RECEPTOR SPECIFICITY IN VARIOUS PERIPHERAL ZONES OF THE INTEROCEPTIVE ANALYZER

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At present it is not known to what extent the different reflexogenous zones of the interoceptive analyzer are specialized to particular chemical stimuli of the internal medium.

On the one hand, various chemical and pharmacological substances such as acetylcholine, nicotine, adrenalin, serotonin, veratrine and others cause excitation of the viscera (intestine, kidneys, spleen and heart), muscles, sinocarotid and cardio-aortal regions, lesser circulation, etc. On the other hand, it may be taken as established that certain of the interoceptive zones, for example the carotid gland, are differentially sensitive to adequate stimuli and particularly to a reduced oxygen tension in the arterial blood. By recording afferent impulses in single vagal fibers it has been shown [17] that specialized receptors are present in the gastric mucosa, and that some are excited by acids and others by alkalis.

To study their differential sensitivity we have investigated the response of the intestinal chemoreceptors to two stimuli: one was hydrochloric acid, which normally reaches the intestine from the stomach, and the other was reduced oxygen tension, which is an adequate stimulus to the chemoreceptors of another zone – the sinocarotid region. As a control, experiments were also carried out in which a low oxygen tension was applied to the chemoreceptors of the carotid gland.

METHOD

The experiments were carried out on cats under urethane anesthesia. Potentials were picked up from the fine afferent nerve fibers innervating the duodenum and jejunum. In the first set of experiments the stimulus was 0.01 N or 0.1 N hydrochloric acid, and it was applied to the duodenum and jejunum while normal blood circulation was maintained; during the second set of experiments the effect of reduced oxygen concentration on the small intestine receptors was investigated. For this purpose, in some of the experiments the animals breathed a mixture of 98% nitrogen and 2% oxygen, which markedly reduced the partial pressure of oxygen in the arterial blood supply to all organs including the small intestine. In other experiments the small intestine was isolated from the general circulation and was perfused with an oxygenated Ringer-Locke solution at 37° and at constant pressure; this was periodically replaced by an oxygen-free solution.

The potentials from the afferent nerves were led off from buried electrodes similar to those used by O. M. Zamyatina [2]. They were recorded on a two-channel OB2 oscillograph constructed in the experimental works of the AMN SSSR.

RESULTS

An initial recording of the electrical activity of the afferent nerves of the duodenum and jejunum was made before applying any stimuli. In some of the experiments the amplitude of the potential oscillations was insignificant, amounting to a few micro-volts and scarcely exceeding the noise level of the amplifier (Fig. 1, a, b); in other experiments, well-marked impulses having amplitudes of the order of 10 μv were obtained (Fig. 2, a).

The injection of 1-1.5 ml of 0.01 N hydrochloric acid into the lumen of the duodenum caused an increase of impulses, or caused impulses to appear when they had previously been absent. The latent period varied from 20–30 seconds to 3–5 minutes according to the experiment, and the increase of impulses was maintained for

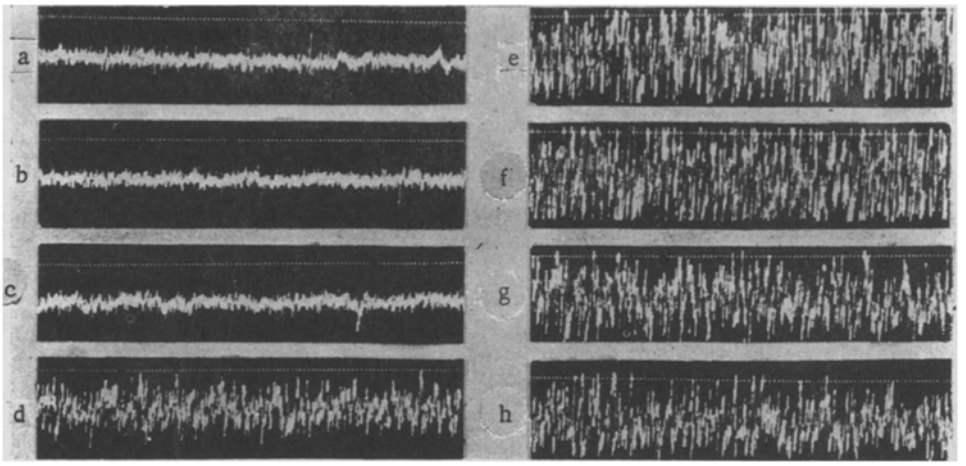

Fig. 1. Impulses in the afferent nerve from the duodenum. a) Initial level; b, c, d, e, f, g, h) 30 seconds, and 1, 2, 5, 10, 25, and 30 minutes after injecting 0.01 N HCl into the lumen of the intestine.

30 minutes or more. In Fig. 1, d, it can be seen that two minutes after applying the stimulus there is a marked increase in the amplitude of the impulses, which increases further during the next ten minutes (Fig. 1, e, f); after 10 and 20 minutes (Fig. 1, g, h) there is some falling off of the impulses, although the level remains higher than before the stimulus was applied. In the afferent nerve from the jejunum there was no noticeable change in the number of impulses.

Similar results were obtained in experiments where there was considerable electrical activity in the afferent nerves before the stimulus was applied. Again there was an increase in activity in the nerve from the duodenum, but none in that from the jejunum.

When 0.01 N hydrochloric acid was introduced into the lumen of the jejunum, there was no increase of impulses in the afferent nerve (Fig. 2, I, a – b). A marked increase could be observed only when acid of concentration 0.1 N was used. Then the latent period varied from 30 seconds to 5 minutes in different experiments. In Fig. 2, II, a – h, it can be seen that the impulses increased at the third minute, and continued to increase until the fifth and tenth minute; the rate remained high till the fifteenth and twentieth minutes, and had not returned to the original value even 60 minutes after the acid had been given.

Therefore, the action of hydrochloric acid on the mucous membrane of the duodenum and jejunum causes a marked and maintained increase in the number of impulses in the afferent nerves. However, in order to stimulate the receptors of the jejunum it was necessary to use a ten times higher concentration of the stimulus than was required for the duodenum.

It should be noted that there is a considerable interval, usually extending to several minutes, between the time at which the chemical stimulus is applied to the mucous membrane and the moment when the increase in impulses occurs. We deduced, therefore, that the excited receptors do not lie at the surface of the mucuous membrane, and the electrical activity which we recorded in the nerve fibers results from the excitation of receptors lying within the intestinal wall.

As a test we carried out several experiments in which the 0.01 N hydrochloric acid was added to the Ringer-Locke solution with which the intestine was perfused. There was then an immediate increase in the rate of impulses in the afferent nerve, and there was no definite latent period. It can be seen from Fig. 3, a, b, that there is a marked increase in the activity from the afferent nerve of the small intestine, even during the time the hydrochloric acid is being introduced into the perfusate, and the increase reaches a maximum immediately the acid ceases to be given. The increased impulsation was maintained only for 12 – 20 seconds (Fig. 3, c) and after as little as 30 seconds the nerve activity had returned to normal (Fig. 3, d).

The considerable difference in the duration of the latent period and in the period of action of the stimulus when the solution was introduced into the lumen of the intestine appears to be due to differences in the rate at which it gained access to the receptors, and in the duration of the contact. The fact that the latent period was very prolonged when the acid was introduced into the intestine, and very short when mixed with the perfusate,

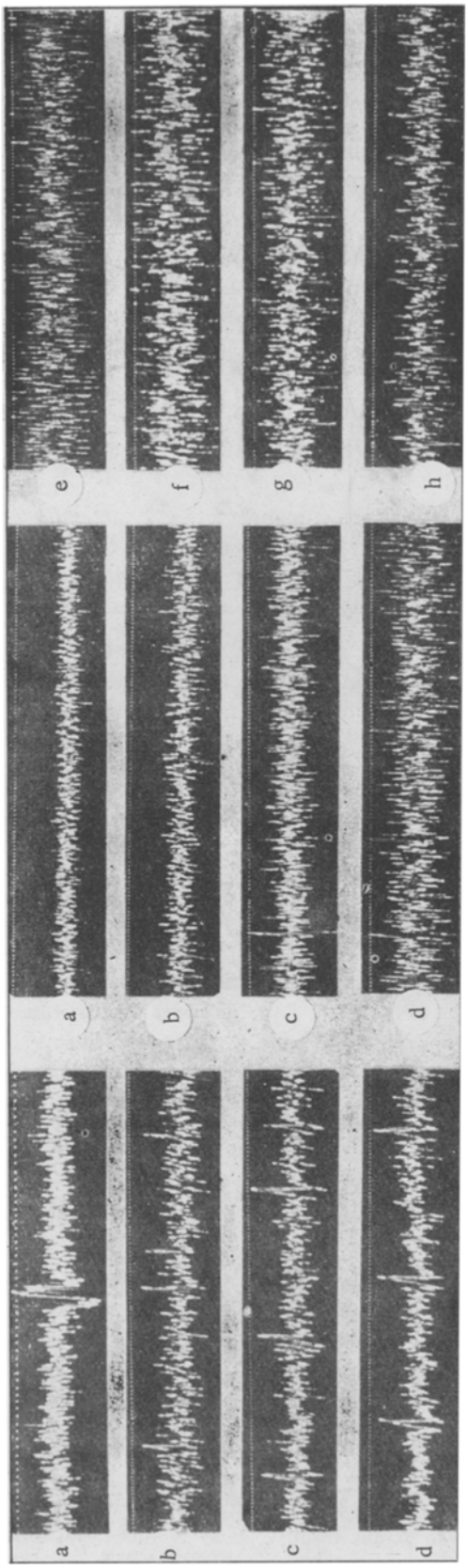

Fig. 2. Impulses in the afferent nerve from the jejunum. I a and II a) Initial level; I b,c,d,) 30 seconds, and 5 and 20 minutes, after injecting 0.01 N HCl into the intestinal lumen; II b,c,d,e,f,g,h) 2,3,5,10,15,20 and 60 minutes after injecting 0.1 N HCl into the intestinal lumen.

confirms the idea that the receptors are situated within the intestinal wall. In the second set of experiments, a simultaneous record was made of the activities in the nerves from the carotid sinus and from the jejunum when the oxygen tension in the arterial blood was reduced. After a mixture of 95-93% nitrogen with 5-7% oxygen had been breathed for only 15-20 seconds, there was an increase in the impulses from the sinus nerve indicating excitation of the chemoreceptors of the carotid gland. However, during this period and in the subsequent 3-5 minutes, during which the animal breathed the reduced oxygen mixture, there was no increase in the electrical activity in the afferent nerve from the jejunum.

A similar result was obtained in experiments in which Ringer-Locke solution containing a low partial pressure of oxygen was used to perfuse a portion of intestine which retained only nervous connection with the rest of the animal. Despite the very low oxygen partial pressure, which was obtained by raising the solution to boiling point and passing nitrogen through it for a long time, neither in the first nor in subsequent treatments was there any increase in the number of impulses. Only in two of the 40 experiments was there some slight increase in the impulses in the afferent nerve. Thus the low partial oxygen pressure which causes an increase in the electrical activity in the sinus nerve is without effect on the impulses in the intestinal nerve.

It may be concluded that the chemical receptors of the different zones have a selective sensitivity, at any rate with respect to certain adequate stimuli. A low oxygen partial pressure represents a stimulus for the receptors of the carotid gland, but does not stimulate the chemoreceptors of the intestine. In addition, even within the intestine there is also a differential sensitivity to hydrochloric acid, as between the duodenum and the jejunum.

O. N. Zamyatina [2] demonstrated excitation of the intestinal receptors occurred on feeding animals with meat and on introducing amino acids and glucose into the intestinal lumen. Her results and ours indicate that different peripheral interoceptive zones are specialized to their proper stimuli, and show little if any response to stimuli which are adequate for the chemoreceptors of a different zone. It is probable that this differential sensitivity is associated with the evolution of specialized chemoreceptive zones.

Also, a large number of studies [1, 3 – 9, 11, 15, 16, 18] have shown that many substances such as nicotine, veratrine, acetylcholine, lobeline, adrenalin, serotonin, potassium chloride, sodium bicarbonate, disodium hydrogen phosphate, and lactic, carbonic, and acetic acids stimulate all the interoceptors. Many of these stimuli are universal and excite both chemo- and mechanoreceptors disposed in different organs, including receptors of the carotid gland as well as tactile, thermal and pain receptors.

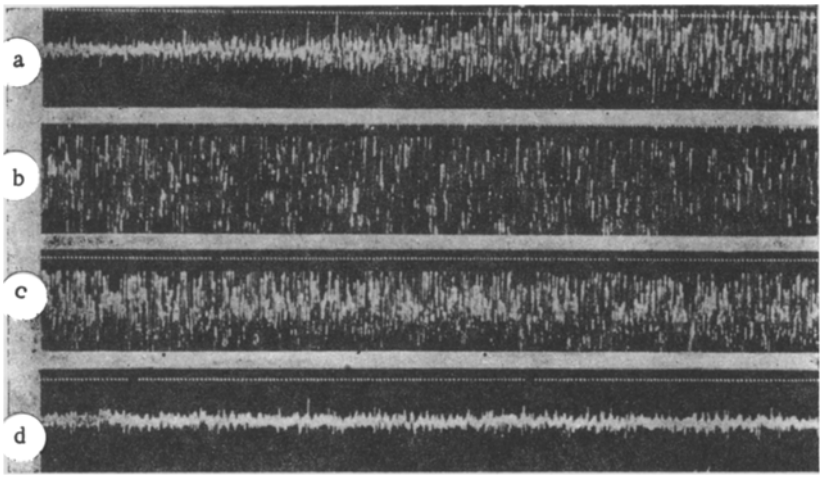

Fig. 3. Impulses in the afferent nerve from the small intestine. a) During the injection of 0.01 N HCl into the perfusate; b,c,d) 2,15 and 30 seconds after the injection.

However, many authors [10, 12, 13, 14, 19] have shown that hexamethonium, tetraethylammonium, and tubocurarine block the nonspecific sensitivity of the receptors to pharmacological stimuli, so that the latter can no longer excite all kinds of receptors; however, the sensitivity of the receptors to the adequate stimulus is preserved. For example, under the influence of hexamethonium, the receptors of the carotid gland can no longer be stimulated by acetylcholine and nicotine, but they remain sensitive to a reduced oxygen partial pressure; the baroreceptors of the carotid sinus also retain their sensitivity to pressure changes, and the tactile receptors remain sensitive to mechanical stimulation.

Thus, the exicitation which develops through the action of a number of drugs has a different mechanism from that which distinguishes the adequate stimulus. We may therefore suppose that the fact that a number of substances can stimulate all the receptors must not be interpreted as indicating that they all have a common adequate stimulus.

We have shown that the intestinal receptors are not excited by a low oxygen pressure, which is, however, an adequate stimulus for the chemoreceptors of the sinocarotid zone, and that the receptors of the duodenum and jejunum have different sensitivities to hydrochloric acid; from these and from published results we may conclude that there is a specialization of the peripheral interoceptors to different adequate stimuli.

SUMMARY

A solution of 0.01 N HCl was introduced into the lumen of the cat and it was found that there was an increase in the number of afferent impulses from the duodenum, and that a similar increase occurred when 0.1 N HCl was introduced into the jejunum. The increase in the impulses shows a long latent period lasting from 30 seconds to 5 minutes, and the effect is maintained for as long as 30 or even 60 minutes. Introduction of 0.01 N HCl solution into the perfusate provoked a brief increase of rapid onset in the afferent impulses from the jejunum. Reduction of the partial oxygen pressure of the blood or of the perfusate increased the number of impulses from the sinus nerves, but had no such effect on the nerves from the intestine. Therefore, different portions of the peripheral interoceptors show a selective sensitivity to various stimuli.

LITERATURE CITED

1. Anikina N. A., Byull. Éksptl. Biol. i Med. 42, 7, 8 (1956).
2. Zamyatina O. N., Proceedings of the Physiol. Inst. [in Russian] (Moscow-Leningrad, 1954) Vol. 3, p. 193.
3. Kulaev B. S., Byull. Éksptl. Biol. i Med. 45, 6, 17 (1958).
4. Lebedeva V. A., Byull. Éksptl. Biol. i Med. 34, 11, 17 (1952).
5. Ugolev A. M., Khayutin V. M. and Chernigovskii V. N., Fiziol. Zhurn. SSSR, No. 1, 117 (1950).
6. Khayutin V. M., Byull. Éksptl. Biol. i Med. 34, 8, 1 (1952).
7. Chernigovskii V. N., The Afferent System of the Internal Organs [in Russian] (Kirov, 1943).
8. Chernigovskii V. N., Proceedings of the Military and Naval Medical Academy [in Russian] (Leningrad, 1949) Vol. 17, p. 395.
9. Aviado, D. M. and Schmidt, C. F., Physiol. Rev. 1955, v. 35, p. 24.

10. Brown G. L., Gray J. A. B., J. Physiol. 107 (London, 1948) p. 306.
11. Comroe J. H., Schmidt C. F., Am. J. Physiol. 12 (1938) p. 75.
12. Diamond J., J. Physiol. 130 (London, 1955) p. 513.
13. Dodt E., Scouby A., Zotterman Y., Acta Physiol. Scand. 28, (1953) p. 101.
14. Douglas W. W., Gray J. A. B., J. Physiol. 119 (London, 1953) p. 118.
15. Euler U. S., Liljestrand G., Zotterman Y., Scand. Arch. Physiol. 83, (1939) p. 132.
16. Heymans C., Neil E., Reflexogenic areas of the cardiovascular system, (London, 1958).
17. Iggo A., Quart. J. Exp. Physiol. 42 (1957) p. 398.
18. Landgren S., Neil E., Zotterman Y., Acta Physiol. Scand. 25 (1952) p. 24.
19. Witzleb E., Pflüg. Arch. ges. Physiol. 269 (1959) p. 439.

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