THE ACTION OF CARBONIC ACID AND NOVOCAINE ON THE INTEROCEPTORS OF THE ILEOCECAL REGION

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At the present time there is a generally accepted concept in physiology of the presence in the intestinal tract of two types of interoceptors: mechano-and chemoreceptors. However, the functional characteristics of these receptors have not yet been studied systematically. V. A. Lebedeva has expressed a hypothesis on the possible variations in the physiological qualtities of the mechano-and chemoreceptors, which are shown in particular in their different sensitivity to the lack of oxygen.

There are also reports on depressing the excitability of chemoreceptors as well as mechanoreceptors of the intestinal tract and bladder in the conditions of prolonged contact with hypercapnic solution [1, 2, 4].

To prove the reflex nature of the effects observed during chemical and mechanical stimulation of the receptors of the internal organs, novocaine was used by V. N. Chernigovsky [5] and his co-workers. In concentrations of 0.5-2% it lowered or depressed the excitability of the interoceptors, which was accompanied by the disappearance of reflexes from the receptor field under investigation.

In connection with the data about the depressing action of carbonic acid and novocaine on the interoceptors, an attempt was made to compare the sensitivity of the mechano-and chemoreceptors of the intestinal tract to each of these agents separately and to show the ranges of the novocaine concentrations, in which the dissociation of the mechano-and chemoreceptors' sensitivity takes place.

The perfusion method of an intestinal loop, isolated from the general circulation, with intact nervous connections, developed by V. N. Chernigovsky, permits a simultaneous study of various groups of intestinal receptors during the action of the same agent.

The ileocecal region was chosen as the object for the study of the comparative sensitivity of the mechano- and chemoreceptors of the intestinal tract to hypercapnia and novocaine.

EXPERIMENTAL METHOD

The experiments were conducted on cats under urethane narcosis (25% solution). An area of the ileocecal angle together with the mesentery was perfused by oxygenated Ringer-Locke's solution at 37-38° at a pressure of 100 mm mercury. Attention was especially directed to the conservation of nervous connections. Carbonic acid or novocaine was applied to the receptors of the ileocecal region by switching the perfusion to the corresponding solution. A cannula was tied into a part of the colon connected to a system for distending the perfused area, and also serving as an outlet for the transudate. The pressure in the opening in the perfused area, the arterial pressure in the common carotid, the respiration rate and the rate of the perfusion were recorded on a kymogram by means of a drop recorder.

The mechanicoreceptors were stimulated by distending the intestine with air. The height of pressure in the intestinal opening varied between 100 to 130 mm mercury. The reflexes from the chemoreceptors were produced by nicotine (10-100 γ), which was introduced into the perfusate flow. After recording the initial size of the reflexes ("background"), a hypercapnic solution or the novocaine solution was allowed to flow through for 1-3 minutes. After 1/2 -1 minute following the switching of the perfusion to the basic solution, the same stimulations were applied with an interval of 1-1 1/2 minutes. Further, combinations of the stimuli were repeated every 3-5 minutes, in various orders, to show the dynamics of the reflexes' re-establishment.

EXPERIMENTAL RESULTS

The action of the carbonic acid on the mechano-and chemoreceptors of the ileocecal region. Altogether 15 experiments were made, the results of which are shown in the table.

As can be seen from the findings shown in the table, after perfusion with hypercapnic solution for 1-3 minutes, the diminution of reflexes from the mechanoreceptors was observed in 12 tests out of 26, and from the chemoreceptors in 19 out of 28. Also the reflex reactions of the chemoreceptors changed in all experiments after the action of the carbonic acid, whereas the reflexes in response to mechanical stimulations remained unchanged in 3 experiments (Figure 1).

The character of the changes in the reflexes	Number of tests	
	reflexes of the mechano-receptors	reflexes of the chemo-receptors
Complete depression	7	7
Diminution	12	19
Absence of changes	3	0
Increase	4	2

When the mechanical and chemical stimulations were applied during the time of the flow of the solution saturated with carbonic acid, the reflex responses were absent.

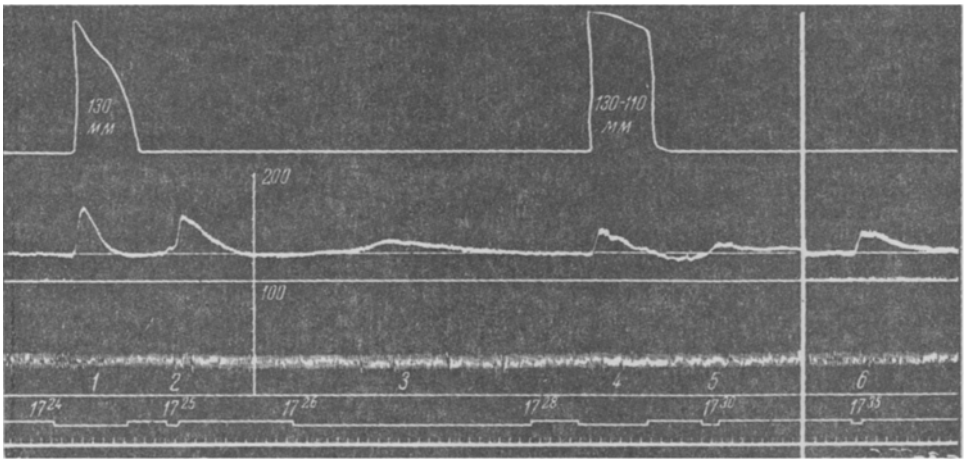

Fig. 1. The reflex changes in the arterial pressure in response to increased pressure in the opening of the perfused part of the intestine up to 130 mm mercury (1, 4) and to the introduction of 10 γ nicotine (2, 5). After a 2 minute perfusion with carbonic acid (3) the reflex to the introduction of 10 γ nicotine (5) decreased more than to the increase in pressure in the intestinal opening (4). The reaction of the blood pressure to the introduction of 10 γ nicotine (6) after 7 minutes following the action of carbonic acid. Experiment of January 22, 1954. Narcosis-urethane. Interpretation of the curves (from top to bottom): pressure in the intestinal opening, arterial pressure, initial level of arterial pressure, rate of perfusion, respiration, zero line of the manometer, mark of stimulation, mark of time (5 seconds).

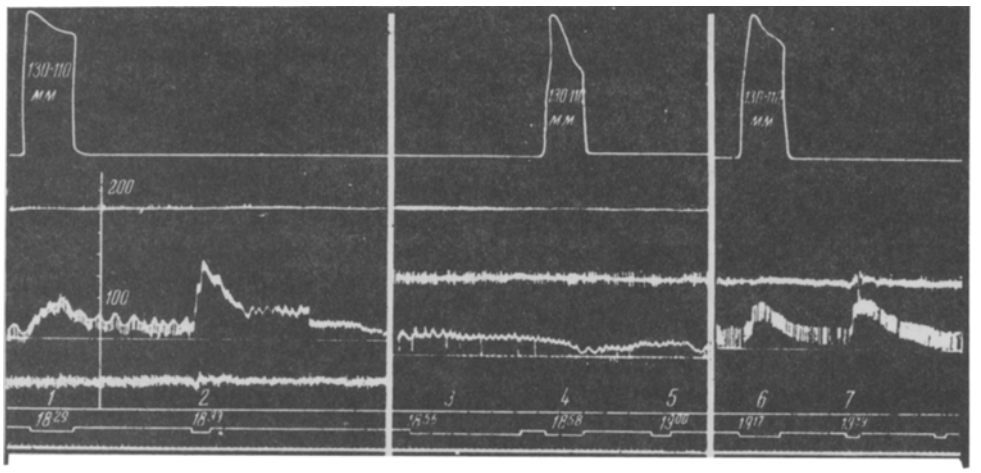

Fig. 2. The reflex changes in the arterial pressure in response to increasing the pressure in the intestinal opening up to 130 mm of mercury (1, 4, 6) and to the introduction of 100γ nicotine (2, 5, 7). After $1^1/_2$ minute perfusion with 100 mg% (0.1%) solution of novocaine (3) the reflexes were absent both from the mechano- and chemoreceptors (4, 5). After 20 minutes the reflex from the mechanoreceptors (6) was completely reestablished, but from the chemoreceptors (7) it did not reach its initial height. Experiment of April 12, 1954. Narcosis-urethane. Interpretation of the curves (from top to bottom): pressure in the intestinal opening, rate of perfusion, arterial pressure, initial level of the arterial pressure, respiration, zero line of the manometer, mark of stimulation, mark of time (5 seconds).

The reestablishment of the reflex reactions after the action of carbonic acid was observed in 10 out of 22 tests on stimulating the mechanoreceptors and only in 2 tests out of 26 on stimulating the chemoreceptors. These findings can also serve as indication of the greater sensitivity of the chemoreceptors as compared to the mechanoreceptors to the action of carbonic acid.

The action of novocaine on the mechano- and chemoreceptors of the ileocecal region. 18 experiments were conducted using 100, 50 and 25 mg% solutions of novocaine. The experimental conditions were identical to those of the first series.

Seven experiments were conducted using a perfusion of novocaine solutions in the concentration of 100 mg% (0.1%). In all the experiments, after perfusing the novocaine solution for 1-3 minutes through the vessels of the intestinal loop, the reflexes to the stimulation of the chemoreceptors as well as the mechanoreceptors were completely absent (Figure 2). Only in one experiment, an insignificant pressor reaction on applying mechanical stimulation was observed.

In experiments with perfusion of a novocaine solution in the concentration of 50 mg% (6 experiments, 7 tests) a complete depression of the interoceptor reflexes was noted in 4 cases. In 2 tests the reflexes from the chemo- as well as from the mechanoreceptors were not changed. In one test the reflex in response to chemical stimulation was absent, but the reflex to the intestinal distension remained.

On diminishing the novocaine concentration to 25 mg% (5 experiments, 7 tests) a complete switching off of the interoceptors was observed only in 2 tests(after a 3 minute perfusion with novocaine), the interoceptor reflexes remained also in 2 tests (Figure 3, A) and the dissociation of the sensitivity to novocaine, with the preservation of the stretch reflexes was observed in 3 tests (Figure 3, B).

The difficulty of the study of the functional properties of the mechanoreceptors in the perfusion conditions is connected with the growing edema of the intestinal wall and the filling of its opening with transudate, causing inconsistency in the mechanoreceptors' reflexes in the given conditions of the experiment. In connection with this, three control experiments were made, recording the reflexes from the mechano- and chemoreceptors during perfusion. It was shown that in these conditions the reflexes from the chemoreceptors do not change materially for 1 1/2-2 hours. The reflexes from the mechanoreceptors, as a rule, diminish towards the end of the first hour, and disappear completely towards the end of the second hour.

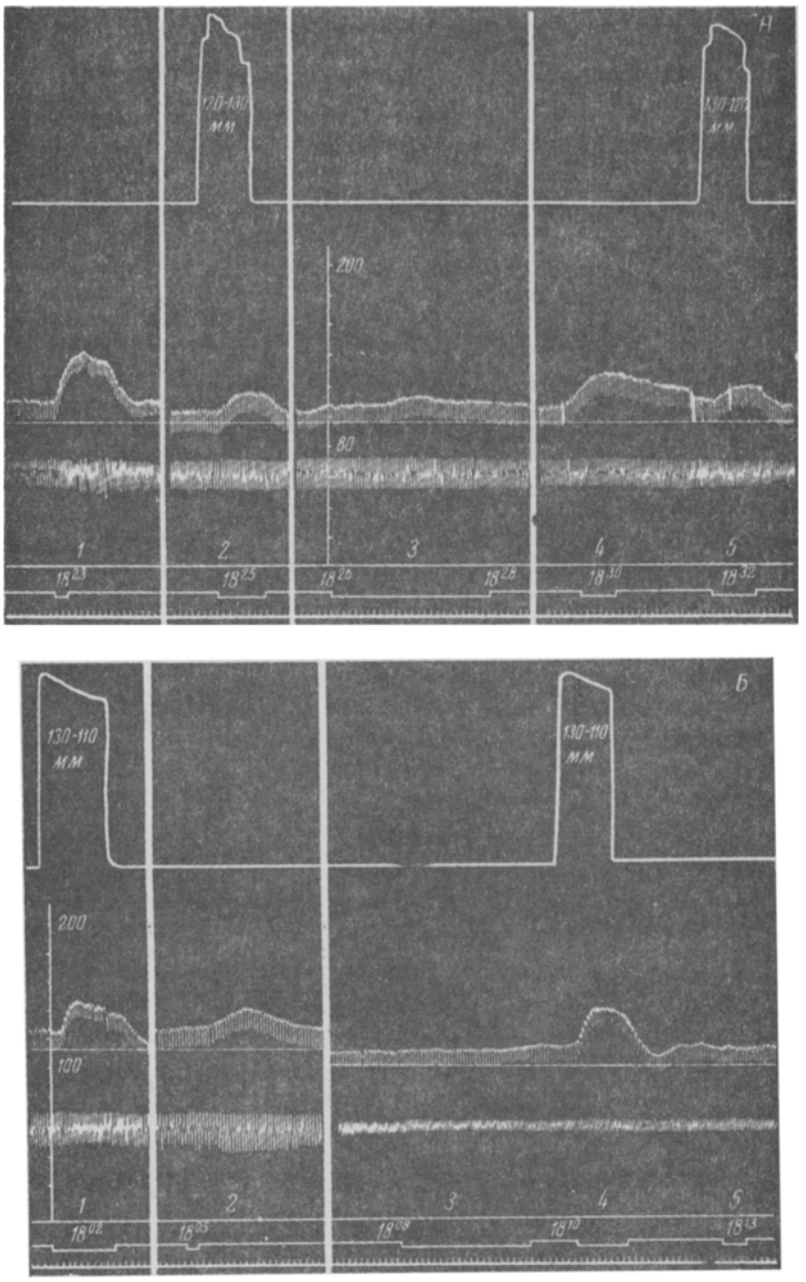

Fig. 3. A) Reflex changes in the arterial pressure during stimulation of the mechanoreceptors of the intestine (2, 5) and during the introduction of 100 γ of nicotine (1, 4). After a 2 minute perfusion with 0.025% solution of novocaine (3) the reflexes from the interoceptors remained (4, 5). Experiment of April 14, 1954. Narcosis-urethane. B) Reflex changes in the arterial pressure in response to the increase in pressure in the intestinal opening up to 130 mm mercury (1, 4) and to the introduction of 10 γ nicotine (2, 5). After 1 1/2 minute perfusion with 0.025% solution of novocaine (3) the reflex from the mechanoreceptors (4) was not changed and the reflex from the chemoreceptors is absent (5). Experiment of April 19, 1954. Narcosis-urethane. Interpretation of the curves (from top to bottom): pressure in the intestinal opening, arterial pressure, initial level of arterial pressure, respiration, zero level of the manometer, mark of stimulation, time mark (5 seconds).

It must be emphasized that in spite of the unfavorable conditions which the mechanoreceptors of the perfused organ are in, they have proved to be more stable to hypercapnia and novocaine than the chemoreceptors.

Note should be taken of the results of the control experiments, which show that with the strength of the stimulators and the time intervals used, the sequence of the mechanical and chemical stimulations did not influence the character of the reflex reactions.

Thus, the results obtained permit an evaluation of the unequal sensitivity of the mechano-and chemoreceptors to the action of certain chemical agents (e. g. carbonic acid, novocaine, etc.). Novocaine as well as solutions saturated with carbonic acid distinctly lower the excitability of theinteroceptors – mainly that of the chemoreceptors and to a lesser degree that of the mechanoreceptors.

LITERATURE CITED

[1] N. A. Lapshin, [Papers of the Military-Naval Medical Academy] (In Russian) (Leningrad, 1951) Vol. 29, pp. 46-62.

[2] V. A. Lebedeva [The Problems of the Interoceptor Physiology] (In Russian) (Moscow-Leningrad, 1952) 1, pp. 273-304.

[3] V. A. Lebedeva , Byull. Eksperim. Biol. i Med. Vol. XXXV, pp. 5-10 (1953).

[4] V. A. Lebedeva and V. M. Khayutin, [The Problems of the Interoceptor Physiology] (In Russian) (Moscow-Leningrad, 1952) No. 1, pp. 305-310.

[5] V. N. Chernigovsky, [The Afferent Systems of the Internal Organs] (In Russian) (Kirov, 1943).