ELECTROPHYSIOLOGICAL INVESTIGATION OF THE MECHANISM OF CHEMORECEPTION

COMMUNICATION I. CHANGE IN AFFERENT IMPULSES IN THE INTESTINAL NERVES THROUGH THE INFLUENCE OF CHEMICAL STIMULI ON THE RECEPTORS (NICOTINE AND ACETYLCHOLINE)

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Until recent times no systematic investigations devoted to the electrophysiological characterization of the impulses arising on stimulation of the chemoreceptors of the internal organs had been undertaken.

The present work was conducted to provide material for an electrophysiological characterization of the impulses arising in the intestinal receptors on chemical stimulation. We concentrated on the intestine because the reflex influences upon stimulation of its chemoreceptors have been studied in the greatest detail.

In the literature there are a number of papers devoted to electrophysiological investigation of the impulses of the receptors of the intestinal membrane.

Thus, Gammon and Bronk [11] studied the activity currents of the abdominal nerve and demonstrated their links with the activity of the Vater-Pacinian corpuscles. Gernandt and Zotterman [12] investigated the activity currents of the fine nerve branches of the intestines, paying particular attention to the influence of painful stimuli.

Brown and Gray [10] observed the appearance of impulses in the intestinal nerves when nicotine and acetylcholine were introduced into the intestinal vessels. However the authors did not describe the impulses electrophysiologically.

The afferent impulses from the receptors of the stomach wall in relation to various functional states of this organ have been investigated in papers by V. E. Delov, P. A. Kiselev, N. A. Adamovich and O. N. Samyatina [1]. O. N. Zamyatina [2] studied the bioelectrical potentials in peripheral segments of the mesenteric nerves and fine nerve branches of the intestinal wall in connection with different functional states of the digestive apparatus and also under artificial influences increasing the activity currents of the intestines (heat, stimulation of motor activity, effect of digestive products of carbohydrates and albumins, etc). The author notes that on the basis of active digestion and also in conditions of prolonged starvation and in the presence of the above mentioned influences the activity currents flowing in the mesenteric nerves were intensified. An exception was the action of glucose. In the nerves of the intestinal wall there arose in this case a special kind of impulse: the maximum amplitude of the potentials did not exceed 25-30 μv; the minimum was scarcely higher than the level of sound of the actual intensifier. The total frequency of the impulses was not more than 80 hertz.

However, in these investigations the chemical stimuli were introduced either directly in the blood stream [10] or in the lumen of the intestines [2] and thus the receptors may have reacted not only to the chemical stimuli but also to the resulting change in the general blood pressure. The latter complicates assessment of the effect of the direct influence of the chemical stimuli.

The method of perfusion employed by us, which is routine in study of the reflexes of the internal organs, makes it possible to investigate the receptors independent of fluctuations in general blood pressure.

By removing the possibility of chemical stimuli entering the general blood stream this method at the same time enables one to investigate the relation between change in electrical activity of the intestinal nerves and the reflex change in blood pressure arising when chemical stimuli are introduced in the intestinal vessels, which also was part of the object of our work.

EXPERIMENTAL METHODS

The investigation was carried out in acute experiments on cats under urethane narcosis; the urethane was introduced intravenously in the animal with slight ether narcosis. The chemical stimuli were added to the Locke-Ringer solution perfusing the isolated section of the intestines, connected through the nervous system to the organism. In a number of experiments natural blood supply was maintained and the chemical stimuli were introduced in the relevant arteries. The electrical potentials of the peripheral segments of the mesenteric nerves were recorded as were those of the peripheral segments of the rami intestinales (referred to by us later on as the nerve branches of the intestines or the intestinal nerves). The latter were not exposed at the entrance itself to the intestinal wall, but somewhat higher, and the Vater-Pacinian corpuscles situated along the nerve branches were not excised. The activity currents of the nerve were led off by means of silver electrodes to the intensifier, the frequency description of which was linear in the range of 10 to 300 cps. The electrical potentials of the nerve were recorded by means of the Schleifer oscillograph. The sensitivity of the apparatus was 2 μv per 1mm ray deviation.

The experiments were carried out in a screen chamber. Simultaneous with recording of the bioelectrical potentials, blood pressure in the carotid artery (by means of a mercury manometer) was registered on a kymograph. We investigated the effect of nicotine and acetylcholine, which are the most often used chemical stimuli in experiments for study of the internal organ reflexes.

EXPERIMENTAL RESULTS

Effect of nicotine. We introduced into the perfusate 1 ml nicotine solution at concentrations of $1 \cdot 10^{-5}$, $1 \cdot 10^{-4}$ and $1 \cdot 10^{-3}$. As is clear from Fig. 1, B, under the influence of nicotine there occurs an afferent impulse with a definite electrophysiological characterization: amplitude up to 35 μv, frequency 80-90 cps (We arbitrarily describe this in the article as "slow"). With the emergence of this impulse upon introduction of nicotine in the intestinal vessels a rise in blood pressure was observed.

In our experiments the impulses of this type arose on introduction of nicotine into the vessels both in the nerve trunks of the mesenteric plexus and in the intestinal nerves. As regards the impulses from the Vater-Pacinian corpuscles, which we shall arbitrarily describe as "fast", they usually did not increase directly after introduction of nicotine. In a series of experiments a certain intensification of the "fast" impulses arising considerably later than the manifestation of the "slow" impulses was observed. In order to establish more accurate time relationships between the emergence of the impulses in the afferent nerve and changes in blood pressure we made a timed comparison with simultaneous recordings of the reflex change in blood pressure in response to introduction of nicotine and the change in afferent impulses (Fig. 2).

As is clear from Fig. 2 the curve of change in afferent impulses is shifted to the left in comparison with the arterial pressure curve. Consequently, the impulses arise earlier (latent period $1\frac{1}{2}$ seconds) than the change in the blood pressure reflex response, the latent period of which equals 5 seconds. The maximum impulse (35 μv) occurred in 4-9 seconds from the commencement of the action of the stimulus. The maximum increase in blood pressure was observed at the 19th second. At that moment the impulse had already fallen to 15 μv. It completely disappeared even before arterial pressure returned to normal.

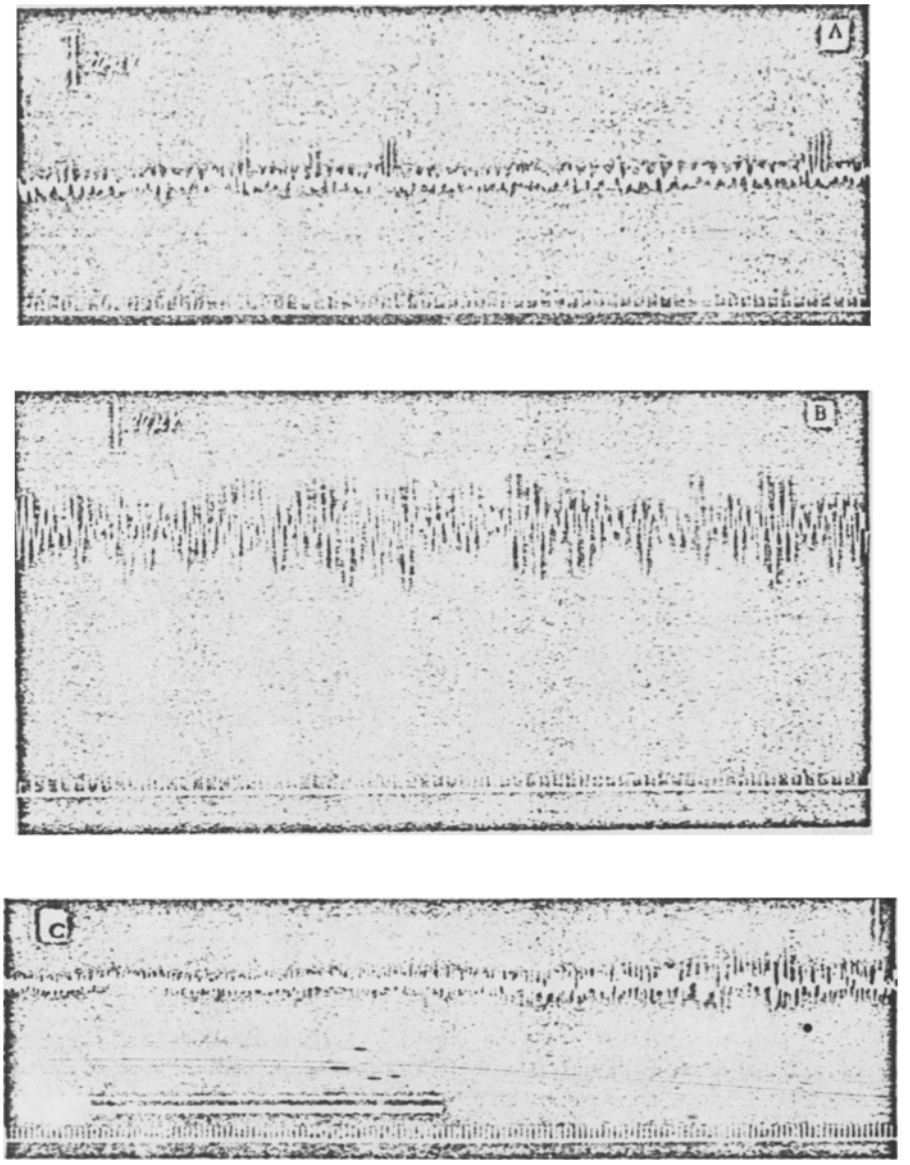

Fig. 1. Change in electrical activity of peripheral terminus of nerve branch of intestines upon introduction of nicotine (100 γ) and acetylcholine (100 γ) into intestinal vessels. A – Original electrical activity of intestinal nerve; B – electrical activity of nerve after introduction of 100 γ nicotine; C – change in electrical activity of peripheral terminus of intestinal nerve upon introduction in intestinal vessels of 100 γ acetylcholine. Significance of tracings (top to bottom: for A and B: activity currents of peripheral segment of intestinal nerve, indication of time (50 cps), for C: activity currents of peripheral terminus of nerve branch of intestines, indication of introduction of acetycholine, indication of time (50 cps). Beginning at Fig. 1, C and thereafter (Figs. 3 and 4) the oscillogram scale is only half the size.

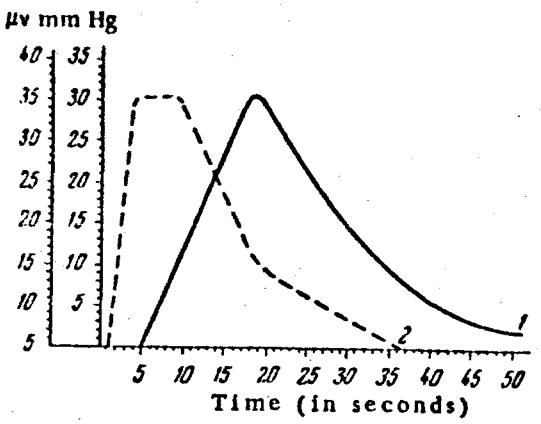

Fig. 2. Comparison of changes in blood pressure (1) and impulse in nerve branch of intestines (2) upon introduction of 100 γ nicotine in the intestinal vessels. 1) Change in blood pressure; 2) change in amplitude of bioelectrical potentials (in μv). Original level of blood pressure at commencement of experiment taken as zero; original level of amplitude of currents of activity in nerve – 5 μv.

Similar relationships, constantly observed, between the appearance of the impulse of the type indicated ("slow") and the reflex change in the arterial pressure upon introduction of chemical stimuli provide apparent proof that this kind of impulse in the experiments gives rise to reflex changes in the arterial pressure.

Effect of acetylcholine. Introduction in the intestinal vessels of acetylcholine at concentrations from $1 \cdot 10^{-5}$ to $1 \cdot 10^{-2}$ also produced, alongside reflex changes in arterial pressure (pressor effect), the appearance of "slow" impulses in the nerve trunks of the mesenteric plexus and fine nerve branches of the intestines.

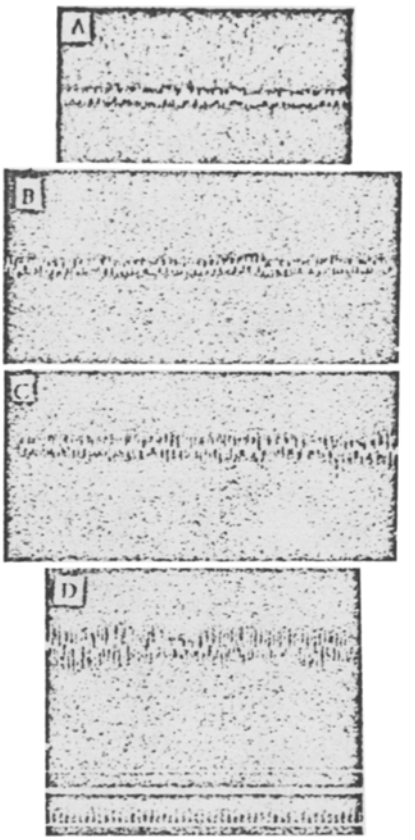

Fig. 3. Change in electrical activity of peripheral segment of intestinal nerve upon introduction of nicotine at various concentrations in intestinal vessel. A) Original electrical activity of intestinal nerve; B, C, D) electrical activity of this nerve after introduction of 1 ml nicotine at concentrations respectively of $1 \cdot 10^{-5}$, $1 \cdot 10^{-4}$, and $1 \cdot 10^{-3}$.

As is clear from Fig. 1, C, "slow" impulses started even during introduction of the stimulus. The changes in the "fast" impulses directly after introduction of the stimulus are considerably less marked.

We investigated the relationship between the concentrations of the chemical stimuli introduced (nicotine and acetylcholine) and the intensity of the impulses arising in the afferent nerve and also the reflex changes in arterial pressure. It is clear from Figures 3 and 4 that with an increase in the concentrations of the chemical stimulus the intensity of the resulting impulses in the intestinal nerve increases. Parallel with this increase, where the concentrations of the stimulus are increased, the value of the reflex change in arterial pressure, recorded by us, also rose.

The marked parallelism in the changes in the indices confirms the correctness of our hypothesis concerning the link of the reflex changes in blood pressure with the appearance of the "slow" impulses.

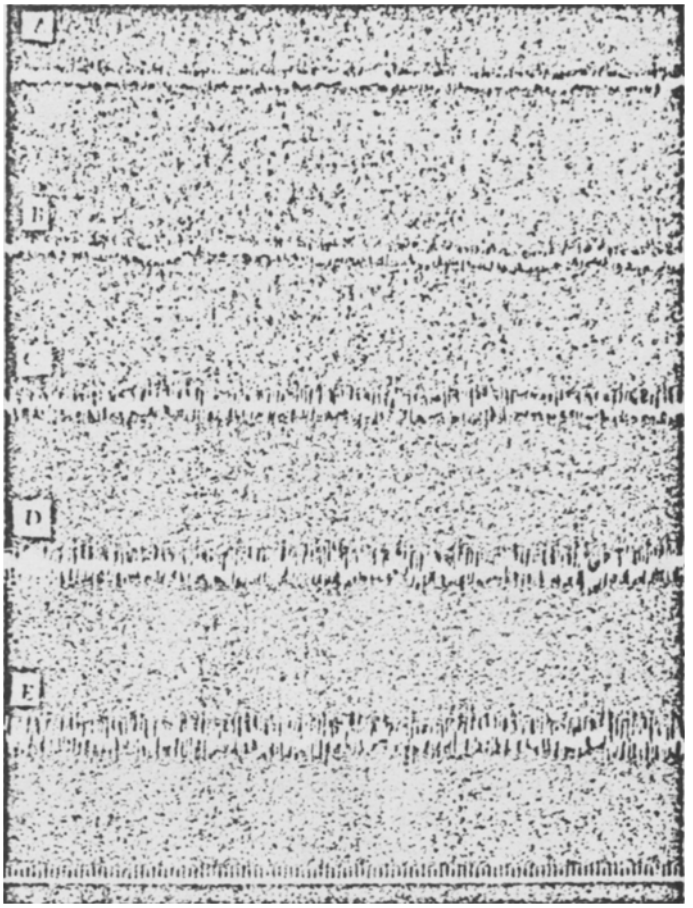

Fig. 4. Change in electrical activity of peripheral segment of intestinal nerve upon introduction of acetylcholine at various concentrations in intestinal vessels. A) Electrical activity in intestinal nerve before introduction of acetylcholine: B, C, D, E) same after introduction of 1 ml acetylcholine solution at concentrations respectively of $1 \cdot 10^{-5}$, $1 \cdot 10^{-4}$, $1 \cdot 10^{-3}$ and $1 \cdot 10^{-2}$.

DISCUSSION OF RESULTS

Under the influence of the chemical stimuli employed by us in the mesenteric and also in the intestinal nerve branches there appeared an afferent impulse with a definite electrophysiological character which we have termed "slow". Analogous impulses of the receptors of the intestinal wall were first recorded in the experiments of O. N. Zamyatina in conditions which were described in detail above. Since it is known that acetylcholine and nicotine produce contraction of the smooth musculature of the intestines, the hypothesis may be put forward that the impulses we observed and the reflex change in blood pressure upon introduction into the perfusate of the chemical substances indicated are associated with the motor activity of the intestines and consequently with stimulation of the mechano- and not the chemoreceptors. However, in relation to nicotine this hypothesis is clearly not justified since in special experiments it was demonstrated that the impulses arise much earlier than intensified motility of the intestines.

The reflex changes in blood pressure under the influence of nicotine also occur earlier than intensification of the motor activity of the intestines, which was shown in the experiments of V. N. Chernigovsky [3, 9] and is confirmed in our investigation.

In the case of the effect of acetylcholine the question is more complicated because of the stronger influence exerted by it on the motor activity of the intestines. To solve this question special investigations are required.

Our findings show that the reflex changes in blood pressure are caused by the appearance of "slow" impulses This conclusion is confirmed also by the absence of orderly changes in the "fast" impulses when chemical stimuli were introduced into the intestinal vessels. Accordingly the electrophysiological characterization of the potentials arising in the afferent nerve of the intestines under the influence of chemical stimuli (nicotine, acetylcholine) and the connection between these impulses and the reflex changes in blood pressure were established.

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