# AN INVESTIGATION OF THE PERIPHERAL NERVOUS INTERACTIONS OF THE VASCULAR SYSTEM IN THE SMALL INTESTINE

S. S. Musyashchikova

From the Laboratory of Blood Circulation and Respiration (Head– Prof. G. P. Konradi) of the I. P. Pavlov Institute of Physiology (Dir.– Academician K. M. Bykov), Leningrad
(Presented by Academician V. N. Chernigovskii)
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The relative constancy of the blood pressure level in the organism is maintained by central and peripheral mechanisms. It is known [5, 6] that after transection and removal of the spinal cord the arterial pressure can be preserved at a relatively high level (60-90 mm Hg). Therefore, after exclusion of the central influences on the tonus of the vessels the peripheral mechanisms provide for the maintenance of a relatively high level of blood pressure. Reactions have been described, caused by stimulation of receptors and being carried out following the removal of the central nervous system (so called viscerovisceral, or peripheral, reflexes). The first ones were described by N. M. Sokovnin [12]. Subsequently, these reflexes were studied by many authors [3, 10, 13-17] in isolated organs of the lesser pelvis; the existence of peripheral reflexes was shown in animals after removal of the spinal cord [1, 4, 7, 9, 11, 18, 19]. Several authors regarded them as axon reflexes, while others postulated the existence of synaptic connections in the peripheral ganglia [17].

It can be postulated that for the regulation of the vascular tonus local reflex arcs must have essential importance. Confirmation of this can be found in the work of E. N. Speranskaya-Stepanova [13]. Using frogs, she demonstrated vascular reactions to stimulation of the central end of the sciatic nerve following removal of the spinal cord and transection of the adjacent sympathetic trunks.

The purpose of this investigation was to study the effects of changing the vascular tonus in one intestinal loop on the vascular tonus of another portion of the small intestine in animals with an intact nervous system and after removal of the spinal cord.

## EXPERIMENTAL

The experiments were carried out on cats with an intact nervous system (narcosis was performed with the use of uretane, in a dose of 0.5–1.3 g/kg) and on cats first subjected to removal of the entire spinal cord below the last cervical segment. The spinal cord was removed both immediately before the experiments and 1-4 days prior to its beginning, using a somewhat modified version of N. F. Popov's method [8]. Removal of the spinal cord was performed under deep anesthesia (nembutal, 80-90 mg/kg), the spinal canal being opened over the first thoracic segment and over the croup. The spinal cord (without the dura mater) was forced out with a flexible rod coated with a mixture of wax and vaseline. In several cases, in order to increase the survival rate of the animals, the operation was carried out in two stages: initially only transection of the spinal cord was performed, and, after 24 hours, it was removed. Following the operation the animals were warmed and given subcutaneous injections of ephedrine (1.5 ml of a 5% solution). In order to completely exclude the influence of the central nervous system on the reactions of the vessels the vagosympathetic trunks in the neck were transected 40 minutes before the experiment.

Two portions of the small intestine were isolated as far as their vessels were concerned, and were perfused with oxygenated Ringer-Lock's solution, using the method of V. N. Chernigovskii [16]. Perfusion of the vessels was done individually, i.e. the artery of each section of the intestine was joined to a separate perfusion system. The pressure level of the solutions was set at a uniform height, approximately corresponding to the mean pressure in the carotid artery. Glass canulae were inserted into the free ends of the intestinal tube, in order to withdraw the fluid collecting within. In all the experiments the nicotine, histamine, acetylcholine, and hypertonic NaCl solution (20%) were injected into the mesenteric artery at the proximal part of the intestine. The interval between injections was 10-15 min.

The blood pressure was recorded in the common carotid artery, using a mercury manometer; respiration was recorded via a canula introduced into the trachea and connected to a Marie's capsule. The amount of perfusate flowing out of the veins of the corresponding intestinal segments was measured with the aid of 2 Marie's capsules [16].

As the experiments showed, the effect of one vascular region of the intestine on another was extremely clear when there was a 3 : 1 relationship between the length of the perfused proximal segment, containing the vessels injected with the stimulus, and the length of the non-stimulated perfused distal segment of intestine. When these

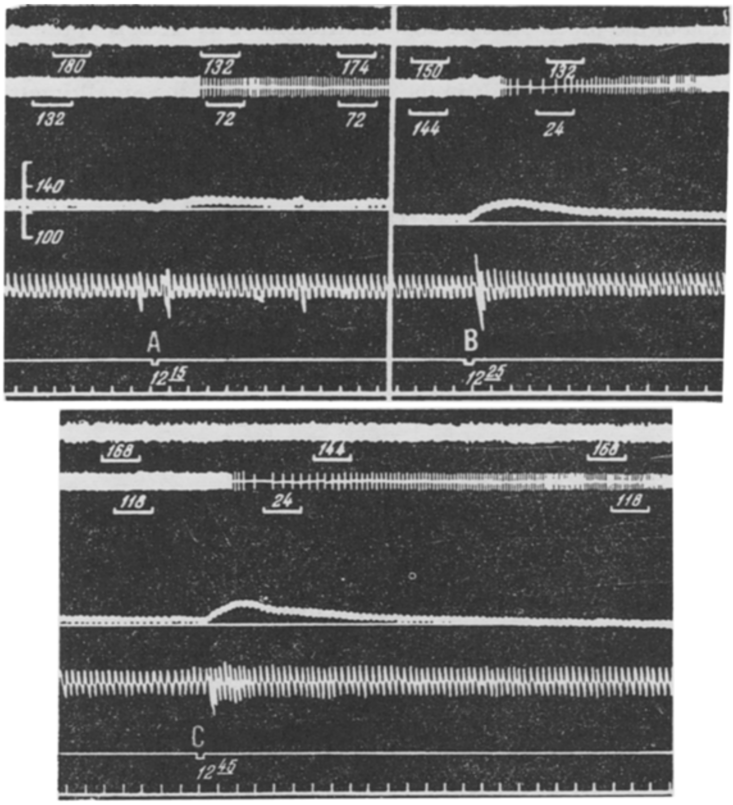


Fig. 1. The effect of nicotine injected into the vessels of the proximal segment of small intestine on the tonus of the vessels in the distal intestinal loop in a cat with an intact nervous system. Experiment performed on April 11, 1959. Uretane narcosis. Perfusion of the two segments of small intestine, isolated as regards their blood vessels, was carried out with oxygenated Ringer-Lock's solution. Meaning of the curves (from above downward): markings of the drops of perfusate flowing out of the vein of the distal "unstimulated" intestinal segment; markings of the drops of perfusate flowing out of the vein of the proximal intestinal segment (chemical stimulant having been injected into its vascular bed); numbers – the number of drops per minute; blood pressure; original level of the blood pressure; respiration; stimulation marking; time markings (5 seconds). A) 0.1 Nicotine $\cdot 10^{-4}$, B) 0.3 nicotine $\cdot 10^{-4}$, C) 0.5 nicotine $\cdot 10^{-4}$.

lengths were equal we did not observe any changes in the lumens of the vessels within the distal portion with the introduction of the stimulating agent into the vascular bed of the proximal intestinal loop. The perfusion rate of both portions of the intestine was kept as steady as possible, so that it approximated the rate of flow of the blood in the intestinal vessels normal for animals with natural blood circulation. The latter was determined in an experiment especially performed for this purpose, involving the perfusion of a portion of the small intestine with blood from a donor. The rate of blood flow, as determined by this method, ranged from 10.8 to 16.4 ml/min. In all the experiments a flow of 1 ml of perfusate corresponded to 15 drops.

## RESULTS

A total of 29 experiments was carried out.

The first series consisted of 12 experiments, performed on animals with an intact nervous system. Under the conditions of our experiment, with the introduction of 20-25 micrograms of nicotine, histamine, acetylcholine, or 0.5 ml of a 20% NaCl solution into the mesenteric artery of the proximal perfused portion of the intestine, we observed both a pressor reaction of the blood pressure and constriction of the vessels in this intestinal loop. In certain

Change in the Tonus of the Vessels in the Distal Segment of the Small Intestine Associated with the Action of Nicotine on the Chemoreceptors of the Proximal Segment of the Small Intestine

| Number of trials | | | Decrease in venous outflow secondary to action of stimulus (in % of original) | | Number of repeated reactions possible |
|---|---|---|---|---|---|
| total | with a positive reaction | with a negative reaction | in the proximal segment | in the distal segment | |
| Intact animals | | | | | |
| 12 | 12 | 0 | 57 | 20 | 10-12 |
| Animals with the spinal cord removed | | | | | |
| 14 | 11 | 3 | 60 | 17 | 3 |

Note: Nicotine dosage was equal to 30-50 micrograms.

trials this was preceded by an increase in the outflow rate of the perfusate, lasting 5-8 seconds; this was possibly related to injection of the solution under pressure. Along with this we observed reflex changes in the vascular lumina of the neighboring intestinal loop. In many of the experiments the reflex changes in the tonus of the vessels situated within the neighboring intestinal segment were reflected by a decrease in the amount of outflowing perfusate, and lasted 20-120 sec. In some of the trials (8 out of 86) instead of a decrease in the venous outflow of the distal intestinal segment we observed its increase, despite the normal decrease in venous outflow seen in the proximal segment of the intestine following the administration of the stimulus. Constriction of the vessels in the proximal intestinal loop, following injection of the above mentioned chemical agents, was considerably greater than the vascular contraction in the distal loop of intestine (Fig. 1).

With the administration of 30-50 micrograms of nicotine, the decrease in outflow from the proximal segment of intestine was equal to an average of 57%, while in the distal intestine the reduction was only 20% of the original level (see table).

The degree to which these reactions were manifested, and their duration, depended, within certain limits, on the strength of the acting chemical stimulant: with an increase in its dosage the contraction of the vessels in both segments of the intestine was stronger and of longer duration (see Fig. 1). However, we did not find a linear relationship between the strength of the stimulus and the effect observed.

Under the conditions of this method (recording the drops of perfusate) the latent periods of the reactions cannot be expressed in absolute numbers, since with a gradual decrease in the number of outflowing drops it is not always possible to determine the beginning of the reaction precisely. In addition, under the conditions of perfusion of an organ it is difficult to judge the moment when the stimulus begins to act on the receptors. Finally, the rate of perfusion fluctuated in the different experiments, depending on the diameter of the tube and canula through which the solution was conducted. The relative figures for the latent periods of the reactions in arterial pressure (from the moment of injection into the artery of the proximal intestinal segment) were in the range of 4-7 sec. The reactions of the vessels in the same intestinal segment began after 10-30 sec. The time of onset of the vascular contractions in the distal segment of the intestine ranged within the same limits. In the animals with the intact nervous system the change in the lumen of the vessels of both intestinal loops arose with every repeated injection.

In the control experiments, with the injection of the same volume of physiological saline into the lumen of the vessels, the venous outflow remained unchanged in both intestinal loops. Following injection of novocain (0.5 ml of a 2% solution) into the perfused vessels of the proximal intestine, the pressor reflex in the blood pressure associated with the introduction of chemical stimuli into these vessels disappeared, as well as the reactions of the ves sels in both this portion of the intestine (in which the novocaine was injected) and the neighboring segment. Experi ments performed on animals after respiration and the heart beat had stopped, but with continued perfusion of the intestinal loops under observation, showed that after injection of the chemical substance into the proximal segment of the intestine the vessels contracted; the stronger the stimulus, the greater was the contraction. Under these conditions the perfusion rate in the distal portion of the intestine naturally did not change.

The second series consisted of 14 experiments, carried out on animals following the removal of their spinal cords. In the beginning of the experiment the arterial pressure in these cats was equal to 80-130 mm Hg, and, as the experiment progressed over a period of 3-4 hours, gradually decreased to 60-70 mm (to a lesser degree, a reduction in the blood pressure was also noted in the experiments on the animals with the intact nervous system).

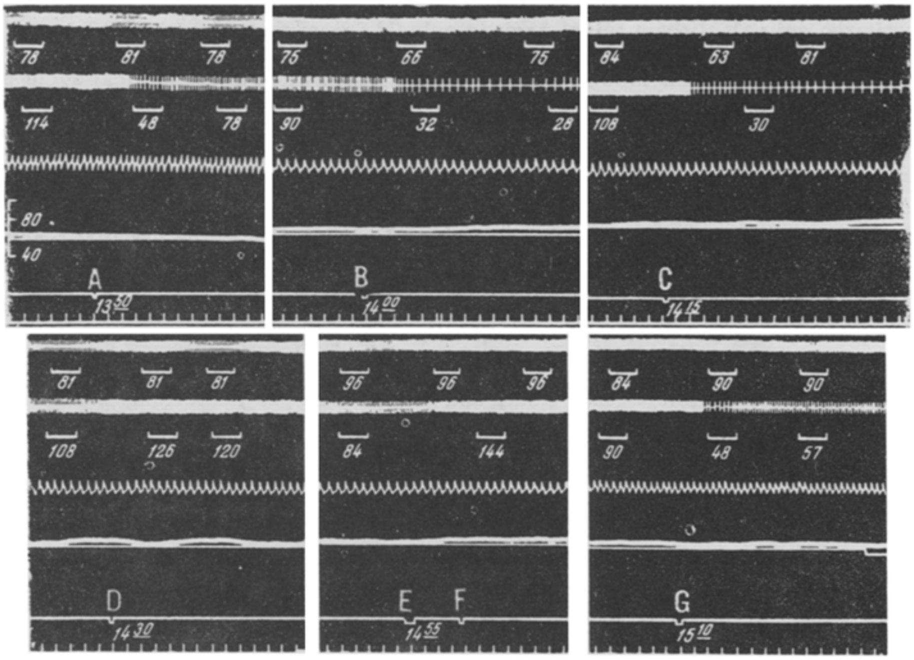


Fig. 2. The effect of nicotine, physiological saline, and novocaine, injected into the vessels of the proximal loop of small intestine, on the tonus of the vessels in the distal intestinal loop, in cats, following the removal of the spinal cord below the last cervical segment. Experiment performed on April 9, 1958. Uretane narcosis. Perfusion of both portions of the small intestine carried out with oxygenated Ringer-Lock's solution. Designations are the same as in Fig. 1. A) 0.1 Nicotine $\cdot 10^{-4}$, B) 0.3 nicotine $\cdot 10^{-4}$, C) 0.5 nicotine $\cdot 10^{-4}$, D) 0.5 physiological saline, E) 1.0 novocaine, F) 0.5 nicotine $\cdot 10^{-4}$, G) 0.5 nicotine $\cdot 10^{-4}$.

The results of this series of experiments showed that the effect from one vascular region of the small intestine is transferred to the vessels of the other even after the removal of the spinal cord below the last cervical segment. The results of one of these trials are presented in Fig. 2.

It can be seen that the introduction of 30 micrograms of nicotine into the artery of one intestinal loop caused constriction of the vessels in the other perfused loop; with elevation of the dose of nicotine to 50 micrograms the vascular contraction was more marked. However, here, just as in the case of the animals with the intact nervous system, the relationship between the degree of vascular contraction and the strength of the acting stimulus was not a direct proportion. The threshold for the vascular reaction in the distal intestinal segment to the stimulus injected into the proximal intestinal segment, in animals deprived of their spinal cord, was higher than in the animals with the intact nervous system. In the latter, the vascular reaction in the "unstimulated" intestinal segment always appeared upon injection of 10 micrograms of nicotine (see Fig. 1), while in the animals without the spinal cord the reaction was only observed upon injection of an average of 30 micrograms of nicotine. The magnitude of the contraction (in percents of the original level), in vessels directly exposed to the action of the chemical agent, did not essentially differ in the operated animals from the analogous reactions in the animals with the intact nervous system (see table).

This vascular reaction in the "unstimulated" intestinal segment of the animals with preliminarily removed spinal cords disappeared after injection of 1.0 ml of a 1% solution of novocain into the vessels of the "stimulated" intestine (see Fig. 2). However, we did not succeed in obtaining restoration of the reaction after the novocain was flushed out.

One of the essential differences of these reactions in the animals without the spinal cord was their instability concerning repeated stimulations. The maximal number of repeated vascular reactions to the introduction of the chemical stimulus was equal to an average of 3 when the stimulus dose was increased with each new injection, whereas in the animals with the intact nervous system the reaction was repeated after 10-12 injections.

The effect from one vascular region of the intestine on the other, observed in the intact animals in 100% of the trials, took place in the animals without spinal cords in only 78.6% of the cases (see table).

Thus, the results of the experiments showed that with the administration of a chemical agent to vessels in a portion of the small intestine vascularly isolated but retaining a neural link with the organism, changes occur in the vascular lumina, not only in this intestinal loop, but in its neighbor. These vascular reflexes not only occur in animals with an intact nervous system, but also following the removal of the spinal cord from the last cervical segment down to the croup, and after transection of the vagosympathetic trunks in the neck. Apparently, these reactions belong to the peripheral reflex class, described in the literature. In distinction to the vascular reactions in the animals with the intact nervous system, the vascular influences from one portion of the small intestine on the other were unstable, and disappeared with repeated stimulation. There is evidence in the literature on the inconstant nature of the peripheral reflexes. Thus, S. I. Gal'perin and V. N. Chernigovskii [2], studying the contraction of the urinary bladder secondary to electrical stimulation of the sciatic nerve following removal of the spinal cord, observed a decrease in the effect with repeated stimulations. Kuntz and Saccomanno [19], describing peripheral reflexes in the intestine, also pointed out their instability with repeated stimulations. Based on the available data on peripheral reflexes, it may be concluded that the effect from one vascular region of the small intestine on another is realized via vegetative ganglia.

## SUMMARY

Chemoreceptors of the proximal area of the small intestine were stimulated in cats with an intact nervous system and in the same animals with their spinal cord removed below the last cervical segment. The effect produced on the vascular tone of the distal section of the small intestine was studied. Two vascularly isolated intestinal sections were perfused with Ringer-Lock solution. After injecting 10-50 $\gamma$ of nicotine, histamine, acetylcholine, and 0.5 ml of 20% sodium chloride solution into the artery of the proximal intestine there occurs a constriction of the vessels in both intestinal sections. These reflex effects were noted in the animals with intact nervous systems, as well as in those with removed spinal cord and bilaterally divided sympathetic and vagus nerves on the neck. The effects exercised from one vascular area of the small intestine on the other in animals devoid of spinal cord are unstable and easily disappear on repetition of the reflex.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

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