

ON THE SELECTIVE EFFECT OF SOME CHEMICAL IRRITANTS
ON REFLEXES FROM CHEMORECEPTORS
COMMUNICATION 5. EFFECT OF SUBARACHNOID INJECTION OF STREPTOMYCIN ON REFLEXES
FROM CHEMORECEPTORS, MECHANORECEPTORS, AND AN AFFERENT SOMATIC NERVE

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Streptomycin, when injected intramuscularly or intravenously, exhibits a profound depressing effect on reflexes from the chemocenters of the small intestine, kidneys, spleen, and carotid sinus, as was established by us previously [2, 5, 6]. In contradistinction to this, the antibiotic, under the same experimental conditions, does not exhibit such an effect, or produces it to a much lower degree, if unconditioned reflexes arising from mechanical stimulation of the bladder, stomach, small intestine, or the central portion of the tibial nerves are considered. The above-mentioned property of streptomycin appears in experiments in which blood pressure and respiration serve as the indicator, as well as in experiments in which the leukocyte picture of the peripheral blood serves as the indicator. These observations led us to the conclusion that streptomycin exhibits a selective effect on the reflexes on the chemoreceptors by way of a direct influence of the central portions of the afferent part of the reflex arc. Taking account of the fact that the antibiotic, injected intramuscularly or even intravenously, penetrates to the brain in insignificant amounts [1, 4, 7, 8], it was necessary to assume a high sensitivity of the corresponding parts of the central nervous system to streptomycin directly. We believe that this assumption can be checked to a certain extent by experiments in which streptomycin is introduced into the submeningeal space of the brain. If following such a mode of administration the antibiotic exhibited its characteristic influence on the interoceptor reflexes, rapidly and in moderate doses, then the assumption that it acts on the central part of the reflex arc would receive additional confirmation.

METHODS

We carried out the experiments in cats anesthetized with urethane. We recorded the respiration and the blood pressure in the carotid artery. We made a record of the reflexes on smoked kymograph paper.

The chemoreceptors of the carotid sinus were stimulated by the intravenous injection of 0.15-0.2 ml of 0.15% cytone.* We produced the reflexes of the chemoreceptors of the intestine by the method of V. N. Chernigovsky. We produced the reflexes of the chemoreceptors and mechanoreceptors of the pericardium by the method of C. K. Drinker [8].

We injected streptomycin (the calcium chloride complex) into the subarachnoid space. By the method described by V. S. Galkin [3], with the aid of a special needle, we made a puncture in the atlanto-occipital membrane. Then with a syringe we removed fluid and injected the corresponding volume (1-2.5 ml) containing various doses of streptomycin.

* Transliterated. Probably a Russian trade name.

RESULTS

In the first series of experiments the influence of subarachnoid injection of streptomycin on the reflexes from the chemoreceptors of the carotid sinus was studied.

First of all it was established that the reaction of the animals to subarachnoid injection of streptomycin depends both on the concentration of the preparation injected and on the dose. Following injection of the antibiotic in a concentration of 40,000 units per ml and higher, there generally ensued cessation of breathing and a considerable lowering of blood pressure. In a series of experiments the animals succumbed. This impelled us to employ streptomycin in a concentration of 25,000 units in 1 ml physiological saline. Doses of streptomycin up to 50,000 units with moderate concentrations of the antibiotic in the injected fluid as a rule were well tolerated by the animals. There was observed merely a slowing of respiration and diminution of the respiratory motions. Doses exceeding 50,000 units led in some cases to an alteration of the respiratory rhythm and in some to cessation. The blood pressure also declined. However it should be noted that in separate experiments animals tolerated doses of streptomycin greater than 55,000 units.

In control experiments on the influence of the injection of saline alone into the subarachnoid space the reflex to cytotoxine did not change, rarely became somewhat, though negligibly, weaker.

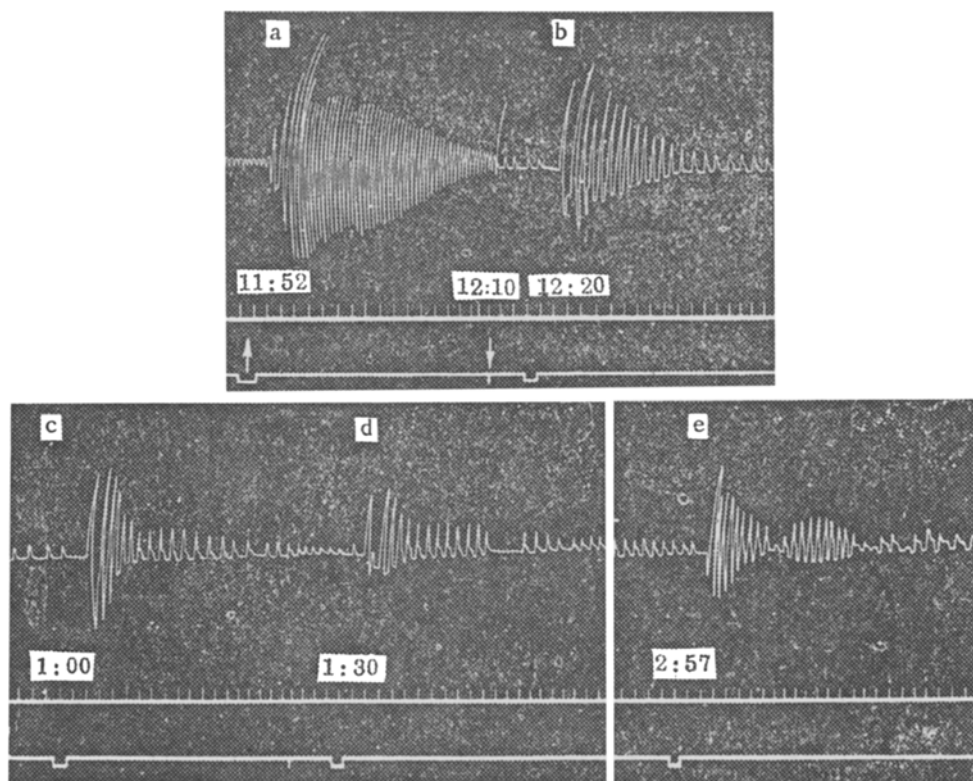


Fig. 1. Effect of subarachnoid injection of streptomycin on the respiratory reflex produced by cytotoxine. a) reflex to cytotoxine before the injection of streptomycin, b, c, d, e) reflex to cytotoxine after injection of 52 thousand units of streptomycin. Experiment No. 275, January 22, 1955. Cat weighing 2.8 kg. Significance of curves (from top to bottom); respiration, time signals (5 seconds), records of stimuli:

↑ - reflex before injection; ↓ - reflex after injection.

Under the influence of subarachnoid injection of streptomycin (30-40-50-60,000 units) the initial reflex from the chemoreceptors of the carotid sinus produced by cytotoxine was sharply depressed in 9 out of 10 experiments. Only in one experiment was this effect negligible.

Even at the first check of the reflex to cytotoxone, which in the majority of experiments was carried out 7-10 minutes after the subarachnoid injection of streptomycin, there was evident a distinct depression of the respiratory reaction. This was expressed as a considerable diminution of the increase in amplitude and frequency of the respiratory motions and also a considerable shortening of the time of the respiratory reaction (Fig. 1).

In separate experiments the reflex to cytotoxone was tested 3-4 minutes after the injection of streptomycin. Even in these cases there was a marked depression of the respiratory reflex.

About 20-25 minutes after the subarachnoid injection of the antibiotic the depression of the respiratory reaction to cytotoxone in most of the cases reached its maximum. In experiments the maximum depressive effect of the streptomycin appeared a little later, 30-40 minutes after the injection of the preparation.

A distinct depression of the reflex to cytotoxone generally lasted the whole period of observation, i.e., 1 1/2-3 hours.

In 13 experiments of a second series we investigated the influence of streptomycin on the reflexes arising from stimulation of the chemoreceptors of a perfused intestinal loop. The calcium chloride complex of streptomycin was injected into the subarachnoid space in a dose of 17.5-36,000 units per animal in 1-1 1/2 ml of saline. Before and after injection of the antibiotic we established the magnitude of the reflexes from the chemoreceptors of the small intestine to CO₂, acetylcholine, and nicotine.

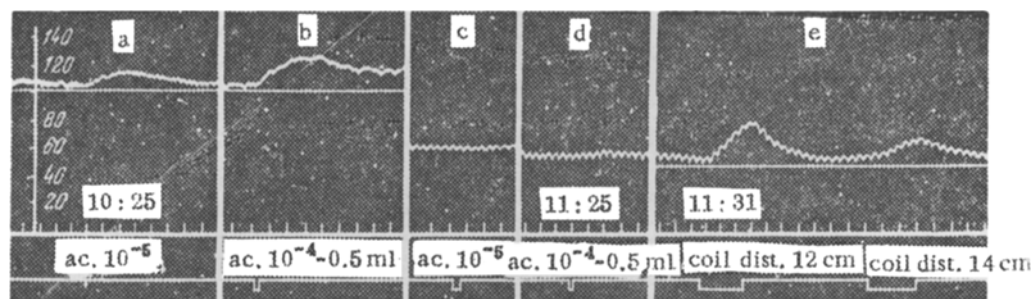


Fig. 2. Effect of subarachnoid injection of streptomycin on reflexes of chemoreceptors of small intestine. a,b) original reflex; c,d) under the influence of streptomycin (injected into the subarachnoid space at 10:33 in dose of 30 thousand units) the reflexes disappeared; e) under these conditions the excitability of the tibial nerve remains high (threshold reflex produced in control experiments with an induction coil distance of 14-17 cm) Experiment No. 337 on March 1, 1955. Cat weighing 3.4 kg. Meaning of curves (from top to bottom): Blood pressure, time signals (5 seconds), records of stimuli.

Under the influence of the injection of streptomycin into the subarachnoid space of the brain the reflexes from the chemoreceptors in the greatest portion of cases disappear completely or are decreased more than 60% (Fig. 2).

In 4 experiments there ensued complete suppression of all reflexes arising from stimulation of the chemoreceptors of perfused intestine. A marked effect developed 3-5-13 minutes after injection of the antibiotic and remained steady for 1 1/2-2 hours of observation. It is important to note that the depression of the reflexes from the chemoreceptors was not caused by a paralyzing effect of the antibiotic on the vasomotor center. This latter is confirmed by experiments in which it was established that in the presence of complete depression of the reflexes from the chemoreceptors of the small intestine the excitability of the vasomotor center to impulses arising from the stimulation by electric current of the tibial nerve remained sufficiently high (Fig. 2). In the remaining cases streptomycin produced a not completely equal depression of the reflexes from the chemoreceptors when given various stimuli.

In 8 experiments the effect of the antibiotic on reflexes produced by acetylcholine in various concentrations was observed. In 4 experiments the effect of streptomycin on reflexes produced by acetylcholine in dilutions of 10^{-5} and 10^{-6} was studied. Out of these the reflexes disappeared in three, and in one was decreased by 50%. In 4 cases acetylcholine was employed in a dilution of 10^{-4} ; in two of these the reflex was completely suppressed, in one case decreased by 75% in one 22%. Acetylcholine in a dilution of 10^{-3} was employed in 6 experiments. In one of these the reflex disappeared, in three it decreased by 60-66% in two by 39 and 20%.

In 5 experiments the reflexes from the chemoreceptors were produced by nicotine (10^{-6} and 10^{-5}). Under the influence of streptomycin in one case the reflex disappeared completely, in the others it decreased by 54-66-72-88%.

The reflex to CO_2 , tested in 2 experiments, also decreased: in one by 84% in the other by 66%.

Thus, in spite of the unequal stability of different reflexes in different experiments, in all observations without exception subarachnoid injection of streptomycin produced pronounced depression of the reflexes from

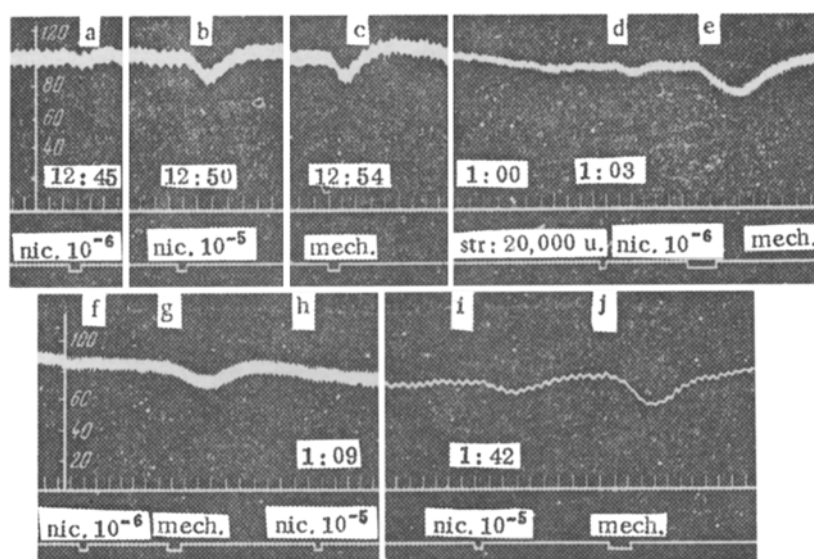


Fig. 3. Effect of subarachnoid injection of streptomycin on reflexes from chemoreceptors and mechanocenters of the pericardium. a,b,c) original reflexes; d,e,f,g) profound depression and subsequent partial recovery of reflexes from chemoreceptors after subarachnoid injection of streptomycin (20 thousand units at 1:00); h,i,j) at this time the reflex from the mechanocenters almost undiminished in magnitude. Experiment No. 409 on July 13, 1955. Cat weighting 3.8 kg. Meaning of curves as in Fig. 2.

the chemoreceptors. This effect, as in the first group of observations, developed quickly, in the course of the first 5-10-15 minutes, barely 20-30 minutes after injection of the streptomycin into the subarachnoid space. On prolonged observation of the reflexes referred to, a marked stability of the depressive effect of the antibiotic on the reflexes from the chemoreceptors was noted when the preparation was injected into the subarachnoid space.

In the third and last series of experiments we studied the effect of subarachnoid injection of streptomycin on the reflexes from the chemo- and mechanocenters of the pericardium. We injected streptomycin in the same dose as in the previous experiments. It was established that subarachnoid injection of streptomycin produces profound depression of the reflexes from the chemoreceptors of the pericardium, which sets in soon after the injection of the antibiotic. In contrast to this the reflexes from the mechanocenters of the pericardium, in

our observations, did not change or decreased negligibly, which is clearly visible on the kymogram, presented in Fig. 3.

Thus in all three series of experiments it was demonstrated that on injection of streptomycin into the subarachnoid space of the brain, blocking of the reflexes from the chemocenters of various reflexogenic zones ensues. It results from the employment of moderate doses of the antibiotic and maintains itself very constant. The depressive action of streptomycin on the reflexes from the chemoreceptors was not accompanied by significant alteration in the reactivity of the vasomotor center to the reflex influence from the mechanoreceptors and a peripheral afferent somatic nerve.

These conclusions, following from our observations, allow one to conclude that streptomycin, when introduced into the central nervous system, exhibits a direct blocking action on the central portion of the afferent part of the reflex arc, beginning with the tissue chemoreceptors. Therefore the above mentioned assumption as to the point of action of streptomycin on the interoceptor reflex arc receives additional confirmation.

SUMMARY

Data are reported on the effect of subarachnoid injection of streptomycin on reflexes from the chemoreceptors of the carotid sinus, small intestine, and pericardium. Anesthetized cats were used in the experiments. Reflexes from the zones mentioned to chemical stimuli were profoundly depressed by streptomycin. Reflexes from mechanoreceptors, on the contrary, were almost unchanged. The excitability of the vasomotor center, when the tibial nerve was stimulated, remained quite high. It is concluded that streptomycin blocks directly the central portions of the afferent part of the chemoreceptor reflex arc.

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* In Russian.

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