CHANGES IN THE INTEROCEPTIVE REFLEXES IN DOGS UNDER THE INFLUENCE OF NARCOTICS

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The aim of the present investigation was to study the interoceptive reflexes in dogs without preliminary anesthesia or decerebration.

The action of anesthetics was investigated by the administration of various doses ranging from small amounts causing no change in the animal's behavior to doses causing a state of profound narcosis.

EXPERIMENTAL METHOD

Experiments were carried out on dogs trained to a procedure enabling the recording of the blood pressure without anesthesia.

Interoceptive reflexes were induced by stimulation of the mechanoreceptors of the stomach and rectum, and of the clamped carotid artery brought near the surface in a skin flap (for a description of the method, see papers [9, 10]).

In the experiment various anesthetics were used in the form of a 2.5% aqueous solution: hexobarbital in doses of 0.01-0.134 g/kg, evipan sodium — 0.005-0.116 g/kg, sodium amytal — 0.005-0.09 g/kg, chloralose — 0.005-0.15 g/kg (1% aqueous solution), chloral hydrate — 0.03-0.5 g/kg (10% solution in physiological saline) and urethane — 0.166-1.72 g/kg (20% aqueous solution); the dose of ether was measured at the time of the experiment from the amount actually consumed (before the experiments the animals were given 0.005 g/kg of morphine subcutaneously).

All the anesthetics (except ether) were injected intravenously after a recording had been made of the initial interoceptive reflexes.

In all, 67 experiments were carried out on 11 dogs.

EXPERIMENTAL RESULTS

As a result of the administration of the anesthetics mentioned above, phasic changes were observed in the pressor interoceptive reflexes of the animal.

After small doses or during slow (fractionated) anesthesia an increase in the pressor reflexes and a reduction in the threshold of stimulation could be observed (especially after stimulation of the mechanoreceptors of the rectum). This phase of the change in the reflexes was observed in the absence of any form of alteration in the animal's behavior, was often difficult to detect and, as a rule, was transient. With the onset of sleep or at an earlier period of the action of the anesthetics the second phase of change of the reflexes was observed — their decrease and depression.
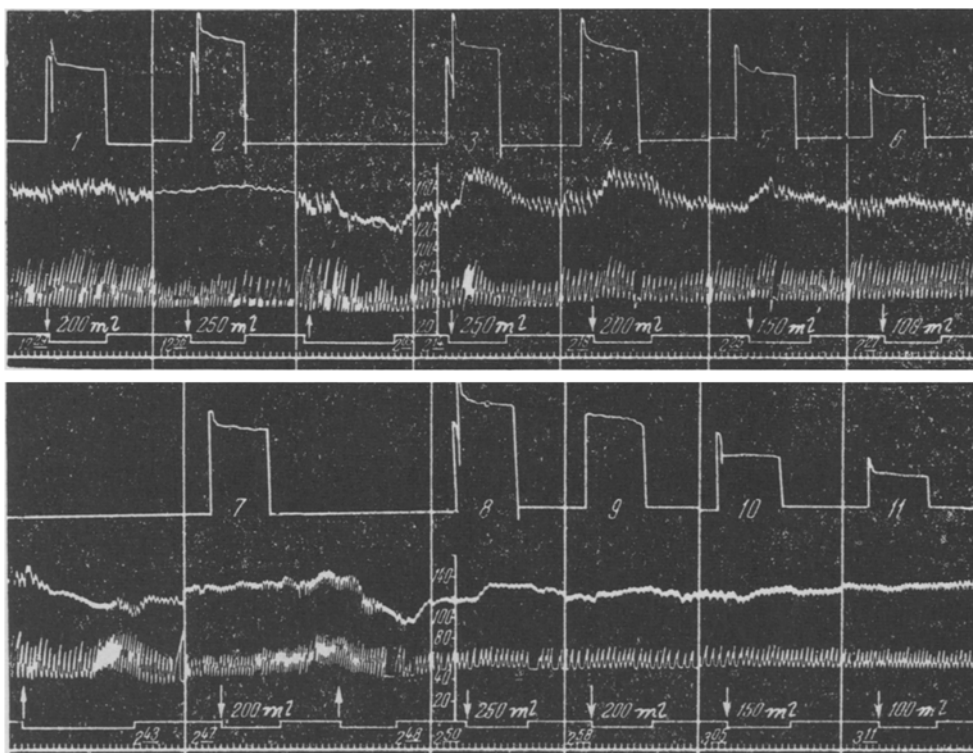
* Deceased.

Fig. 1. Changes in the interoceptive reflexes during fractionated intravenous injection of evipan sodium (dog Dzhanka, experiment dated February 11, 1956).
Significance of the curves (from above down): pressure within the organ, arterial pressure, respiration, zero line of the arterial pressure (also the stimulus marker), time marker (5 seconds). 6 and 11) Reflex in response to injection of 100 ml of air into the rectum (↓); 5 and 10) the same in response to 150 ml; 1, 4, 7, 9) the same to injection of 20 ml; 2, 3, 8) the same to injection of 250 ml; ↑) injection of evipan sodium (12, 24 and 14 mg/kg).

When an anesthetic dose was given continuously the phase of increased interoceptive reflexes died out, and a considerable decrease or total suppression of the pressor reflexes was then at once observed.

In several cases depressor changes in the blood pressure were observed, and these usually increased in magnitude with further doses of anesthetic. As the depth of anesthesia lessened, the depressor changes in blood pressure decreased and the pressor reactions were subsequently restored.

Examples of the experiments in which the phasic changes in the pressor reflexes during anesthesia took place as described may be seen on the accompanying kymograms.

During fractional injections of evipan sodium (Fig. 1), for instance, after a dose of 12 mg/kg a considerable increase of the pressor reflexes was observed in response to stimulation of the mechanoreceptors of the rectum and a fall in the thresholds of stimulation (well marked by comparison of tracings 1 and 2 with 3 and 4). Furthermore reflexes appeared also in response to subthreshold stimulation (injection of 150 and 100 ml of air, tracings 5 and 6). Further addition of evipan sodium lowered the increased pressor reactions.

The extinction of the first phase and suppression of the pressor reflexes during continuous injection of an anesthetic dose of sodium amytal (46 mg/kg) are shown in Fig. 2, in which the depressor changes in the blood pressure in response to inflation of the stomach (tracing 8), appearing instead of the pressor reflex (tracing 1) are seen to be not sharply pronounced. With deeper anesthesia (for example with a dose of 0.134 g/kg of hexobarbital) depressor reactions were observed with a significant fall in the blood pressure. The carotid sinus pressor reflex was also considerably decreased in the period of narcotic sleep, and there was observed in addition a
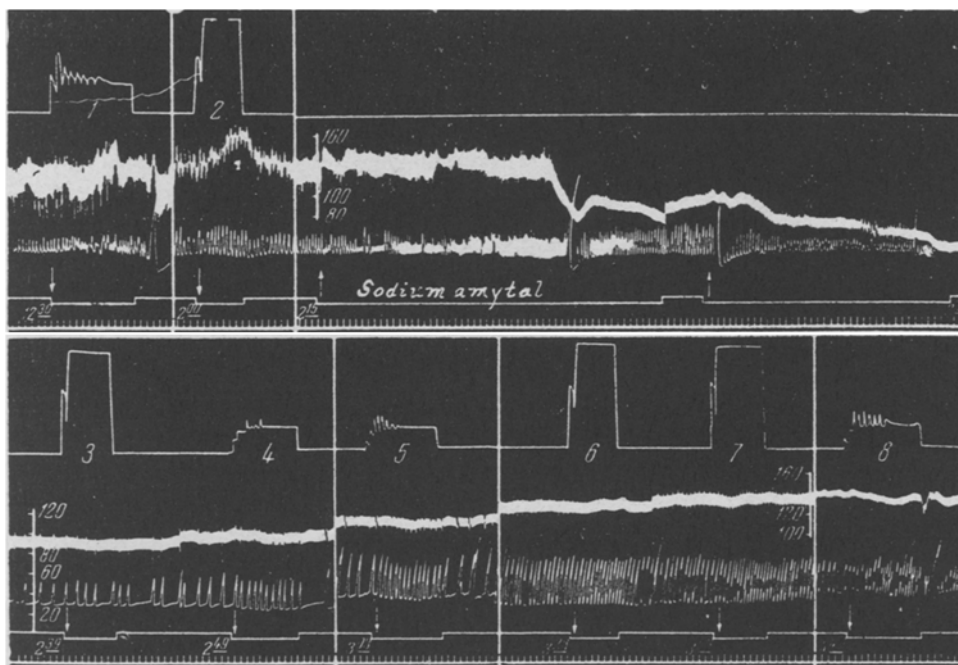
Fig. 2. Changes in the interoceptive reflexes in response to intravenous injection of an anesthetic dose of sodium amytal (the dog Dzhanka, experiment dated May 24, 1956). Significance of the curves as in Fig. 1. 1,4,5,8) Reflexes in response to injection of 1200 ml of air into the stomach ($\downarrow$); 2, 3, 6, 7) reflexes in response to injection of 350 ml of air into the rectum; $\uparrow$) injection of sodium amytal (46 mg/kg).

distinctive depressor reaction which appeared after removal of the clamp from the carotid artery.

The results of special control experiments showed convincingly that the changes described in the interoceptive pressor reflexes were not the result of the duration of the experiment nor of repetition of the stimulus.

As an additional control of the results of the investigations the reflexes were tested with changes in the depth of anesthesia, and also experiments were carried out in which various volumes of physiological saline were administered to animals.

As may be seen from Fig. 3, the reflex reactions of the blood pressure in response to repeated interoceptive stimulation in a prolonged control experiment during which physiological saline was given, continued without appreciable change.

The standard pattern of the phasic changes in the interoceptive reflexes during anesthesia indicated that, in principle, the action of all the anesthetics used was the same.

If, however, the doses causing the first and second phases of the changes in the pressor reflexes were compared with the anesthetic doses (in our experimental conditions), a difference was found in the degree of the inhibiting effect of the different anesthetics on the interoceptive reactions which we studied.

The most marked depression of the interoceptive reflexes was caused by sodium amytal and chloral hydrate. The phase of increase of the reflexes and also their subsequent decrease appeared in response to injection of these drugs in doses significantly smaller than the minimal doses having a narcotic effect. Thus even before the onset of sleep the interoceptive reflexes in response to the injection of chloral hydrate and sodium amytal were, as a rule, considerably reduced.

Injection of chloralose also reduced the reflexes even before injection of an anesthetic dose. However, in the first phase of action the pressor reflexes were increased to a greater extent (than by sodium amytal and chloral hydrate), although this period was also quite short in duration.
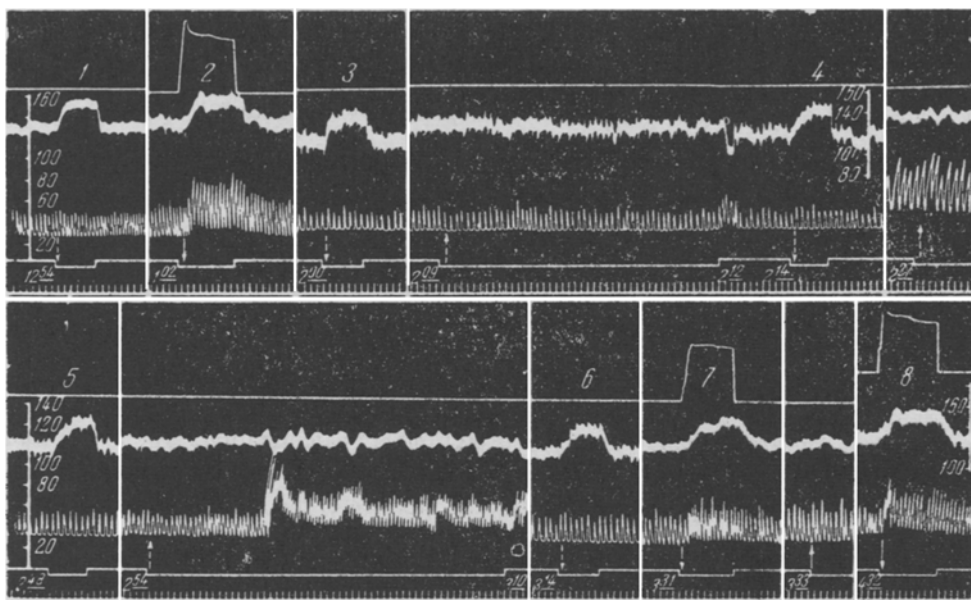
Fig. 3. Interoceptive reflexes in a control experiment (in response to the intravenous injection of physiological saline (the dog Pamir, experiment dated October 18, 1956). Significance of the curves as in Fig. 1. 1,3,4,5,6) Reflexes in response to clamping the carotid artery (↓); 2, 7, 8) reflexes in response to injection of 200 ml of air into the rectum (↓); ↑) injection of physiological saline (20, 20, 40 and 20 ml).

In contrast to these narcotics, hexobarbital and evipan sodium reduced the reflexes only after sleep had been induced in the animal. Furthermore, in some experiments in which hexobarbital was injected in fractional doses, increased reflex reactions could be observed even in the period of profound sleep.

In the experiments with ether an obvious and prolonged increase took place in the interoceptive reflexes, in some cases maintained throughout the whole experiment in spite of the adequate depth of the ether anesthesia, which was especially marked after preliminary depression of the reactions by administration of morphine.

Urethane occupied a special place among the anesthetics. After the phase of increase of the interoceptive reflexes, with increasing depth of urethane anesthesia by fractional injection of the drug (between phases I and II) a period ensued of normalization of the reflexes, which corresponded to the end of the period of excitation and the beginning of light anesthetic sleep (in a dose of .73-109% of the anesthetic dose).

Following preliminary inhalation of ether this period occurred later, at a dose equivalent to 100-160% of the minimum anesthetic dose (under these conditions of anesthesia). This is an important factor because such a level of anesthesia is in practice adequate for the performance of acute experiments and also in view of the more common usage of ether-urethane anesthesia in experimental practice.

On testing the other anesthetics we observed an intermediate phase of normalization of reflexes only in the experiments in which fractional injections of chloralose were given. However, this period was very transient and appeared in response to a dose equivalent to 43-57% of the anesthetic dose, i.e. before the animal fell asleep.

Hence, in light anesthetic sleep, with the exception of sleep induced by ether, urethane, and sometimes, hexobarbital, we always observed decreased interoceptive reflexes.

A particularly pronounced depressing effect on the interoceptive reflexes was shown by narcotics which are widely used in clinical practice for therapeutic purpose (sodium amytal and chloral hydrate).

On the bais of the results obtained we cannot agree with Gero's view [3] that the therapeutic action of narcotic drugs (in sleep therapy) is effected in a period of increase of interoceptive reflexes.

This hypothesis is unlikely, since the phase of increase of the interoceptive reflexes is very brief and (in

particular for chloral hydrate and sodium amytal) it is observed only at the very beginning of administration of the narcotics, at a dose which is till insufficient to have a hypnotic action.

Furthermore, clinical and experimental observations have shown that sleep therapy is effective only in those cases when it is essential to produce protective inhibition, in contrast to states when it is important to activate the protective functions of the body, since the latter are depressed by narcotics [2].

These observations also confirm the fact that the phase of increase of reflex reactions, if it arises at all, is less important during narcotic sleep than the depression of reflexes, which is predominant under such conditions.

The view that a temporary suppression of the interoceptive reflexes may be of therapeutic importance in certain diseases is held at the present time by clinicians and also has experimental grounds in its favor [12, 1, 4, 8, 5, 7, 6, 10, 11 etc.].

SUMMARY

Experiments were performed on dogs without their preliminary narcotization. The author studied the effect of various anesthetics on the reflex changes of the blood pressure occurring in interoceptive stimulation. Phasic changes were noted in interoceptive reflexes with the increase of the doses of anesthetics (at first they increased and later decreased, became depressed and inversed).

In fractional administration of urethane (especially after the preliminary inhalation of ether) the period of normalization of the reflexes was noted. By this urethane differs from other anesthetics.

Is is assumed that the depressing effect of the anesthetic on the interoceptive reflexes (especially in the administration of chloral hydrate and sodium amytal) plays the main role in the mechanism of sleep therapy in clinical conditions.

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* In Russian.

** Original Russian pagination. See C. B. Translation.