced by Electroshock in Mice

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A prerequisite for the genesis of epileptic activity in the brain is deficiency of inhibitory, in particular GABA-ergic, mechanisms [2]. GABA-ergic inhibition results from activation of the $GABA_A$-receptor complex consisting of subunits that bind GABA, benzodiazepines, and barbiturates [10]. These subunits mutually potentiate each other, and this increases the activity of the whole complex and thus leads to an increased chloride current, which causes hyperpolarization inhibition of the neuron [3,9,12].

The present study was undertaken to examine the efficacy of the combined use of two drugs that act on the above-mentioned subunits, namely diazepam (which stimulates GABA activity by increasing the frequency with which the chloride channels open [9,13]) and phenobarbital (which acts by prolonging the open state of these channels [6,11]), as well as of sodium valproate, which enhances the inhibitory GABA-ergic mechanisms by raising the GABA levels in the brain [8].

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MATERIALS AND METHODS

The experiments were conducted on 350 noninbred mice weighing 18-24 g. The animals were kept in the vivarium under ordinary conditions and fed a standard diet. Anticonvulsive activity of the drugs and their combinations was assessed by the maximal electroshock test. The current (40 mA for 0.4 sec) was delivered from an electrostimulator (ENS-01, Lvov) through auricular electrodes (the electrostimulation procedure is described elsewhere [4]). The dose that prevented the occurrence of convulsions in 50% of the animals (ED_{50}) was taken as the index of activity of the drugs after their separate or joint administration. The value of ED_{50} was determined in each particular case by the conventional method of Litchfield and Wilcoxson using computer software. For the analysis and subsequent evaluation of the effects from

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