THE EFFECT OF DISTURBANCES IN ACETYLCHOLINE AND SYMPATHIN SYNTHESIS ON THE REGULATION OF URETERAL MOTOR ACTIVITY

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The results of the few works that have been devoted to the role of the chemical mediators – acetylcholine and adrenalin – in the mechanism for neural regulation of ureteral motor function are rather contradictory. There are data [2, 18, 20, 22] indicating that acetylcholine intensifies the peristaltic contractions of the ureters, while, on the contrary, a number of investigators have observed hypotonia of the ureters under the influence of this agent [22], or a dual, indeterminate effect [19, 21]. According to the investigations of several authors [22, 23, 24], adrenalin intensifies the motor activity of the ureters. Yet there is also evidence that adrenalin exerts an inhibitory influence on the peristaltic activity of the ureters, both when they are isolated and in the intact organism [2, 18].

In previous investigations [11], we showed that participation of the chemical mediators (adrenalin and acetylcholine) in the mechanism for the reciprocal reactions of the ureters, associated with stimulation of the peripheral end of the splanchnic nerve, in the form of inhibition of the motor activity in the ureter on the side of the stimulation, and intensification on the contralateral side. In this case, the blood coursing from the renal vein on the side of the stimulation showed an increased concentration of adrenalin (sympathin), while on the opposite side there was a marked rise in the concentration of acetylcholine, as compared with the level of these agents in the blood before stimulation of the splanchnic nerve.

In this report, we decided to approach elucidation of the role played by the indicated chemical agents in the mechanism for regulation of ureteral motor activity, and in particular, in accomplishing the reciprocal reaction, by means of an artificial disturbance in their synthesis within the organism. For a temporary disturbance in the process of acetylcholine formation, we used the method of extirpating a portion of the pancreas [5, 4, 7, 9], while for a disturbance in the synthesis of sympathin, we cauterized the medullary layer of the adrenals [3, 9].

EXPERIMENTAL METHOD

The experiments were carried out on dogs, we performed graphic recording of the ureteral contractions in short-term experiment conditions, using the method of Kharitonov [17], which employs an apparatus constructed like an oncometer. In order to stimulate the peripheral end of the splanchnic nerve under the diaphragm, we used an induction current from a Zimmerman sliding coil, fed by a storage battery with a force of 2.5 volts; stimulation was accomplished with a distance of the inductor coils 20-30 mm greater than the stimulation threshold. In order to stimulate the posterior spinal radicles, we performed a laminectomy in the area of T 10-13 and L 1. The peripheral end of the isolated and transected posterior radicals at the level T 11– L 1 was connected with immersion electrodes, and subjected to stimulation with the induction current under the same conditions. Some of the observations were carried out on intact animals (control), and the others – on dogs that were first subjected to partial depancreatization or cauterization of the medullary layer of the adrenals. In the depancreatized animals (60 experiments), observations were performed from the 3rd to the 16th day after the operation. In the dogs that underwent cauterization of chromaffin tissue in the adrenals (56 experiments), observations were made from the 3rd to the 20th day after the operation. Some of the operated animals (27 experiments) received a daily, compensatory [1, 3, 7, 9] injection, into the femoral vein, of 1–1.5 ml of acetylcholine (in a concentration of 1 : 100,000) or 1–1.5 ml of adrenalin (in a concentration of 1 : 1000). The acetylcholine or adrenalin were not given to the dogs on the day the experiments were set up.

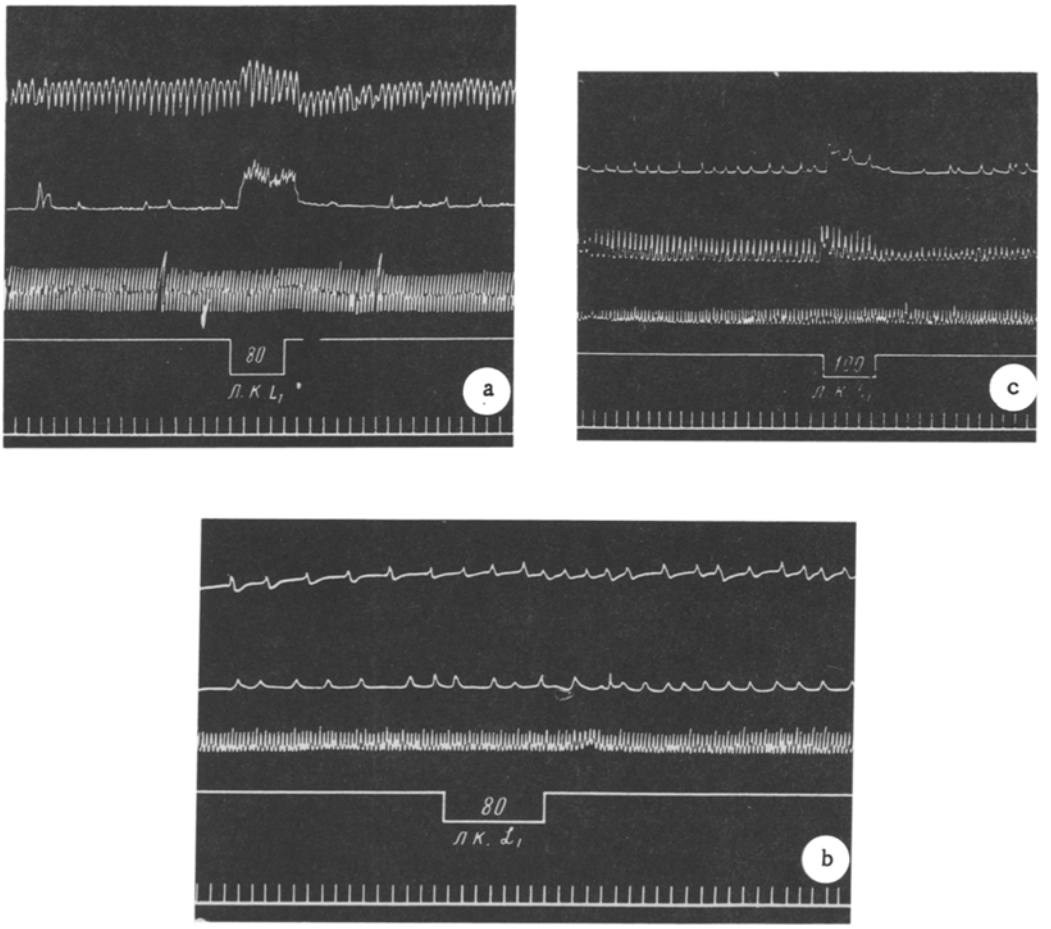

Fig. 1. The effect of stimulating the posterior spinal radicle at the level of L 1, left side, on the motor activity of both ureters. a) In an unoperated dog; b) in a partially depancreatized dog, on the 5th day after removal of a portion of the gland; c) in a dog at the same interval after the above operation plus intravenous injection of acetylcholine. Meaning of the curves (top to bottom), here and in the other figures: contractions of the right ureter, contractions of the left ureter, respiration, stimulation marks, time markings (5 seconds).

Our most recent investigations showed that removal of a portion of the pancreas also substantially alters the character of the effect exerted by the splanchnic nerve on the peristaltic activity of both ureters.

On the 3rd-4th day after the operation, stimulation of the peripheral end of the splanchnic nerve, as in the case of the unoperated animals (Fig. 2a), caused inhibition of the motor activity in the ureter on the side of stimulation, and intensification of peristalsis in the contralateral ureter. Earlier [11], we showed that such reciprocal reaction is connected with excitation of the posterior radical fibers that are included in the composition of the splanchnic nerve; these fibers also cross over to the contralateral side, where they exert a dominant effect. This corresponds to the morphological data on the crossed innervation of the ureters, both by the posterior radicles and sympathetic nerve fibers [12, 14]. In this case, on the same side as the stimulation we observed an inhibitory influence from the nerve fibers of sympathetic origin.

On the 5th-7th day after the operation, stimulation of the splanchnic nerve no longer caused intensification of the motor activity in the contralteral ureter, but, on the contrary, depressed its contraction and, as before, exerted an inhibitory action on the motor activity of the ureter on the same side as the stimulation, up to complete disappearance of the peristaltic waves (Fig. 2b). The inhibitory influence of the splanchnic nerve on the motor activity of both ureters was quite clearly demonstrated, and was accompanied by prolonged sequelae (decrease in the muscle tonus of the ureter, depression of the peristaltic contractions). Thus, at certain intervals after the operation, the

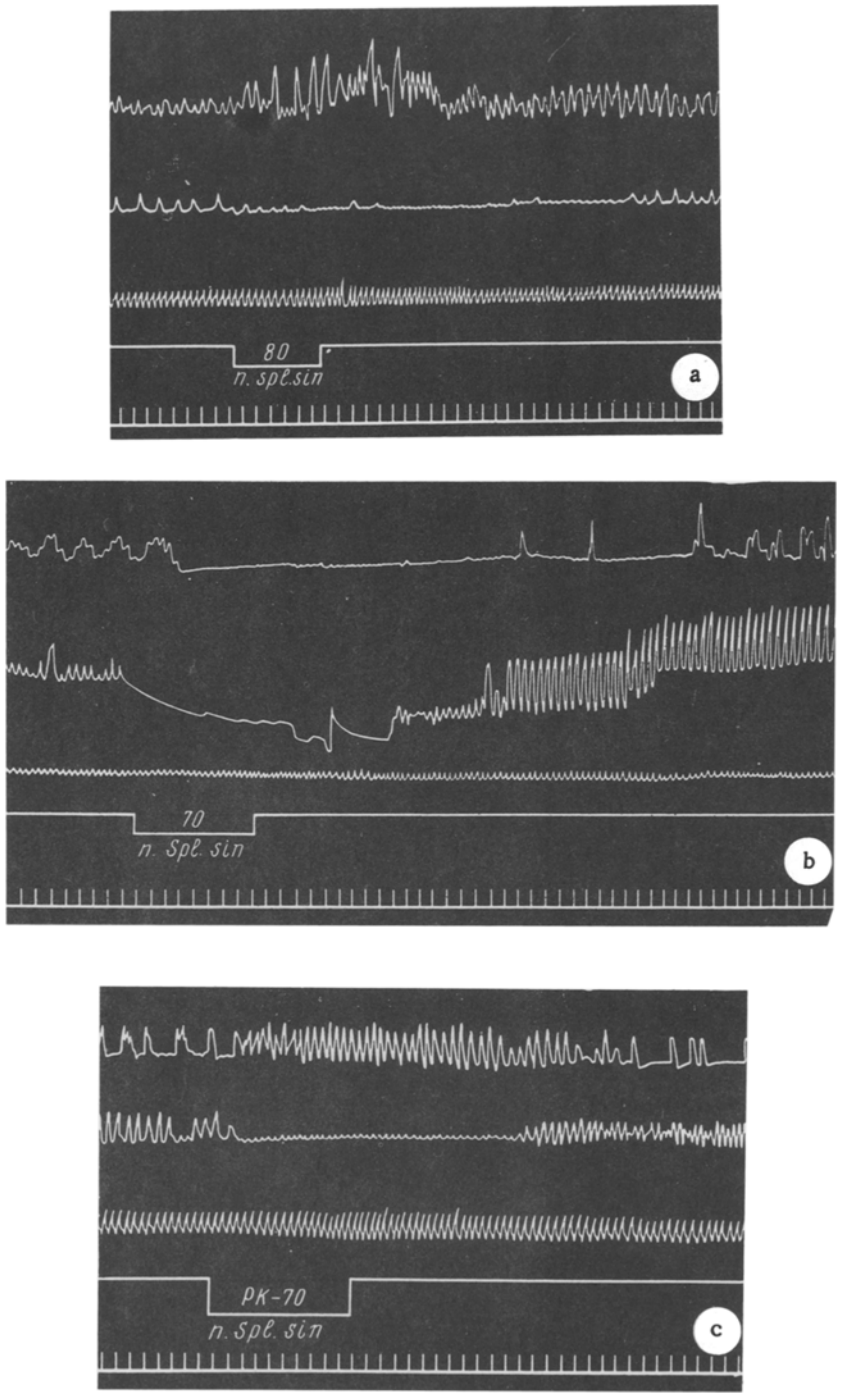

Fig. 2. The effect of stimulating the peripheral end of the left splanchnic nerve on the motor activity of both ureters. a) In an unoperated dog; b) in a dog on the 5th day after partial depancreatization; c) in a dog on the same day after the operation, but that received injections of acetylcholine.

reciprocal reaction of the ureters associated with stimulation of the splanchnic nerve disappeared in the depancreatized animals. At later intervals, the normal reaction of the ureters to stimulation of the splanchnic nerve was restored.

In the animals that received acetylcholine in the postoperative period, on the 5th-7th day after depancreatization, as in the control, stimulation of the peripheral end of the nerve, in the majority of cases, caused inhibition of

the tonus and peristaltic activity of the ureter on the side of the stimulation. On the opposite sidefrom the stimulated nerve, as in the normal animals, the motor activity of the ureter was intensified: the amplitude of the peristaltic waves increased or the rhythm of the contractions accelerated (Fig. 2c).

Thus, with disturbance of acetylcholine synthesis under conditions of partial depancreatization, the stimulatory action of the posterior radicle fibers on the motor activity of the ureters, when the fibers are excited by stimulation of the peripheral end of the splanchnic nerve, is either weakened or completely lost. Under these conditions, the sympathetic fibers exert an inhibitory influence which is stronger, not only on the motor activity of the ureter on the side of the stimulation, but also on the contralateral ureter, while under normal conditions the stimulatory action of the posterior radicle fibers predominated. Injection of the operated animals with acetylcholine normalized the functioning of the posterior radicle sensory fibers, and hence, restored the normal reciprocal reaction of both ureters following stimulation of the peripheral end of the splanchnic nerve on one side.

In the animals that underwent cauterization of the medullary layer in their adrenals, we also observed a certain weakening in the automatic activity of the ureters. On the 3rd-4th day after this operation, stimulation of the peripheral end of the splanchnic nerve, as in the normal animal, caused depression of the peristalsis in the ureter on the side of stimulation, and intensification of this activity on the opposite side. On the 5th-10th day after the operation, the inhibitory effect on the side of the stimulation completely dropped out; sometimes, we even observed a motor reaction in the form of an increase in the frequency of the peristaltic contractions. On the opposite side, the stimulatory effect was constantly retained, which was manifested in some of the experiments by an increase in tonus, in others by an increase in the frequency of the peristaltic contractions, and in still others by a heightening of the strength of the contractions (Fig. 3). Beginning with the 11th day after the operation, the inhibitory influence of the splanchnic nerve on the motor activity of the ureter on the same side was gradually restored. These changes could be prevented to a significant degree by the daily injection of the operated animals with adrenalin. Thus, the inhibitory influence of the splanchnic nerves on the motor activity of the ureter on the side of stimulation is caused by the activity of sympathetic nerve fibers, whose activity is linked with participation of their chemical mediator-sympathin. Disruption of the synthesis of the latter weakens the inhibitory influence of the splanchnic nerve on the ureter of the same side, down to its complete disappearance, with retention of the stimulatory action on the contralateral ureter, due to the posterior radicle fibers that enter into that nerve's composition.

The performed investigations confirm our previous conclusion [11] that the splanchnic nerves exert an inhibitory effect on the motor activity of the ureter on the same side, due to the activity of the sympathetic nerve fibers, and a stimulatory action on the contralateral ureter, through involvement in the reaction of the posterior radicle fibers that enter into the composition of the nerves. Apparently, the latter is accomplished in the intact organism according to the axon-reflex type [6, 10, 15].

The inhibitory action of the sympathetic nerve fibers on the contractile activity of the ureters is linked with the participation of their mediator-sympathin, while the stimulatory action of the posterior radicle fibers is accomplished through the participation of acetylcholine.

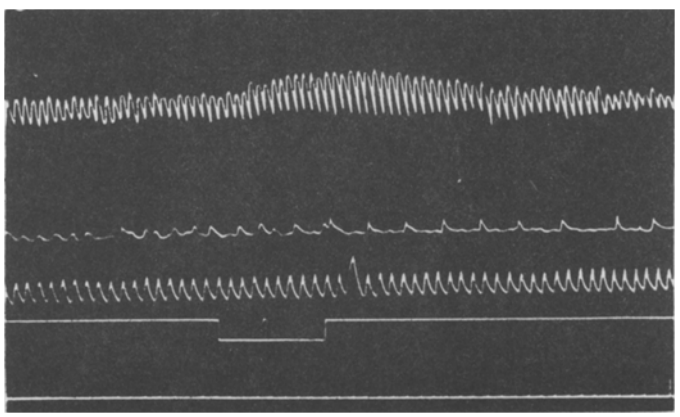

Fig. 3. The effect of stimulating the peripheral end of the left splanchnic nerve on the motor activity of both ureters, on the 9th day after cauterization of the chromaffin tissue of the adrenal glands.

Participation of acetylcholine in the mechanism of action of the posterior radicle fibers is also corroborated by data in the literature [1, 8, 13, 16]. Disruption of the synthesis of these mediators, particularly in hormonal insufficiency of the pancreas – a deficit in the hormone lipocain [4, 5] and disturbances in the adrenalin-secreting functioning of the adrenals, leads to essential changes in the neural regulation of ureteral motor activity.

SUMMARY

The splanchnic nerves exert an inhibitory effect on the motor activity of the ureter on the side stimulated, due to the activity of sympathetic fibers, and also produce a stimulatory effect on the contralateral ureter, through involvement in the reaction of the posterior radicle fibers that enter into the composition of the nerve. The inhibitory effect is produced with the participation of sympathin, and the stimulatory one – with acetylcholine. Disturbances in the chemical synthesis of these mediators, under conditions of partial depancreatization or cauterization of the medullary layer of the adrenal glands, leads to marked disturbance in the neural regulation of ureteral motor activity.

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