THE RELATIONSHIP BETWEEN THE BLOOD PRESSURE REFLEX ARISING IN THE PRESSORECEPTORS OF THE SMALL INTESTINE AND METABOLISM IN THE RECEPTOR AREA

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The interoceptors are intimately connected with the tissues of the organs in which they are located. One may suppose, therefore, that the metabolism in the tissues and consequently also in the interoceptors is one of the essential features which change the nature of the response from these interoceptors. Confirmation of the correctness of such a view is found in the work of V. N. Chernigovsky, V. A. Lebedeva and M. L. Belenky [1, 5], from which it is apparent that a change in metabolism in the chemoreceptors of the carotid sinus effected by various means (the action of carbon dioxide, cyanides, lack of oxygen, inhibition of glycolysis by means of sodium flouride and monoiodoacetic acid) leads either to a change in the strength of the reflex or to a distortion of the reflex response arising from these interoceptors.

In the present research we set before ourselves the task of studying the influence of changes in metabolism in the wall of the small intestine, and thus also in the pressoreceptors located in the intestinal wall, on the nature of the reflex response arising from these pressoreceptors.

A. A. Ukhtomsky [6] considered that excitation in nervous tissue, and consequently also in the receptors, consists in the harmony of two processes: the production of a peak of action current and a compensation reaction which restores readiness to produce a new peak of action current. The restoration of normal excitability, as was shown by A. A. Ukhtomsky and his co-workers, takes place as a result of the metabolism of this tissue, the essential links of which are the disintegration of adenosinetriphosphate, the disintegration of phosphocreatine, glycolysis and, according the contemporary data, respiratory oxidation as well. Inasmuch as glycolysis is one of the slowest parts of the compensation reaction, one may suppose that strengthening or weakening it can correspondingly strengthen or weaken the compensation reaction in the receptors, thereby changing the intensity of the afferent impulsation arising in them and consequently the intensity of the corresponding reflex response. The more intensive the compensation reaction, i. e., the more rapidly the tissue is prepared for the production of a new spark of excitation, the greater will be the amount of impulsation which a receptor can conduct in a unit of time; in other words, the lability of the receptor increases. When the compensation reaction is weakened, the opposite relationships will prevail.

We studied the influence which is exerted by a strengthening or weakening of glycolysis in the wall of the small intestine on the nature and magnitude of the reflex obtained during irritation of the pressoreceptors located in this intestinal wall. Our previous research [3, 4] showed in prolonged experiments on dogs with isolated intestinal loops that the reflex influence of one intestinal loop on the secretion and motor activity of another loop changes with a strengthening or weakening of glycolysis. If prior to irritation of the pressoreceptors substances are injected which some way or another intensify carbohydrate metabolism in the tissues of the intestinal wall, and at the same time in the pressoreceptors located in it (epinephrine, glucose, glucose with insulin), a strengthening of the reflex can be noted. Inhibition of glycolysis in the intestinal wall by means of monoiodoacetic

acid leads, on the contrary, to the prevalence of inhibitory influences from those pressoreceptors being stimulated.

In the experiments described below this problem was resolved by observing the reflex effects of the pressoreceptors of the small intestine not on its motor and secretory activity, but on blood pressure. The blood pressure reflex arising in the pressoreceptors of the small intestine was selected by us in view of its great clearness and stability.

EXPERIMENTAL METHODS

The experiments were performed on cats under urethane narcosis (1 g of urethane per kg of body weight injected intraperitoneally), which were injected against a background of ether narcosis.

Blood pressure was recorded in the carotid artery. The abdominal cavity was opened and a loop of the small intestine withdrawn. Irritation of the pressoreceptors of the small intestine was accomplished with a rubber balloon (at 60-80 mm of mercury) which was introduced into the intestine or with a rubber collar located on the outside of the intestinal loop which also created a pressure against the outside of the loop amounting to 60- of mercury. Inasmuch as irritation of the pressoreceptors by pressure on the outside of the intestine produced a more distinct reflex change in blood pressure than irritation of the pressoreceptors of the same portion by inflating the balloon on the inside, we chose the first method of stimulation. In all of the experiments we employed a 10-15 minute irritation. In addition we did not apply continuous, but rather rhythmic stimulation: 10 constrictions of the intestine during 10-15 minutes of irritation.

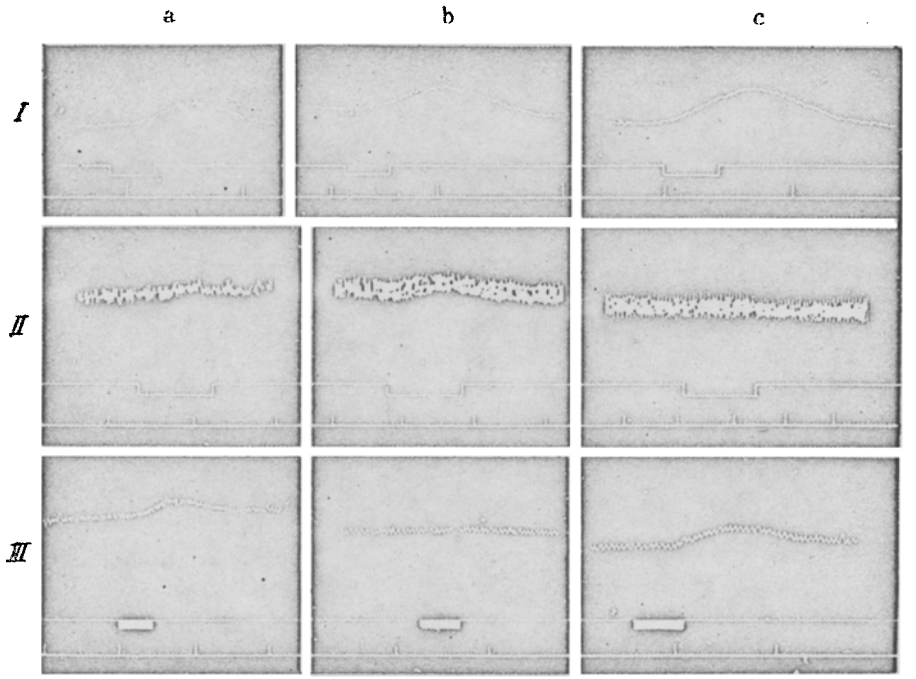

Fig. 1. The blood pressure reflex arising in the pressoreceptors of the small intestine before and after the influence of various substances on the receptor area. I. a) Normally; b) 5 minutes after injection of epinephrine; c) 15 minutes after injection of epinephrine; II. a) normally; b) following injection of glucose; c) following injection of insulin; III. a) normally; b) after injection of monoiodoacetic acid; c) after the addition of lactic acid. From above down: blood pressure record, mark indicating the irritation, time scale (30 seconds).

EXPERIMENTAL RESULTS

Mechanical irritation of the pressoreceptors of the small intestine results in a short-term rise in blood pressure. Prior cocainization of the serosa of the small intestine leads to the disappearance of the reflex. The

reported elevation of blood pressure can be observed arising from any portion of the small intestine. It is more distinctly marked in male cats than in females: the reflex described was observed in 15 out of 16 male cats, while it was absent in two out of three females and was very weakly expressed in the one.

After the blood pressure reflex was obtained from one portion of the small intestine, through the needle of a syringe there was injected into the lumen of that portion a substance which exerts an influence on glycolysis: epinephrine, insulin, glucose, glucose with insulin, monoiodoacetic acid, sodium fluoride, dinitrophenol and lactic acid, i. e., agents acting on metabolism in different ways. We considered that, owing to the absorptive capacity of the mucosa of the small intestine, these substances should rapidly enter the intestinal wall. The active agent was also simultaneously applied to the serosa of the portion on which the experiment was being performed.

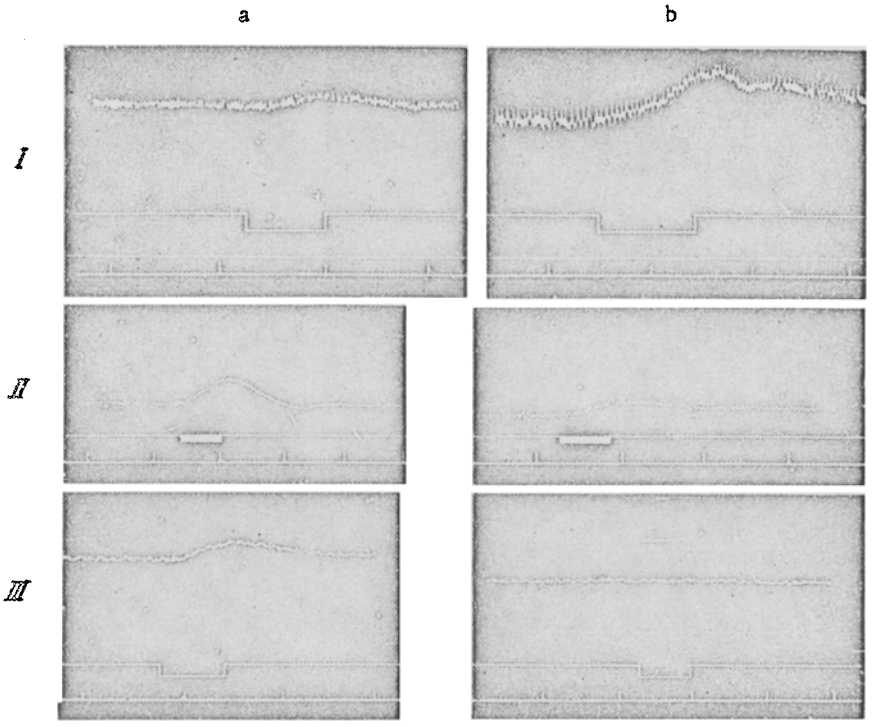

Fig. 2. The blood pressure reflex arising in the pressoreceptors of the small intestine before and after the influence of various substances on the receptor area.
I. a) Normally; b) after injection of glucose with insulin; II. a) normally; b) after injection of sodium fluoride; III. a) normally; b) after injection of 2,4-dinitrophenol. Designation of the curves is the same as in Fig. 1.

When the normal pressor reflex was obtained, 1 ml of solution of epinephrine in a dilution of 1:1000 was injected into the same portion. Irritation of the intestine following the injection of epinephrine resulted in a more distinct pressor reflex (Fig. 1,I). Intensification of the pressor reflex was occasionally observed for as long as 20 minutes after injection of epinephrine, but in the majority of the experiments it was maintained only for a period of 10-15 minutes. In those cases in which an original pressor reflex was absent, injection of epinephrine led to its appearance. Injection into the intestine of the same amount of epinephrine in dilutions of 1:10,000 and 1:100,000 did not influence the magnitude of the reflex. Epinephrine cannot produce its proper pressor reflex when injected into the hepatic portal system [2].

Glucose (a 5% solution) was injected in the amount of 3-4 ml, insulin in the amount of 1 ml. These two agents exerted the opposite effect on the reflex arising in the pressoreceptors, a fact which was especially noticeable when from two different portions of the intestine of the same animal initial blood pressure reflexes of the

same magnitude were obtained: if glucose was injected into one of these portions and insulin into the other, the reflex arising from the portion into which glucose had been injected became more distinct, while that arising from the portion which had been subjected to the action of insulin disappeared entirely (Fig. 1,II). The intensifying effect of glucose, however, was considerably less than that of epinephrine. Increasing the concentration of glucose above 5% did not lead to an intensification of the reflex.

If insulin was injected into the intestine together with glucose (1 ml of insulin+4 ml of 5% glucose), the magnitude of the blood pressure reflex increased considerably more than when glucose alone was injected. Therefore the effect produced by the joint injection of insulin and glucose cannot be regarded as the simple summation of the effects of insulin and glucose (Fig. 2,I).

Injection into the intestine of substances which inhibit glycolysis (monoiodoacetic acid, sodium fluoride) as well as dinitrophenol, which curtails respiratory phosphorylation, reduced the magnitude of the pressor reflex or led to its complete disappearance.

Monoiodoacetic acid was injected in the amount of 1-2 ml in dilutions of 1:1000 to 1:100,000. The most marked effect of monoiodoacetic acid took place when it was used in a dilution of 1:1000. Irritation of the pressoreceptors of the small intestine after injection of this agent led at the beginning to reduction, and then to the complete disappearance of the blood pressure reflex arising in these pressoreceptors (Fig. 1,III).

Sodium fluoride (2 ml of a 1% solution), unlike monoiodoacetic acid, did not result in the complete disappearance of the pressor reflex but only reduced it (Fig. 2,II). While mechanical irritation of the small intestine following injection of monoiodoacetic acid produced a weaker and weaker pressor reflex and finally its disappearance, mechanical irritation following injection of sodium fluoride resulted in a depression of the pressor reflex only in the first few minutes after this preparation was used. Subsequently the magnitude of the reflex was rapidly restored. Injection of another dose of sodium fluoride led once again to a considerable reduction in the magnitude of the pressor reflex with the same rapid (within 10-15 minutes) restoration.

2,4-dinitrophenol (4 ml of a 0.05% solution) had an effect similar to that of monoiodoacetic acid: irritation of the pressoreceptors of the intestine following injection initially produced a reduction of the pressor reflex and then its complete disappearance (Fig. 2,III). The disappearance of pressor reflexes was extremely persistent: after dinitrophenol was injected into several portions of the small intestine, reflex elevation of blood pressure could not be obtained from any one of these or neighboring portions for as long as 2 hours after the dinitriphenol was used.

We also tried the following variation of the experiment. After monoiodoacetic acid had led to the disappearance of the pressor reflex, into the same portion of the intestine we injected lactic acid (2 ml of a 0.5% solution), i. e., one of the end products of glycolysis. Irritation of the pressoreceptors of the small intestine after injection of lactic acid led to the restoration of the lost pressor reflex (Fig. 1,III).

Thus the change in the unconditioned interoceptive blood pressure reflex arising in the pressoreceptors of the small intestine depends first of all on the state of metabolism in the receptor area.

In the experiments cited above it was shown that injection into the intestine of substances which intensify carbohydrate metabolism by stimulating glycolysis in one way or another (epinephrine, glucose, glucose with insulin) produces a change in the blood pressure reflex arising in the pressoreceptors of the intestine, manifested by the augmentation of the reflex.

Injection into the intestine of monoiodoacetic acid and sodium fluoride, substances which inhibit glycolysis, of insulin without glucose (diverting the carbohydrate resources to the synthesis of glycogen) and of dinitrophenol, which curtails respiratory phosphorylation, results in the reduction or disappearance of the blood pressure reflex arising in the pressoreceptors of the corresponding portion of the intestine. Injection into the intestine following monoiodoacetic acid of an end product of glycolysis, lactic acid, restores the reflex arising from the corresponding receptor area, which had been lost after use of monoiodoacetic acid.

The results of our experiments agree with the results of our earlier research which included a prolonged experiment and allow one to conclude that in supplying energy for the work of the pressoreceptors of the intestinal wall an essential role is played by metabolic processes of restitution, in particular glycolysis and respiratory phosphorylation.

SUMMARY

Experiments based on recordings of the reflex response of the blood pressure in cats to mechanical stimulation of pressoreceptors in the wall of the small intestine show that different agents affecting tissue metabolism when introduced into the intestinal lumen and applied to its surface cause changes in the reactivity of the intestinal pressoreceptors. Solutions of epinephnine, glucose and glucose with insulin increase the pressor reflex from the intestinal pressoreceptors while solutions of monoiodoacetic acid and sodium fluoride (inhibition of glycolysis) as well as 2,4-dinitrophenol (inhibition of phosphorylation connected with respiration) decrease it to the point of total disappearance. Insulin acts in the same manner; lactic acid restores the reflex inhibited by monoiodoacetic acid.

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