CHANGES IN EXCITABILITY OF THE INTEROCEPTORS OF THE SMALL INTESTINE IN ANAPHYLAXIS (RESULTS OF AN ELECTROPHYSIOLOGICAL INVESTIGATION)

V. A. Lebedeva, B. I. Padegimas, and Yu. L. Pines

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The nervous system is known to play an important role in the mechanisms of development of anaphylaxis and immunity [1, 3, etc.]. In these processes considerable importance is attached to changes in the functional properties of the peripheral receptor structures and, in particular, of the interoceptors [1, 6, 7, 9, 10, etc.]. Reflex changes in the blood pressure have usually been used as the index of the changes in the functional properties of the receptors, and only occasionally [6, 8] has the effect of anaphylaxis on the character of the flow of afferent impulses been studied. During perfusion of the carotid sinus in sensitized animals, L. M. Ishimova [6] and V. I. Kiseleva [8] found a much greater intensity of afferent impulses in the nerve to the sinus evoked by acetylcholine and antigen than in control animals.

In the present investigation the effect of anaphylaxis on the excitability of the receptors of the small intestine was studied in conditions of perfusion and recording the potentials from the afferent intestinal nerves.

EXPERIMENTAL METHOD

Experiments were carried out on 22 cats anesthetized with urethane (1.0-1.5 g/kg). The animals were sensitized by four subcutaneous injections of 1.5 ml of normal horse serum (HS) at intervals of 1-2 days. The incubation period was 14 days. The loop of small intestine used in the experiments was perfused with Ringer–Locke solution (pH 7.4) of the following composition (in mM/liter): NaCl–154, KCl–5.6, $CaCl_2$–2.2, $NaHCO_3$–1.8, glucose–5.5. The rate of perfusion was 40 ml/min. The afferent impulses were recorded in the peripheral ends of the divided intestinal nerves dissected for a distance of 3-4 cm from the intestinal wall. The biopotentials were detected with silver electrodes 4-5 mm apart, and recorded on an oscillograph with a symmetrical amplifier, the frequency characteristic curve of which was linear over the range from 10 to 1500 cps.

In the experiments of series I, carried out on 10 control animals, the threshold doses of acetylcholine causing excitation of the intestinal receptors when injected into the blood vessels of the perfused intestinal loop and into the femoral vein (with a normal blood supply to the intestine) were determined. The same method was used to investigate the reaction of the receptors to the antigen (HS) and its effect on the sensitivity of the receptors to acetylcholine. The same reactions were studied in the experiments of series II on 12 sensitized cats.

EXPERIMENTAL RESULTS

In the control animals the flow of spontaneous afferent impulses in the nerves of the small intestine was usually absent or weak. This was evidently because the experiments were carried out on cats which has fasted for 24 h. As O. N. Zamyatina [5] demonstrated previously, the bioelectrical activity of the intestinal nerves is slight at this period. The intestine may be assumed to be in a state of relative functional rest at this time, and the chemical and mechanical stimuli responsible for excitation of the interoceptors were absent. In the sensitized cats, on the other hand, a well define spontaneous flow of impulses was present in the form of both slow waves (amplitude up to 20 μV) and of fast occillations with a duration of 1-2 msec (amplitude 30-40 μV).

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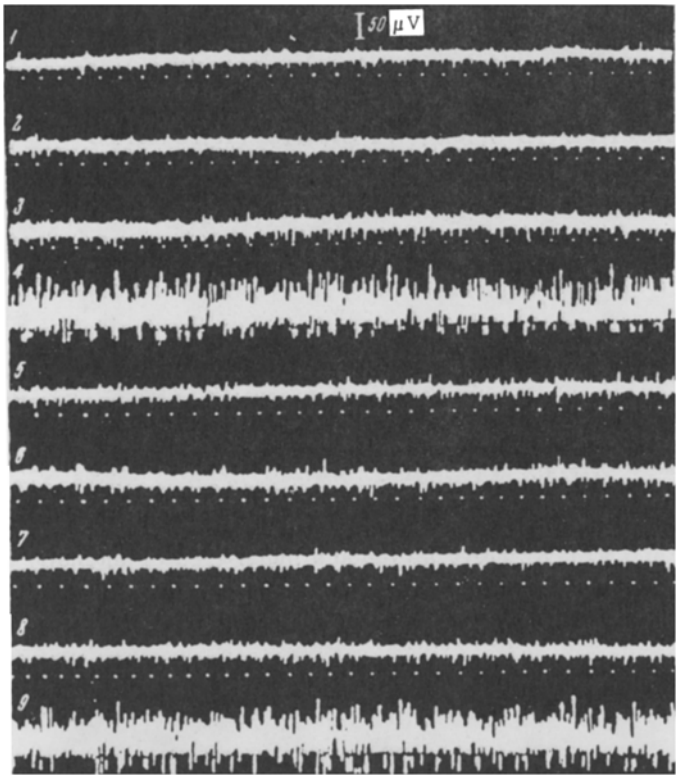

Fig. 1. Afferent impulses in the nerves of the perfused small intestine in unsensitized animals. 1) background; 2-4) 5 sec after injection of 1, 10, and 100 μg respectively of acetylcholine into the perfusate; 5) background; 6) 5 sec after injection of 5 ml horse serum into the perfusate; 7) background; 8, 9) 5 sec after injection of 10 and 100 μg respectively of acetylcholine; time marker 0.05 sec.

During perfusion of intestine, in the usensitized cats threshold doses of acetylcholine, causing an increase in the flow of afferent impulses in the intestinal nerves, had a mean value in these experiments of 10 μV. Injection of 5 ml HS into the perfusion fluid caused no changes in the flow of impulses, and the sensitivity of the receptors to acetylcholine as a rule remained unchanged (Fig. 1).

If the acetylcholine was injected into the general blood stream, the flow of impulses was intensified only when the dose of the drug was 100 μg or more. The receptors did not react to intravenous injection of HS, and their sensitivity to the subsequent injection of acetylcholine remained unchanged.

In the sensitized animals the threshold doses of acetylcholine stimulating the receptors when injected into the vessels of the perfused intestine were lowered to 0.1 μg. In these animals the flow of impulses was intensified also after injection of 5 ml of HS into the perfusion fluid. The action of HS on the receptors led to a decrease in the sensitivity to acetylcholine by more than 100 times (Fig. 2).

If acetylcholine was injected into the general blood stream of sensitized animals the threshold doses of the drug, as in the case of the unsensitized animals, were on the average 100 μg (Fig. 3). In the sensitized animals, however, the flow of afferent impulses was intensified in response to the intravenous injection of 5 ml HS. The excitability of the intestinal receptors then declined (the threshold doses of acetylcholine increased to 500-1000 μg).

The electrophysiological investigation of the functional state of the receptors in the small intestine showed that their excitability was considerably higher in animals sensitized by repeated injections of foreign HS protein than in the controls.

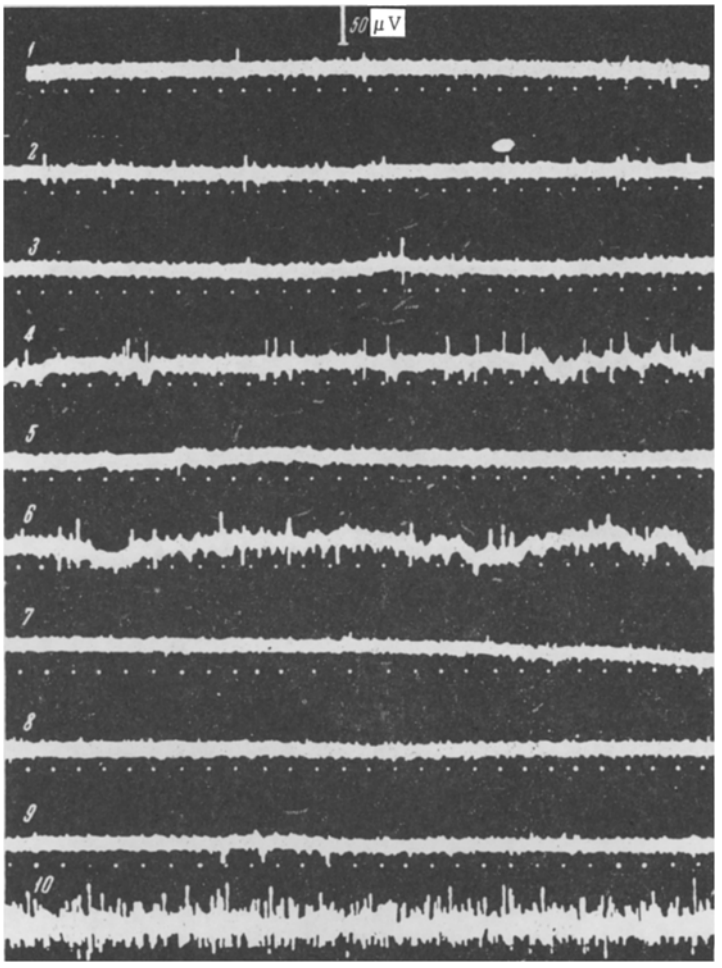

Fig. 2. Afferent impulses in the nerves of the perfused small intestine in sensitized animals. 1) background; 2) 5 sec after injection of 0.1 μg acetylcholine into the perfusate; 3) background; 4) 5 sec after injection of 1 μg acetylcholine; 5) background; 6) 5 sec after injection of 5 ml horse serum; 7) background; 8) 5 sec after injection of 100 μg acetylcholine; 9) background; 10) 5 sec after injection of 1000 μg acetylcholine; time marker 0.05 sec.

It was recently found that the increased flow of impulses evoked by acetylcholine in the peripheral ends of the divided splenic [11] and intestinal [2] nerves is due partly to the stimulant action of this drug on the efferent endings of the corresponding nerves. This effect could not have occurred in the present series of experiments, because an obvious increase in the intensity of the "spontaneous" impulses and also in the intensity of the responses not only to acetylcholine, but also to antigen, was observed. Moreover, a similar increase in the sensitivity of the receptors to antigen, followed by a decrease in their sensitivity to certain chemical substances (acetylcholine, adrenalin, choline, and pilocarpine), has been reported in sensitized animals in which the carotid sinus, the small intestine, the spleen, and the adrenal gland were perfused and reflex changes in the blood pressure were recorded [4, 6, 9, 10].

The results of the present experiments suggest that the interoceptors of the small intestine may participate in the development of sensitization of the organism and in the mechanism of development of anaphylactic shock.

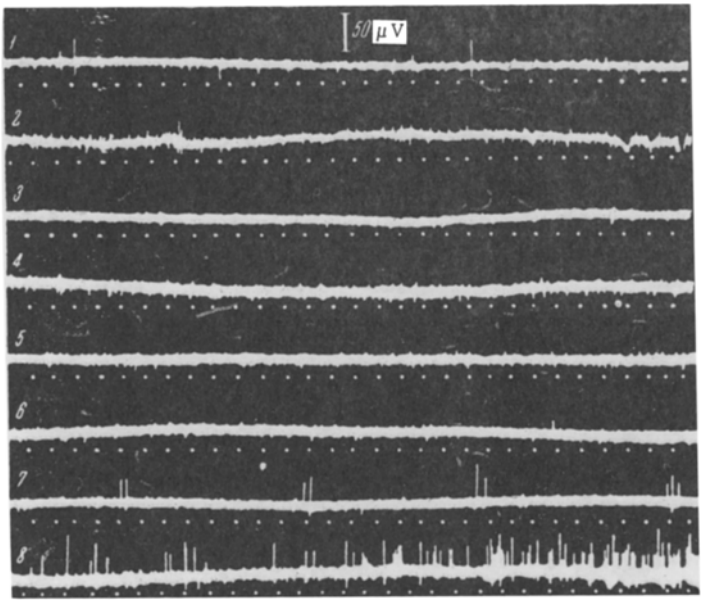

Fig. 3. Afferent impulses in the nerves of the intact small intestine of sensitized animals. 1) background; 2) 10 sec after injection of 100 μg acetylcholine into the general blood stream via the femoral vein; 3) background; 4) 10 sec after injection of 5 ml of horse serum; 5) background; 6) 10 sec after injection of 100 μg acetylcholine; 7) background; 8) 10 sec after injection of 1000 μg acetylcholine; time marker 0.05 sec.

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