# PHYSIOLOGY

## SENSITIZATION OF MECHANOCEPTORS BY ACETYLCHOLINE

I. T. Dzheliev and V. N. Chernigovskii

From the Laboratory of General Physiology (Head – Active Member of the AMN SSSR, V. N. Chernigovskii) Institute of Normal and Pathological Physiology (Director – Active Member of the AMN SSSR, V. N. Chernigovskii) AMN SSSR, Moscow, Received February 19, 1959

It has frequently been demonstrated that several chemical substances can not only stimulate particular chemoceptors, but may also sensitize or desensitize mechanoceptors [2,4]. A detailed review of this subject has been given by A. S. Paintal [3] in his paper at the Twentieth International Physiological Congress. However, there are no references to sensitization or desensitization of the intestinal mechanoceptors.

We have attempted to study the effect of acetylcholine on the mechanoceptors of the small intestine of cats.

### METHOD

The cats were anesthetized with an intravenous injection of 20% urethane solution, and 35 acute experiments were carried out. The ileocecal portion of the intestine was separated, so that it retained only nervous connection with the rest of the body, and its vessels perfused with Ringer's solution. This particular part of the intestine was chosen because well marked reflex changes in arterial pressure and respiration can be elicited from the interoceptors of the ileocecal angle both by chemical and by mechanical stimuli. Solutions of $1:10^7$ – $1:10^3$ of acetylcholine and a 0.1% solution of atropine were used to act on the interoceptors. These substances were introduced into the perfusate through a syringe, the amount injected being usually 1 ml. Also, mechanical stimlation of the perfused section was applied by expanding it with air, whose pressure was measured in millimeters of mercury. Kymographic traces of respiration, pressure in the arterial artery, and of the heart beat (recorded through a membrane manometer) were also made. The rate of perfusion was determined by counting the perfusate drops electrically.

### RESULTS

As a rule, mechanical stimulation of the perfused section produced a reflex elevation of the arterial pressure, and occasionally an increase in the rate and depth of respiration. Usually, a well shown effect was obtained simply by maintaining the pressure in the perfused portion at 60 mm, but sometimes it was necessary to raise it to 80 mm. As a rule, the reflex elevation of the arterial pressure was maintained during the whole period of mechanical stimulation. In a few experiments it returned to its initial level long before mechanical stimulation had ceased.

On introducing acetylcholine into the perfusate, the typical increase in arterial pressure and respiration rate was observed. We first attempted to find whether acetylcholine affects the nature or the extent of the reflex response to mechanical stimulation. For this purpose, experiments were carried out in which the perfused portion was stimulated mechanically before various concentrations of acetylcholine were intoduced into the perfusate. In the great majority of experiments, prior treatment with acetylcholine caused a marked change in the magnitude of the reflex response to stimulation of the mechanoceptors. The results were particularly clearly shown when the moderate or high concentrations of acetylcholine ($1:10^5 - 1:10^4$) were used. In these experiments, after treatment with acetylcholine, the increase in arterial pressure was greater than the initial response.

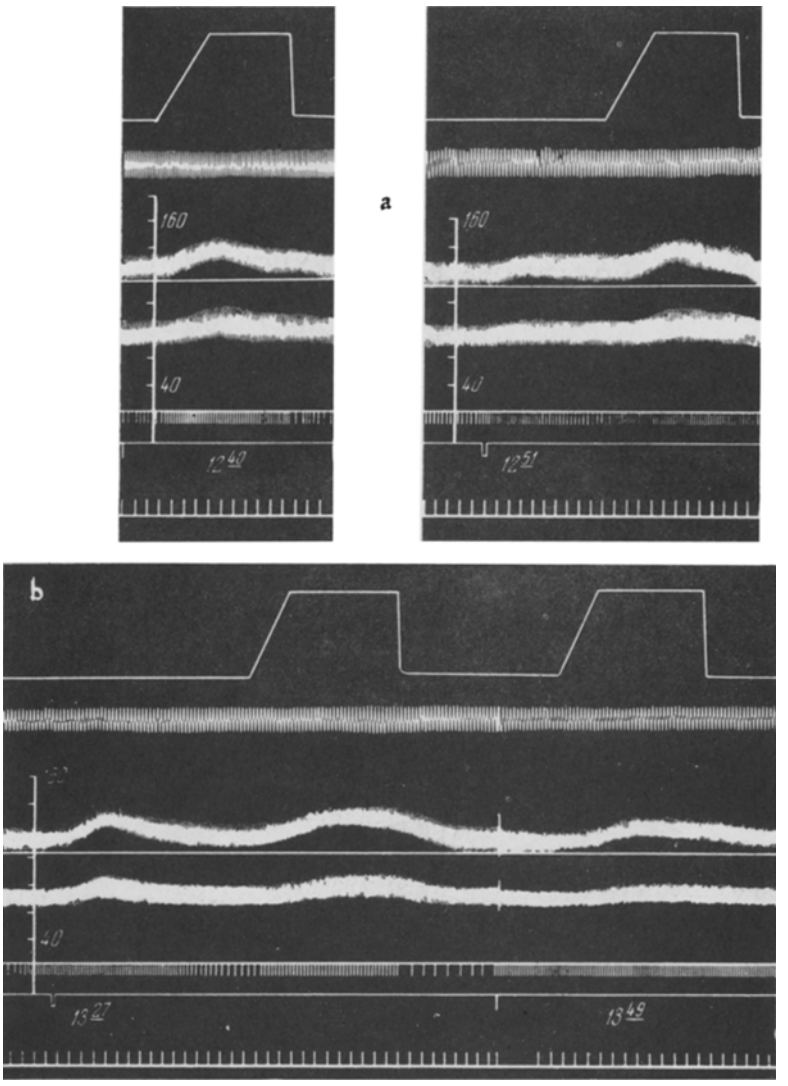


Fig. 1. Variation in the sensitivity of mechanoceptors of the ileocecal portion of the intestine after treatment with acetylcholine. a) No increase in sensitivity to mechanical stimuli with small doses of acetylcholine; b) effect occurs after introducing moderate or large doses of acetylcholine into the perfusate. Curves, from above downwards: strength of mechanical stimulus to perfused loop (in mm mercury), respiration, arterial pressure (in mm mercury), zero line, heart rate, perfusion rate in drops, stimulus marker, time marker (5 seconds).

In 10 experiments, threshold doses of acetylcholine $1:10^7 - 1:10^6$ gave no effect, but the higher concentrations were always effective (Fig. 1,a, b).

The increase in response to mechanical stimulation after treatment with acetylcholine usually developed after 10 minutes. During this period, the reflex remained at the normal level. In some experiments, even the single injection of acetylcholine was sufficient to maintain an increased reflex effect for a period of an hour or more.

If moderate or high concentrations ($1:10^5 - 1:10^3$) of acetylcholine were used, the effect did not always occur immediately. In 7 out of the 30 experiments, the first stimulus applied after giving the drug produced the normal response. Sometimes the reflex was even reduced. Only after the second or third stimulus had been applied, did the marked increase in size of the reflex occur (Fig. 2).

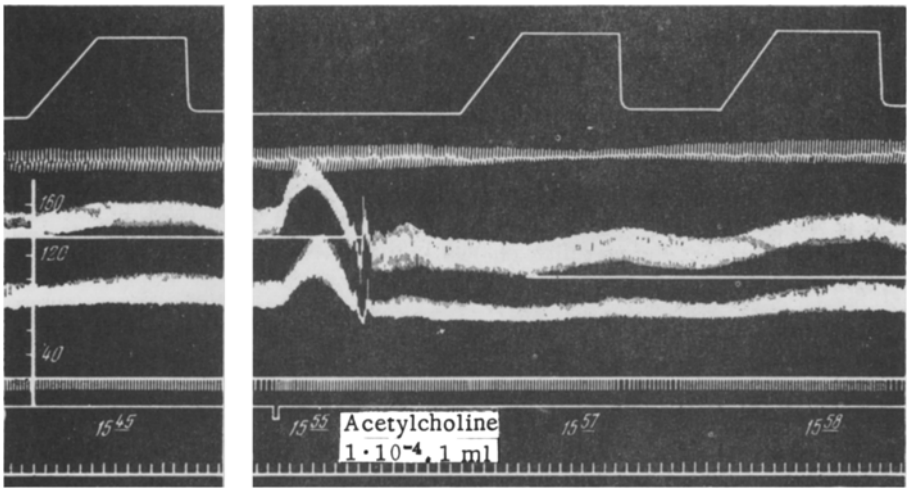


Fig. 2. Gradual increase in sensitivity to mechanical stimulation following moderate or large doses of acetylcholine. Curves as in Fig. 1.

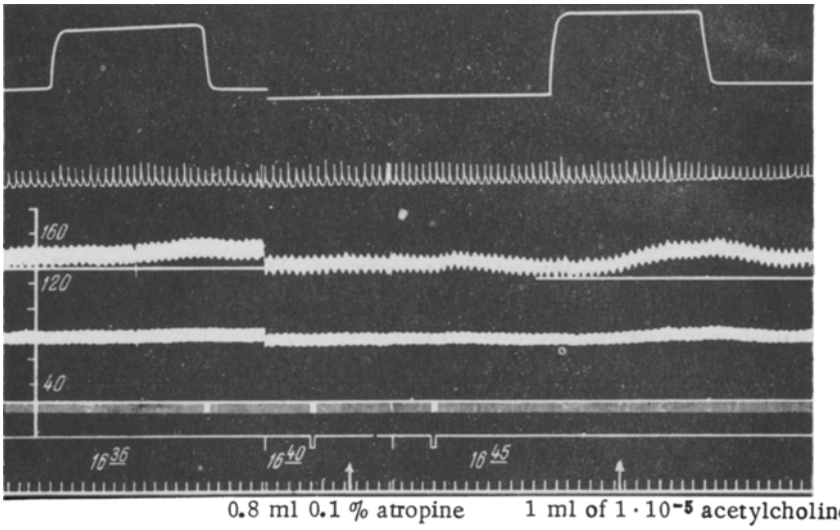


Fig. 3. Increase in the sensitivity of the perfused portion of the intestine to mechanical stimuli following previous treatment with acetylcholine (experiments with atropinized intestinal loop). Curves as in Fig. 1.

In these experiments, the increased sensitivity to mechanical stimuli usually developed over a period of 1-3 1/2 minutes after the first mechanical stimulus was applied. The fact that the effect was mediated by the acetylcholine can be seen from the experiments in which repetitive mechanical stimulation of the interoceptors without previous treatment with acetylcholine caused no increase in the reaction.

Quite frequently, the affect of acetylcholine was to change not only the extent but also the shape of the curve of the reflex response. Normally, after mechanical stimulation had ceased, the arterial pressure rapidly returned to its initial level, but when acetylcholine was given, an after-effect lasting 1.2-20 minutes occurred.

Finally, it must be pointed out that the reflex response to mechanical stimulation following the action of acetylcholine was present in full measure even when the mechanical stimulation of the receptors was delayed until after the direct action of acetylcholine on the arterial pressure and respiration rate had ceased.

When acetylcholine is introduced into the intestinal vessels, in addition to respiratory and circulatory

changes, there is also an increase in peristalsis, and therefore of intestinal tone. Therefore, the increased reflex response to mechanical stimulation which we observed to follow the injection of acetylcholine might be attributed to an increased tone of the intestinal wall, and not to sensitization of the mechanoceptors. To test this possibility, experiments were carriex out in which acetylcholine and mechanical stimulation were used after atropine had been introduced into the intestinal vessels. It was found that a certain dose of acetylcholine, usually 0.5-1 ml of 0.1% solution, still allowed an acetylcholine injection into the perfusate to provide reflex circulatory and respiratory changes, while at the same time peristalsis was completely arrested for at least 40 minutes. This dose of atropine in the perfusate as a rule caused no reflex change in the breathing or blood pressure; only occasionally was there a short, scarcely noticeable increase in arterial pressure.

Despite treatment with atropine, subsequent injection of acetylcholine into the perfusate increased the reflex circulatory and respiratory changes in response to mechanical stimulation, in just the same way as in the previous experiments (Fig. 3).

No response to mechanical stimulation was observed in cases when the injection of acetylcholine either had no effect on arterial pressure and respiration, or when such changes were very small.

The results obtained show that previous injections of acetylocholine into the perfusate increases the reflex response to a mechanical stimulation of this part of the intestine.

Concerning the mechanism, it appears that contact of acetylocholine with the interoceptors increases their sensitivity to mechanical stimulation. The experiments with atropine refute the idea that the observed effects are due to changes in the tone of the intestinal smooth muscle. Further, increasing tone of the wall of hollow organs does not increase but actually decreases the response to mechanical stimulation [1].

It follows, therefore, that the reason for the effect we have observed is due to the ability of acetylcholine to sensitize the intestinal mechanoceptors to their adequate stimulus.

## SUMMARY

The experiments were performed on cats. The ileocecal portion of the intestine in which only the nervous connection with the rest of the body were left intact was perfused. Preliminary introduction of 1 ml of $1:10^5$ – $1:10^4$ acetylcholine into the perfusate causes an increase in the reflex changes in respiration and arterial pressure induced by stimulation of the mechanoceptors of the isolated portion of intestine.

The same effect was observed when the perfused area had been atropinized prior to giving the acetylcholine and stimulating mechanically.

The results show that acetylcholine has a sensitizing effect on mechanoceptors.

## LITERATURE CITED

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* In Russian.