ADAPTATION OF THE INTEROCEPTIVE REFLEXES FROM THE MECHANOCEPTORS OF THE SMALL INTESTINE

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Investigators describing the role of general anesthesia in the adaptation of interoceptive reflexes [1-8] have studied this problem in acute experiments on anesthetized animals.

For this reason the question how adaptation develops to interoceptive stimuli in natural conditions, i.e., in unanesthetized animals, has not yet been studied. Nor it is sufficiently clear to what extent anesthesia modifies the adaptation.

The object of the present investigation was to examine the role of morphinethiopental anesthesia in the mechanism of adaptation of the reflex developing during stimulation of the mechanoceptors of the intestinal wall.

EXPERIMENTAL METHOD

Altogether 3 series of experiments were performed. In series I the character of adaptation of the entero-enteral inhibitory reflex arising during stimulation of the mechanoceptors of the intestinal wall of anesthetized animals was studied. For this purpose, laparatomy was performed on dogs and a rubber balloon with a volume of 1-2 cm^3 was introduced into the lumen of the small intestine to record the contractions of the circular muscle of the intestinal wall; simultaneously by means of an Engelmann's lever, the contraction of the longitudinal muscle of the same segment of intestine were recorded by the usual method.

To stimulate the mechanoceptors of the intestinal wall, a rubber balloon with a volume of 8-10 cm^3, in which a pressure of 20-300 mm Hg was produced, was introduced into the lumen of another portion of the small intestine.

The reaction of the circular and longitudinal muscles of the portion of intestine examined was recorded on a kymograph.

In the experiments of series II these investigations were carried out on 10 dogs in which two intestinal loops had been exteriorized by the Thiry-Vella method or a Thiry-Vella loop and a fistula of the small intestine had been formed 2-3 weeks before the beginning of the experiments. In these experiments balloons were used to record the changes in motor activity of the smooth muscle of the small intestine in response to prolonged and intensive stimulation of the Thiry-Vella intestinal loop. The method of recording was the same as in the previous series.

The experiments of series III were carried out on isolated intestinal loops of healthy dogs perfused with the blood of healthy donors. In these experiments, to examine the direct effect of morphine and thiopental sodium on the contractile activity of the smooth muscle of the intestinal wall, these drugs were injected in doses of 50-500 μg (morphine) and 250 μg-2.5 mg (thiopental sodium) into a catheter inserted into the artery of the perfused loop.

EXPERIMENTAL RESULTS AND DISCUSSION

The experiment of series I showed that in animals anesthetized with morphine (5 mg/kg) and thiopental sodium (50 mg/kg) stimulation of the mechanoceptors of the small intestine produced by a pressure of 60-80 mm Hg in the balloon caused definite inhibition of the motor activity of adjacent areas of the small intestine. From 30 sec to 2 min later, however, the motor activity of the part of the small intestine from which the recordings were made was restored, although stimulation of the interoceptors continued. A further increase of pressure in the stretching balloon to 100-280 mm Hg or more caused further inhibition of motor activity of the small intestine, which again was of short duration and was followed by complete restoration (Fig. 1B). A similar effect was observed when a high pressure in the stretching balloon (over 260 mm Hg) was produced in one stage: after a short (up to 2 min) period

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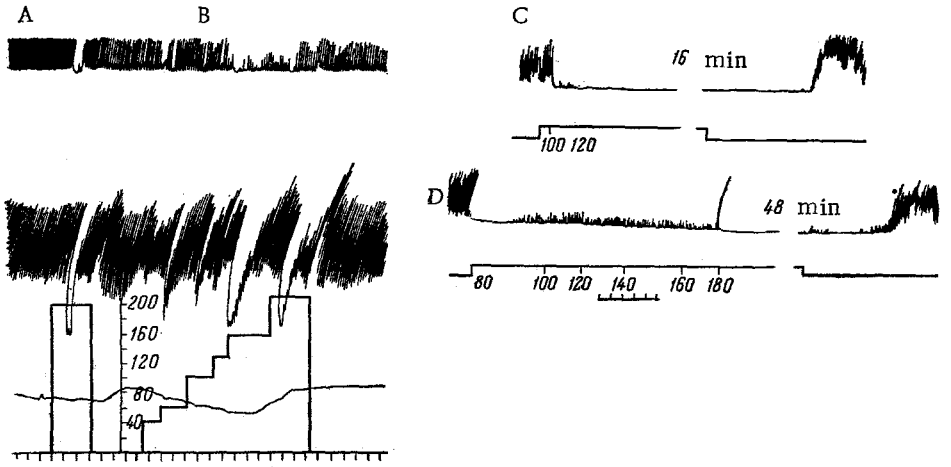

Fig. 1. Entero-enteral inhibitory reflex developing in response to stimulation of the mechanoceptors of the small intestine in anesthetized (A and B) and unanesthetized (C and D) dogs. A and C — pressure in the stretching balloon increased in one stage; B and D — pressure in the stretching balloon increased gradually. From top to bottom: tracing of contractions of the circular and longitudinal muscles, marker of amplitude and duration of stimuli, time marker 1 min.

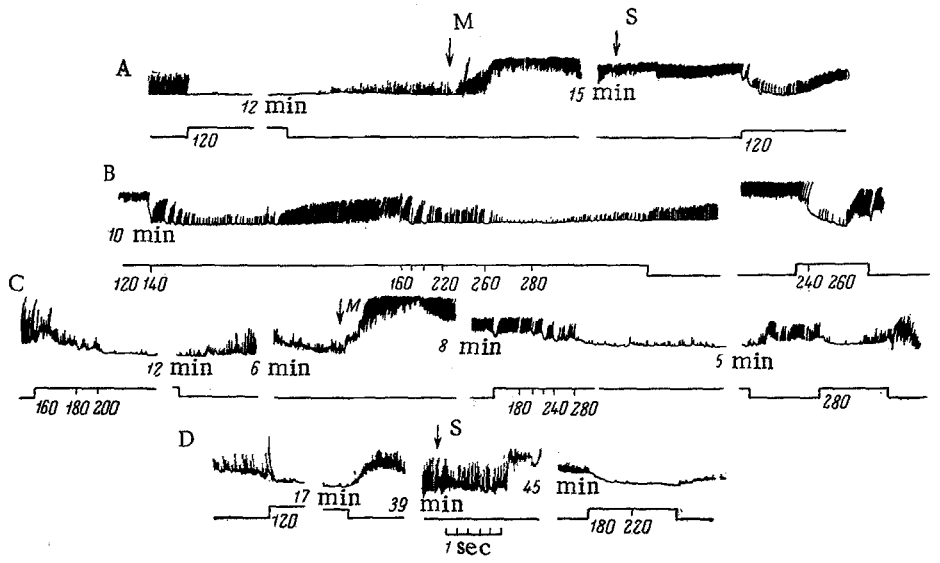

Fig. 2. Development of the entero-enteral inhibitory reflex in dogs after injection of morphine and anesthesia in response to a rapid and a gradual increase in pressure in the stretching balloon. A and B — after injection of morphine and thiopental sodium; C — after injection of morphine; D — after injection of thiopental sodium. Legend as in Fig. 1. The arrows indicate the times of injection of morphine (M) and thiopental sodium (S).

of inhibition, the motor activity of the small intestine was restored, despite continuing stretching of the intestinal loop (Fig. 1A).

In the experiments of series II, carried out on unanesthetized animals, in all cases a threshold level of stimulation of the mechanoceptors of the intestinal loop could be found at which the motor activity in the part of the small intestine from which recordings were made became permanently depressed.

The magnitude of this threshold stimulation varied considerably: the pressure in the stretching balloon at the moment of permanent depression of motor activity ranged from 40 to 180 mm Hg in different experiments. If the threshold stimulus was applied in one stage, the motor activity was immediately depressed and the inhibition persisted until stimulation of the interoceptors ended (for 2-3 h in these experiments; Fig. 1C).

The same effect was observed during a gradual increase in the pressure in the stretching balloon. When a critical level of stimulation was reached, total inhibition of motor activity took place; the activity was restored only after stimulation ceased (Fig. 1D).

In an attempt to discover the causes of this distinct difference between the results of the acute and chronic experiments, in the next series of experiments, after the preliminary establishment of the thresholds of the entero-enteral inhibitory reflex producing permanent inhibition of motor activity, morphine was injected in a dose of 5 mg/kg, or thiopental sodium in a dose of 50 mg/kg, or morphine and thiopental sodium were injected in the same doses consecutively. The character of adaptation of the entero-enteral inhibitory reflex in response to prolonged and intensive stimulation of the Thiry-Vella intestinal loop was again investigated 5-75 min after the injection.

The results of these experiments showed that morphine-thiopental anesthesia produced by consecutive injection of morphine and thiopental sodium led to a distinct reaction of the motor activity in the form of an increase in tone, and initially also in the amplitude of the contractions of the circular muscles of the intestinal wall.

Against this background, a permanent depression of motor activity did not develop whatever the amplitude of stimulation of the mechanoceptors of the intestinal wall, although the amplitude of the contractions diminished slightly (Fig. 2A). The reaction resembled that observed in the acute experiments (see Fig. 1A).

Results similar to those of the experiments of series I were also obtained after one-stage strong stimulation of the interoceptors by distending the balloon immediately to 280 mm Hg (Fig. 2B). In 10 experiments in which the threshold of the entero-enteral inhibitory reflex was studied after injection of morphine alone, it was found that complete inhibition of motor activity in these experiments was never prolonged, regardless of the intensity of stimulation of the interoceptors, although in response to very strong stimulation (240-280 mm Hg) the motor activity of the circular muscle remained sharply depressed through the period of stimulation.

In four experiments in which thiopental sodium (50 mg/kg) alone was injected into the animals, the anesthesia sharply increased the threshold of the entero-enteral inhibitory reflex, although in these conditions a critical level of stimulation could be determined at which permanent inhibition of motor activity developed (Fig. 2C).

To determine whether the decrease in sensitivity of the smooth muscle of the small intestine to the reflex inhibitory influences was connected with the stimulant action of morphine and thiopental sodium on the motor activity of the circular muscle of the intestine, 15 experiments were carried out with perfusion of the isolated loop of the dog's intestine. In 5 of these experiments, thiopental sodium in doses comparable with its blood concentrations during normal thiopental anesthesia (250 μg/ml blood) caused a transient inhibition of motor activity (Fig. 3E), but in larger doses (2.5 mg/ml blood) it caused prolonged depression of the motor activity (Fig. 3D).

The effects observed after injection of morphine into the perfusion fluid in doses of 50-500 μg were inconstant.

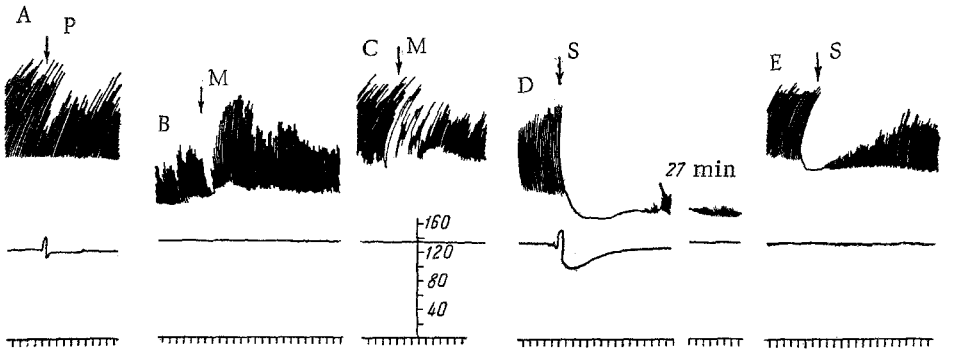

Fig. 3. Effect of morphine and thiopental sodium on the motor activity of the perfused intestinal loop following direct injection of the substances into the blood vessels of the loop. A — Injection of physiological saline (control); B — injection of morphine in doses of 50-500 μg; C — injection of thiopental sodium in doses of 250 μg-2.5 mg. From top to bottom: tracing of contractions of the intestinal muscles, perfusion pressure, time marker 30 sec. The arrows indicate the time of injection of physiological saline (P), morphine (M), and thiopental sodium (S).

In three experiments a slight increase in amplitude was observed without significant change in the tone (Fig. 3B), and in four experiments transient changes in tone took place, although the amplitude of the contractions was actually diminished (Fig. 3C). In 10 experiments the effects were practically indistinguishable from those observed following injection of equal volumes of physiological saline (Fig. 3A).

These experiments demonstrated a clear difference between the character of adaptation of the entero-enteral inhibitory reflexes in the acute and chronic experiments. The results obtained in chronic experiments on anesthetized animals show that this difference cannot be attributed to the conditions of the acute experiment associated with the laparatomy, but were caused by the morphine-thiopental anesthesia.

The results of the experiments with perfusion of the intestinal loop showed that the change in the reaction was due, not to direct stimulation of the intestinal muscle by these drugs, but to the action of morphine and the anesthetic on the central nervous mechanisms regulating motor activity.

The fact that in unanesthetized animals, the inhibition of the motor activity of the small intesting arising in response to prolonged and intensive stimulation of the intestinal wall was of long duration demonstrates that rapid adaptation to interoceptive stimulation does not take place.

It is known that general anesthesia has no direct action on the receptors (Gershuni and Narikashvili), so that it is evident that in the acute experiments the restoration of the motor activity of the intestinal muscle was due not to adaptation of the receptors, but to changes in the state of the nervous centers as a result of the administration of morphine and thiopental sodium.

The results obtained show that the central action of morphine and thiopental, especially if injected at the same time, modifies the reactivity of the centers: adaptation to interoceptive stimuli in these conditions developed much sooner than in the unanesthetized animals.

On the whole the results obtained confirm that adaptation to interoceptive stimulation is not due to changes in the sensitivity of the receptors, but to changes taking place in the centers joining the links of the interoceptive reflexes, as was pointed out previously [3].

LITERATURE CITED

1. P. K. Anokhin and A. I. Shumilina, Fiziol. Zh. SSSR, No. 3, 275 (1947).
2. I. A. Bulygin, Arkh. Biol. Nauk SSSR, 54, No. 2, 65 (1939).
3. V. M. Khayutin, The Mechanism of Adaptation of Unconditioned Interoceptive Reflexes. Candidate Dissertation, Leningrad (1951).
4. A. K. Chuvaev, Some Problems in the Excitability of the Visceral Receptors. Candidate Dissertation, Perm' (1949).
5. V. M. Shirokaya, Abstracts of Proceedings of the Eighth Scientific Session of Volgograd Medical Institute [in Russian], Volgograd (1948), p. 32.
6. E. D. Adrian, The Mechanism of Nervous Action [Russian translation], Moscow-Leningrad (1935).
7. E. Koch, Die reflektorische Selbstenerung des Kreislaufes, Dresden (1931).
8. A. Schweitzer, Die Irradiation autonomer Reflexe, Basel (1937).