ON THE ADAPTATION OF CHEMORECEPTORS

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(Presented by Active Member AMN SSSR V. N. Chernigovskii)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 50, No. 8, pp. 24-28, August, 1960
Original article submitted August 14, 1959

E. D. Adrian [9] first established the fact that various receptors adapt to a constant stimulus. Following him, most investigators limited their study of the phenomena of adaptation to processes occurring directly in the receptor itself [10, 11, etc.]. It was assumed that cessation of reflex reactions during prolonged stimulation results from adaptation of receptors to stimulation. A different tack was adopted by investigators [5, 7, 8] who suggested that in the intact organism adaptation can not be restricted to the receptors, but arises in the analyzer as a whole.

In studying the phenomena of adaptation in the whole organism, A. M. Ugolev, V. M. Khayutin, and V. N. Chernigovskii [7] showed that,in response to prolonged stimulation of the mechanoreceptors of the urinary bladder and intestine,the circulatory and respiratory reflexes, which develop first, disappear although the stimulus continues to act. Analyzing the cause of the adaptation of these reflexes, these authors adduced convincing proof that reflex adaptation was caused by the development of inhibition in the centers. The most conclusive data in this connection are those of V. M. Khayutin [8], who showed in experiments with the cold block of an intestinal nerve during prolonged stimulation of interoceptors that,at a time when the blood pressure had returned to normal, adaptation of the interoceptors still had not taken place, since removal of the cold block produced reflex changes in blood pressure of the same magnitude as at the beginning of the experiment.

Similar results were obtained by T. S. Lagutina [5]. Comparison of the reflex changes in blood pressure with the pattern of afferent impulses during prolonged stimulation of the mechanoreceptors of the urinary bladder, showed that the blood pressure returned to the original level while afferent impulses were still continuing to reach the centers.

It was of interest to determine whether similar interrelationships hold between central mechanisms and the activity of receptors during prolonged application of a chemical stimulus to the receptors.

METHOD

The investigation was performed in acute experiments on cats under urethan anesthesia. The experiments were carried out with perfusion of an isolated segment of intestine having only nervous connections with the organism. The chemical stimuli were injected into the current of perfusing fluid with a syringe for single applications. Prolonged stimulation of receptors was produced with acetylcholine in a concentration of $1 \cdot 10^{-4}$ g/ml by replacing the perfusion fluid (Ringer–Locke solution saturated with oxygen) with the acetylcholine solution. We recorded the pattern of afferent impulses in the intestinal nerves and kept a simultaneous record of the arterial pressure in the carotid artery (with a mercury manometer) on the kymograph. This method has been described in detail in an earlier paper [2].

RESULTS

When 1 ml of acetylcholine solution (in a concentration of $1 \cdot 10^{-4}$ g/ml) was injected with a syringe into the current of fluid perfusing the vessels of the isolated intestine retaining only nervous connections with the organism, reflex elevation of blood pressure occurred, which usually lasted 30-60 seconds (Fig. 1).

With prolonged and continuous stimulation of the interoceptors by acetylcholine at the same concentration,there likewise develops an elevation of the blood pressure at first, which gradually returns to the initial level despite continued stimulation (see Fig. 1b). We will call the time required for this return to normal the "reflex adaptation time," following A. M. Ugolev, V. M. Khayutin, and V. N. Chernigovskii. The reflex effects on arterial pressure that occur upon continuous stimulation of receptors adapt at different rates (requiring from a few tenths of a second to a few minutes) in different experiments, and even during the same experiment. But attention should be paid to the fact that in most experiments reflex adaptation developed within 2-4 minutes, and in some cases,the duration of the reflex

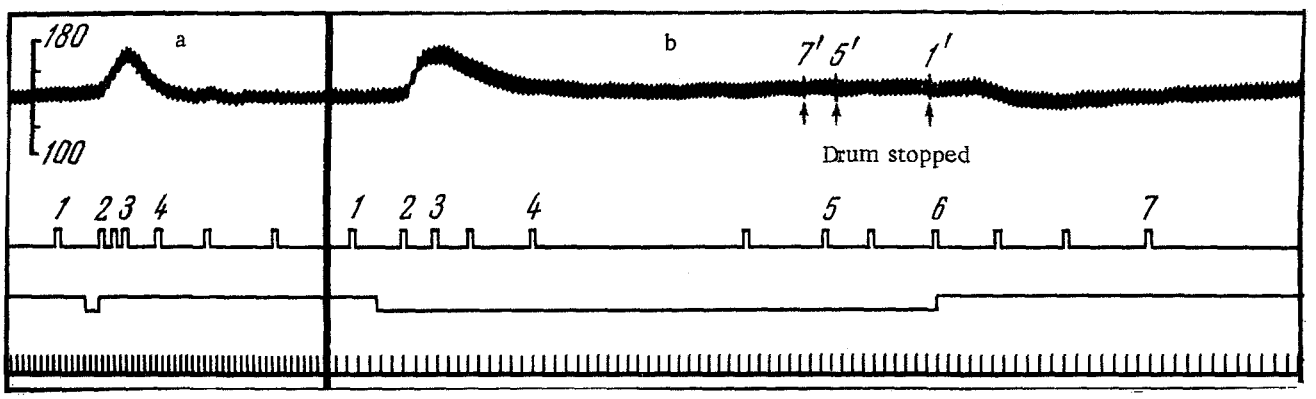

Fig. 1. Reflex changes in arterial pressure accompanying injection of 1 ml of acetylcholine at a concentration of $1 \cdot 10^{-4}$ g/ml into the vessels of the intestine (a) and prolonged passage of acetylcholine in the same concentration through the intestinal vessels (b). Interpretation of curves (from top): recording of blood pressure in the carotid artery; indication of times when oscillograph records were made; injection of acetylcholine; time (5 seconds).

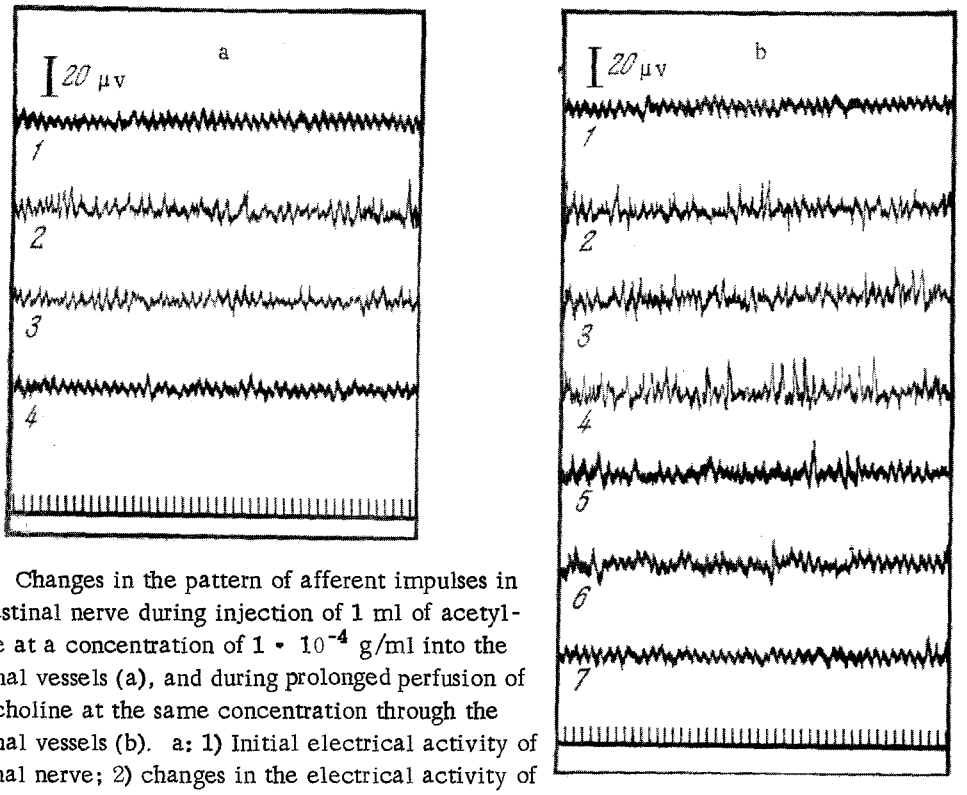

Fig. 2. Changes in the pattern of afferent impulses in an intestinal nerve during injection of 1 ml of acetylcholine at a concentration of $1 \cdot 10^{-4}$ g/ml into the intestinal vessels (a), and during prolonged perfusion of acetylcholine at the same concentration through the intestinal vessels (b). a: 1) Initial electrical activity of intestinal nerve; 2) changes in the electrical activity of the intestinal nerve six seconds after injection of acetylcholine; 3) the same, 20 seconds after injection; 4) the same, 45 seconds after injection; b: 1) initial electrical activity of intestinal nerve; 2) changes in electrical activity of intestinal nerve 10 seconds after beginning of acetylcholine perfusion; 3) the same, 20 seconds after start; 4) the same 65 seconds after start; 5) the same, 10 minutes after start; 6) the same, 17 minutes after start; 7) the same, 1 min 40 sec after start of Ringer-Locke perfusion (time marker – 0.02 sec).

shift in blood pressure accompanying continuous stimulation of receptors was even the same as the duration of the blood pressure shift following a single injection of acetylcholine. In such instances the blood pressure curves sometimes duplicated each other exactly.

Similar variations in the adaptation time of reflex changes in arterial pressure were observed in work cited above [7, 8] with prolonged stimulation of mechanoreceptors of the intestine and urinary bladder. But in our experiments we never observed reflexes lasting for multiples of ten minutes. The longest reflex adaptation time was seven minutes.

When the reflex reaches the level of adaptation, stopping the stimulation of the receptors by switching the perfusion current to pure Ringer-Locke solution produces a drop in arterial pressure to a point below its initial level. This depressor phase is a "release" phenomenon like that observed by A. M. Ugolev, V. M. Khayutin, and V. N. Chernigovskii in their experiments [7]. They interpreted the release phenomenon as a manifestation of inhibition developing in the vasomotor center during prolonged stimulation of the receptors, and clearly exhibited at the cessation of stimulation.

Electrophysiological analysis of the signals from the intestinal receptors during continuous stimulation of those receptors with acetylcholine was carried out by us at the same time as the analysis of the reflex reactions, and showed that during recording of afferent impulses in the intestinal nerves, in response to the injection of 1 ml of acetylcholine in a concentration of $1 \cdot 10^{-4}$ g/ml, there develops a relatively short volley of impulses which usually ends within one minute (Fig. 2a). With prolonged perfusion of acetylcholine solution through the intestinal vessels, the development of the volley of impulses is quite markedly drawn out (see Fig. 2b).

The oscillograms shown in Fig. 2, a and b, were recorded in the same experiment and during the same stimulations as were the kymograms in Fig. 1, a and b. The numerals 1, 2, 3, and so on, on the kymograph records indicate the times when the impulse patterns represented on the oscillograms under the corresponding numerals were recorded. It can be seen from the oscillograms in this experiment that the number of impulses per unit time continues to increase for a considerable period of time (oscillograms 2, 3, and 4), and then diminishes somewhat and remains at a significant level for a rather long time (oscillogram 5); after this, it usually disappears permanently within about half an hour after the beginning of prolonged stimulation.

In the experiment presented in these figures we followed the complete adaptation of the reflex reaction of arterial pressure, with its subsequent "release" at the cessation of stimulation. But we did not observe complete "adaptation" of the receptors, since impulses still kept coming from the receptors (see Fig. 2b, oscillogram 6). This was done intentionally, because, in those experiments where complete adaptation of the receptors was attained during prolonged application of acetylcholine, we failed to observe the "release" phenomenon, which apparently can only appear if there is an abrupt reduction in the rate at which impulses reach the centers.

Thus, electrophysiological investigation of the intestinal receptors during prolonged stimulation shows that these receptors belong in the slowly adapting category. This conclusion agrees with data on the rate of adaptation of other interoceptors. Available information on this subject mainly concerns the receptors of the urinary bladder, which are classified by all authors [1, 3, 4, 10, 11] as slowly adapting.

Comparison of the adaptation time of the reflex shifts in arterial pressure with the adaptation time of the intestinal receptors under prolonged stimulation shows that, when arterial pressure has almost completely returned to the initial level, the rate of impulse generation by the receptors not only has not diminished, but is in fact continuing to increase (see Fig. 2b, oscillogram 4); at a time when the reflex displacement of arterial pressure has adapted completely, the production of impulses remains for a long time at a significant level, adequate to cause a shift in arterial pressure – i.e., the return of reflexes to normal is much faster than the adaptation of receptors.

On the basis of these data we conclude that the return of altered blood pressure to normal during continuous chemical stimulation of intestinal receptors (adaptation to stimulation) is not determined by receptor adaptation, but is apparently the result of the same process of central inhibition whose dominant role in the phenomena of adaptation of interoceptive reflexes has been noted by the authors cited above.

SUMMARY

The subject of this study was the interrelationship between central mechanisms and receptors in the adaptation of reflex blood pressure changes during prolonged action of a chemical stimulus upon the intestinal receptors. The conclusion is drawn that under these conditions the adaptation of the reflex arterial pressure changes is not the result of receptor adaptation, but is mainly due to the involvement of central mechanisms.

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