ELECTROPHYSIOLOGICAL INVESTIGATION OF THE MECHANISM OF CHEMORECEPTION

COMMUNICATION II. CHANGES IN AFFERENT IMPULSES IN THE INTESTINAL NERVES UNDER THE INFLUENCE OF CARBON DIOXIDE AND NOVOCAIN, AND ALSO IN CONDITIONS OF DISTURBED METABOLIC PROCESSES THROUGH THE EFFECT OF MONOIODOACETIC ACID

N. A. Anikina

From the Laboratory of Physiology of the Nervous System (Director-Candidate of Biological Sciences O. V. Verzilova) and of the Laboratory of General Physiology (Director-Acting Member of the Acad. Med. Sci. USSR V. N. Chernigovsky) Institute of Normal and Pathological Physiology (Director-Acting Member of the Acad. Med. Sci. USSR, Prof. V. N. Chernigovsky) Moscow

(Received August 25, 1955. Presented by Acting Member of the Acad. Med. Sci. USSR V. N. Chernigovsky)

The previous communication [1] presented material characterizing the change in electrical activity in the peripheral segments of the intestinal nerves upon the introduction of nicotine and acetylcholine in a liquid perfusing the vessels of the isolated intestine. With this, along with the reflex changes in blood pressure, we observed the emergence in the nerves of the intestines of impulses of a relatively slow type with an amplitude up to 35 μ v and a frequency of 80-90 herz, arbitrarily defined by us as the "slow" impulse.

The connection was established between reflex blood pressure (pressor reactions) and the emergence of this kind of impulse through the effect of the indicated chemical stimuli changes.

In this investigation, we studied the changes in electrical activity of the intestinal nerves with the development of the depressor reactions of blood pressure.

The appearance of such reactions by the effect of novocain on the intestinal receptors, on its introduction into the flow of the liquid perfusing the vessels of the intestines, and also under the influence of carbon dioxide in conditions of disturbed intestinal metabolism induced by monoiodoacetic acid, was demonstrated in the investigations of V. N. Chernigovsky [8], and then of V. A. Lebedeva and V. N. Chernigovsky [6].

Subsequently, the physiological mechanism of the depressor reactions was studied in the works of V. A. Lebedeva [2-4], who on the basis of her findings, without applying the electrophysiological method, arrived at a conclusion concerning the absence of a special depressor impulse. The author attributes the development of the depressor effect under the influence of carbon dioxide, to the decrease or full cessation of the pressor tonic impulse.

The variation in the effect of carbon dioxide on the intestine in normal conditions, and in conditions of disturbance of the tissue metabolism by introducing monoiodoacetic acid, is to be explained, in the view of V. A. Lebedeva [5], by the increased responsiveness in these conditions of the tissue receptors to a different kind of chemical stimuli: such an increase in the responsiveness was demonstrated experimentally by the author. V. A. Lebedeva observed an increase in blood pressure reflex reactions to the effect of chemical stimuli (nicotine, sodium bicarbonate, potassium chloride) after introduction of monoiodoacetates into the intestine. The threshold doses of these stimuli thereupon distinctly diminished. The author explains the change

in the blood pressure pressor reaction, arising under the influence of carbon dioxide on the receptors of the normal intestine, and the blood pressure depressor reaction under the influence of carbon dioxide in conditions of disturbed intestinal tissue metabolism on the basis of the transition of the receptors from a state of excitation to a state of inhibition, in line with the conception of N. E. Vvedensky and A. A. Ukhtomsky, that the "apparatus, finding itself in a state of constant and sufficiently strong activity, is bound more easily to fall into a state of inhibition, than an apparatus which is resting and inactive"

In the present investigation, we studied the change in the bioelectrical potentials of the peripheral segments of the nerve trunks of the mesenteric plexus and the fine nerve branches of the intestines under the influence of carbon dioxide and nicotine on the normal intestines and after poisoning with a monoiodoacetate. The changes in the potentials in these nerves was also studied under the influence of novocain, which caused a depressor reaction of the blood pressure.

EXPERIMENTAL METHODS

The experiments were conducted by perfusion of an isolated intestinal segment having only nerve links with the organism. The chemical stimuli were introduced into the perfusate. We recorded the afferent impulses of the intestinal nerves and at the same time registered the carotid blood pressure (by means of a mercury manometer) on a kymograph.

The method was described in detail in the previous communication [1]. Stimulation by carbon dioxide was carried out by replacing the oxygenated nutrient Locke-Ringer solution by the same solution saturated with carbon dioxide.

EXPERIMENTAL RESULTS

After passage through the intestinal vessels for 20-60 seconds, the carbon dioxide produces, as is known, reflex changes in blood pressure in the form of an increase. This effect was discovered for the first time in the experiments of V. N. Chernigovsky, and then was repeatedly observed in the experiments of V. A. Lebedeva and other co-workers of V. N. Chernigovsky.

We observed upon perfusion of carbon dioxide for 30 seconds through the vessels of the intestines, alongside a blood pressure pressor reaction, the appearance of "slow" impulse of small amplitude, which we described earlier in relation to the influence of chemical stimuli. Where an initial "quick" impulse was present, the latter in some experiments, under the influence of carbon dioxide, grew in intensity (Fig. 1, A and B). It should be noted that the amplitude of the "slow" impulse, arising under the influence of carbon dioxide, was less than with the influence of nicotine and acetylcholine. It showed more distinct changes with the direct introduction of carbon dioxide by injection into the blood stream in conditions of removal of the potentials from the very fine nerve branch of the intestines at the point of its emergence from the intestinal wall (Fig. 1, lower tracing).

With a longer perfusion of carbon dioxide through the vessels of the intestines, the original basic impulse was suppressed to the point of complete disappearance, with subsequent restoration to normal after perfusion of Locke-Ringer solution (Fig. 2). Whereupon an increase in comparison with the original basic amplitude of the bioelectrical potentials was often observed. Prolonged perfusion of carbon dioxide produced suppression both of the "quick" and "slow" impulses.

Of special interest is the study of the electrical activity of the nerve branches of the intestines under the influence of the stimuli already investigated by us on the basis of treating the intestines with monoiodoacetic acid.

The arrangement of the experiments in this case was as follows. At first the substances under study were introduced in the vessels of the intestines before treatment with a monoiodoacetate; the reflex changes in blood pressure and changes in the electrical activity of the nerve branches of the intestines were recorded. Then 4-5 ml 0.01 N solution of monoiodoacetic acid was introduced. After some time (necessary in order to produce "distorted" reflexes from "poisoned" segment of the intestines) we again studied the effect of nicotine and carbonic acid. The very introduction of monoiodoacetic acid caused the appearance of the same kind of "slow" impulses as with the stimuli of the other chemical substances. The effect just as quickly disappeared as with the effect of the other chemical stimuli. The basic impulse, after this, established itself at a somewhat different level. The introduction of nicotine in this condition produced in the nerve branches of the intestines a much

greater impulse than did the same dosage of nicotine on the normal intestines (Fig. 3, A and B).

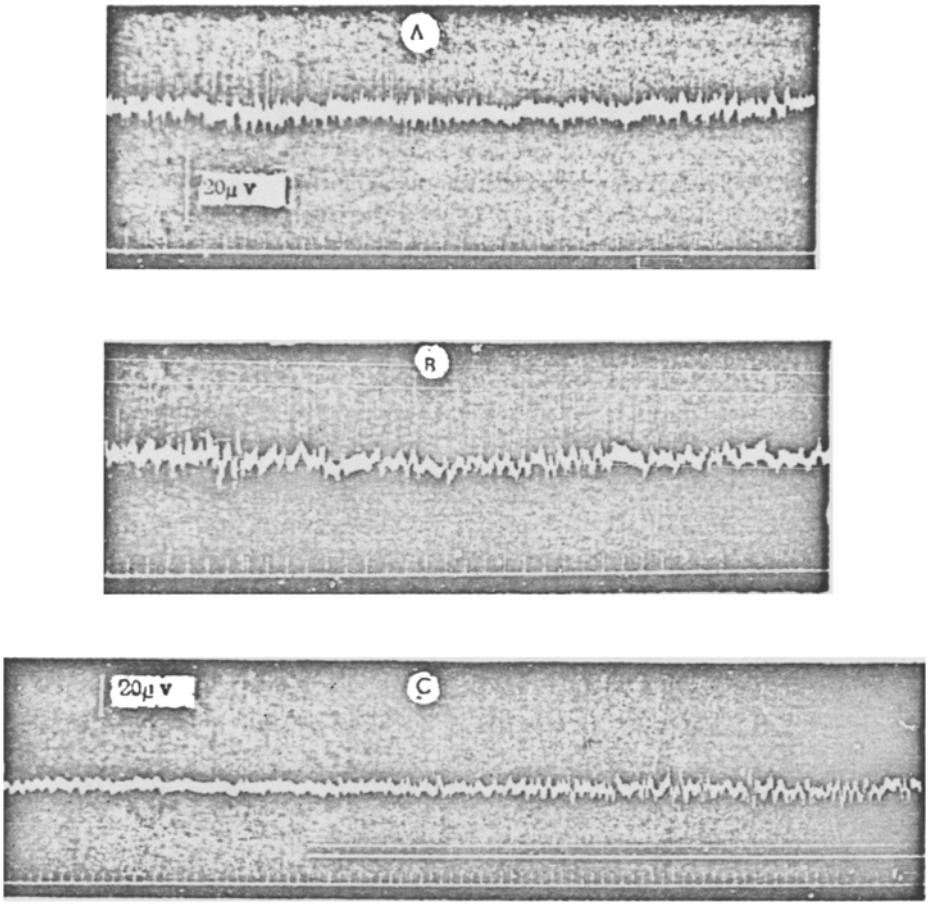

Fig. 1. Change in electrical activity of the peripheral terminus of the intestinal nerve upon infusion of carbonic acid through the vessels of the intestines. A) Electrical Activity of the Intestinal Nerve before Stimulation; B) Electrical Activity of the Intestinal Nerve under the Influence of Carbonic Acid for thirty seconds. Significance of tracings (from top to bottom) for A and B: Currents of the activity of the Intestinal Nerve, Indication of Time (50 herz); for C: Change in Electrical Activity in the Fine Nerve Branch of the Intestines upon introduction in the Vessels of the Intestines of 2 ml hypercapnic solution. Currents of the activity of the intestinal nerve; indication of stimulation (introduction of 2 ml hypercapnic solution), indication of time (50 herz).

Under the influence of carbon dioxide in these conditions, together with the blood pressure depressor reaction, we saw suppression of the original impulse (Fig. 3, D) after only 30 seconds of perfusion of carbon dioxide through the vessels of the intestines (there took place suppression both of the "quick" and "slow" impulses), while with the effect of carbon dioxide for the same length of time on the receptors of the normal intestines, as indicated above, there occurred a strengthening of the afferent impulse (see Fig. 1, B) and of the blood pressure pressor reaction.

Upon further perfusion of carbon dioxide through thevessels of the intestines with a monoiodoacetate poisoning, the impulse disappeared fully in a shorter time than with identical stimulation of the vessels of the normal intestines.

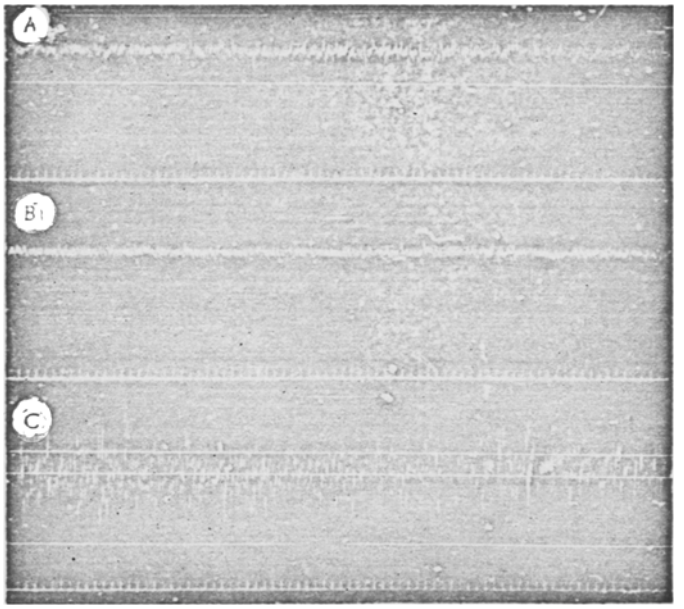

Fig. 2. Change in electrical activity of intestinal nerve upon prolonged infusion with carbonic acid in the vessels of the intestines with subsequent washing with Locke-Ringer solution (in the presence of "Slow" Impulses in the original conditions).
A) Electric Activity of intestinal nerve before stimulation;
B) The same, two minutes after commencement of carbonic acid infusion.
C) The same, five minutes after washing with Locke-Ringer solution.
Significance of tracings (from top to bottom): currents of the activity of the intestinal nerve; indication of time (50 herz).

We also investigated the effects of novocain in a concentration causing a small blood pressure fall. The introduction of novocain produced a depressor reaction of the blood pressure. Recording of currents of the functioning of the peripheral segment of the nerve trunk of the mesenteric plexus (Fig. 4, A and B) showed that with the effect of novocain the original impulse was very quickly suppressed.

DISCUSSION OF RESULTS

As our experiments show, the depressor reflexes, arising under the influence of novocain and carbon dioxide, in conditions of treatment of the intestines with monoiodoacetic acid, are related to the suppression or exclusion of the original basic impulse. It follows from the findings that upon development of the blood pressure depressor reaction, no special "depressor" impulse arises, and there occurs suppression both of the original "slow" impulse which was seen in our experiments, under the influence of the chemical stimuli on the receptors of the intestines, and the "quick" impulse arising upon stimulation of the Vater pacinian corpuscles.

The same conclusion was reached by V. N. Chernigovsky and V. A. Lebedeva on the basis of their experimental investigations. They consider that the reflex fall in blood pressure under the influence of chemical stimuli on the vessels of the intestines depends on the partial or complete absence of the tonic afferent impulses of the sensory apparatus of the intestines.

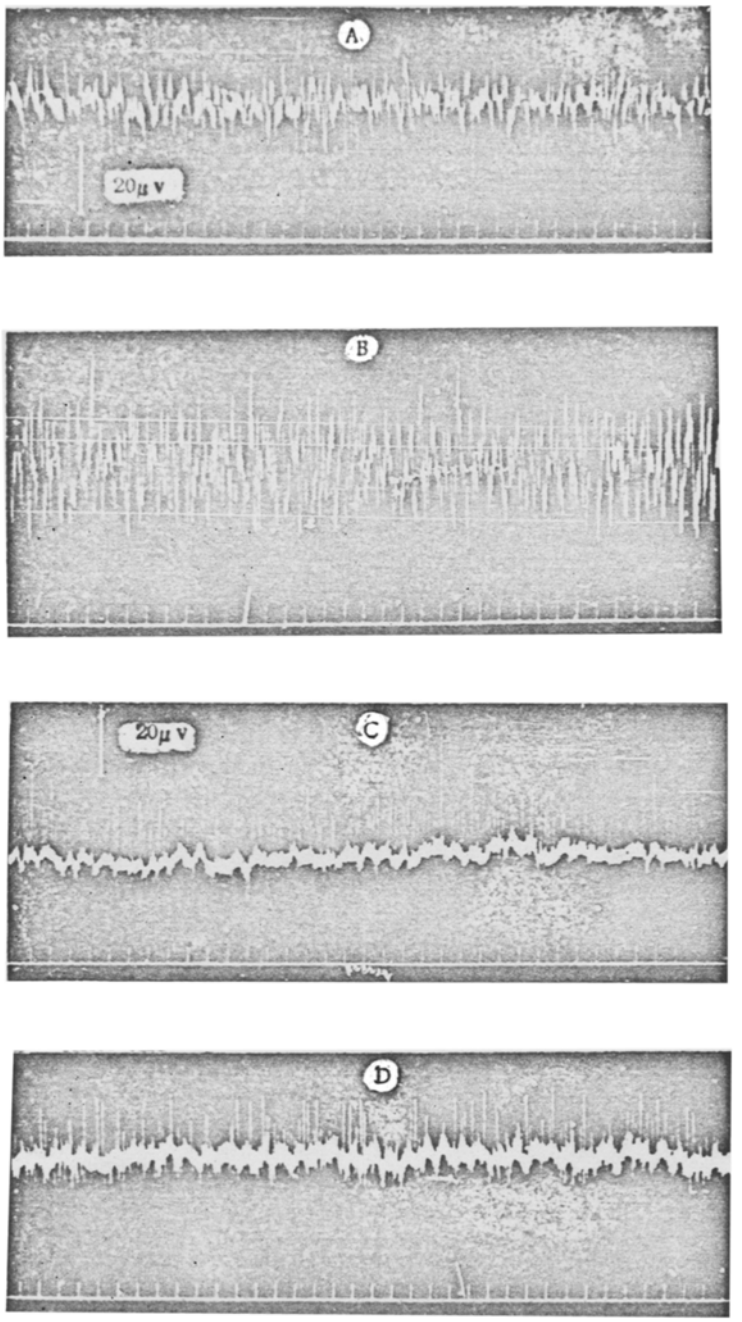

Fig. 3. Change in afferent impulses of intestinal nerve upon introduction in the vessels of the intestines of nicotine and carbonic acid in condition of disturbed metabolism of the intestine by monoiodoacetic acid.
A) Electrical activity of the afferent nerve of the normal intestine upon introduction in its vessels of 100 γ nicotine; B) electrical activity of the intestinal nerve upon introduction in the intestinal vessels of 100 γ nicotine after the effect of monoiodoacetic acid. C) original electrical activity of the intestinal nerve 30 minutes after the effect of monoiodoacetic acid on the intestine; D) reduction of electrical activity of the intestinal nerve in a 30 second period of infusion of carbonic acid in the intestinal vessels (treated with monoiodoacetic acid). Significance of tracings, same as in Fig. 2.

Consequently, in normal conditions, from the receptors of the intestines there is a constant discharge of impulses, conditioning the tonus of the vessels, which is supported by the impulses both of the mechanoreceptors and the chemoreceptors. The hypothesis concerning the existence of such a tonic impulse was put forward by V. N. Chernigovsky [8].

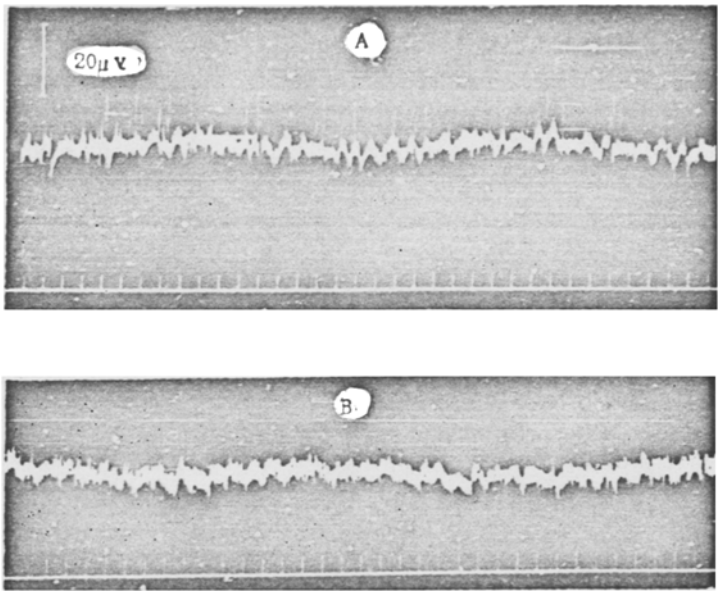

Fig. 4. Change in electrical activity of intestinal nerve upon introduction of novocain in the intestinal vessels.
A) Original electrical activity of intestinal nerve; B) Reduction in electrical activity of intestinal nerve upon introduction of 1 ml 2% novocain solution in intestinal vessels. Significance of tracings same as in Fig. 2.

Under the influence of nicotine, on the basis of treatment of the intestines with monoiodoacetic acid, we demonstrated the increase in the reflex blood pressure changes, and also an increase in the amplitude of the bioelectrical potentials of the afferent nerve as compared with those observed under the influence of nicotine on the normal intestine.

Consequently, in conditions of changed metabolism in the intestines under the influence of monoiodoacetic acid, there is increase in the responsiveness of the receptors of this organ to the chemical stimuli (nicotine). This confirms the findings of V. A. Lebedeva obtained by different experimental methods. As regards her explanation of the results of the experiments showing a rapid exclusion of the chemoreceptors of carbon dioxide on the grounds that the receptors finding themselves in a state of increased sensitivity to the influence of carbon dioxide, more quickly fall into a state of inhibition, we do not have sufficient information to judge the correctness of this hypothesis. Starting from this hypothesis, one should expect before the development of the blood pressure depressor reaction upon the introduction of carbon dioxide, that in a somewhat earlier stage of the effect of monoiodoacetic acid, there should take place a strengthening of the pressor impulsation upon introduction of carbon dioxide. However, we have so far, not observed the strengthening of the intensity of the impulse under the influence of carbon dioxide in these conditions. The experimental investigations in this direction are continuing.

LITERATURE CITED

[1] Anikina, N. A., Byull. Eksptl. Biol. i Med. Vol. 42, No. 7. pp. 8-13 (1956).*

* Original Russian pagination. See C. B. Translation.

[2] Lebedeva, V. A., Byull. Eksptl. Biol. i Med. Vol. 31, No. 6, pp. 400-404, (1951).

[3] Lebedeva, V. A., Byull. Eksptl. Biol. i Med. Vol. 34, No. 11, pp 17-21, (1952).

[4] Lebedeva, V. A., Byull. Eksptl. Biol. i Med. Vol. 35, No. 4, p. 5, (1953).

[5] Lebedeva, V. A., Byull. Eksptl. Biol. i Med. Vol. 38, No. 11, pp. 19-27, (1954).

[6] Lebedeva, V. A., and Chernigovsky, V. N., Byull. Eksptl. Biol. i Med. Vol. 31, No. 3, pp. 153-158, (1951).

[7] Ukhtomsky, A. A., Collected Works* (1950), Vol. 1, p. 29.

[8] Cheringovsky, V. N., Afferent Systems of the Internal Organs* (1943).

* In Russian.