EFFECT OF CENTRAL CHOLINOLYTICS ON LATENT PERIOD OF THE FLEXOR REFLEX AND CORTICAL MOTOR RESPONSE IN RABBITS

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The central muscarine-like cholinolytics amizil and metamizil increased the latent period of the flexor reflex in doses ten times smaller than those of central nicotine-like cholinolytics. Central cholinolytics were ineffective on spinal animals. Interoceptive inhibition from the stomach was strengthened by central cholinolytics. Central cholinolytics had no effect on the latent period of the cortical motor response.

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In this investigation the effect of central cholinolytics was studied on the flexor reflex and the cortical motor response.

EXPERIMENTAL METHOD

Experiments were carried out on 54 rabbits. The latent period of the flexor reflex and cortical motor response was determined by V. V. Zakusov's method [2, 3]. The plantar skin of the rabbit's hind limb and the motor cortex were stimulated with square pulses of threshold intensity from an electronic stimulator.

To analyze the mechanism of action of central cholinolytics on the flexor reflex and cortical motor response experiments were performed on rabbits and interoceptive stimuli applied from the stomach (inflation of a rubber balloon introduced through a fistula to a pressure of 40-50 mm Hg for 20-30 sec) and on animals with the spinal cord transected at the level of the 12th thoracic vertebra. The experiments were resumed 5-6 days after formation of the gastric fistula and also after division of the spinal cord. The central cholinolytics amizil (benactyzine) metamizil (methyldiazine), arpenal* , and spasmolytin (adiphenine hydrochloride) were used in the experiments in a dose of 0.1-10 mg/kg. The drugs were injected intravenously.

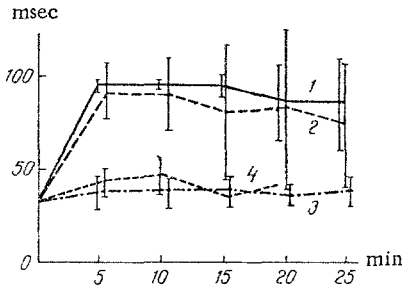

Fig. 1. Effect of central cholinolytics (1 mg/kg) on latent period of flexor reflex. 1) Amizil; 2) metamizil; 3) spasmolytin; 4) arpenal. Here and in Fig. 2, ordinate: duration of latent period of flexor reflex (in msec), abscissa: time (in min).

EXPERIMENTAL RESULTS AND DISCUSSION

The latent period of the flexor reflex of the hind limb of intact rabbits averages 39±1.6 msec. After injection of amizil in a dose of 0.1 mg/kg, an inconstant and transient increase in the latent period of the flexor reflex was observed. The central muscarine-like cholinolytics amizil and metamizil, in doses of 1 and 2 mg/kg, more than doubled the latent period of the flexor reflex. The effect of these two preparations continued for 20-40 min.

Spasmolytin and arpenal, central cholinolytics blocking predominantly nicotine-like cholinergic systems, in a dose of 1 mg/kg did not change the time of the flexor reflex (Fig. 1). Only in large doses did the nicotine-like cholinolytics lengthen the latent period of the flexor reflex. However, even after injection of spasmolytin and arpenal in a dose of 5 mg/kg, the increase in latent period of the flexor

* N-(3-diethylaminopropyl)-2, 2-diphenylacetamide.

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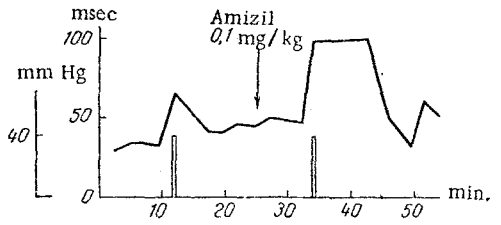

Fig. 2. Effect of amizil (0.1 mg/kg) on interoceptive inhibition of the flexor reflex. Height of columns corresponds to pressure inside stomach. Arrow denotes moment of injection of amizil.

reflex was observed inconstantly. Only in a dose of 10 mg/kg did spasmolytin produce a considerable increase in the time of the flexor reflex for a period of 10-15 min.

The central cholinolytics amizil and metamizil were ten times more effective (in comparable doses) than the central nicotine-like cholinolytics spasmolytin and arpenal. The action of the muscarine-like cholinolytics continued longer. The effect of spasmolytin and arpenal is evidently due to blocking of the muscarine-like, rather than of the nicotine-like cholinergic systems of the brain. This is confirmed by comparing the effective doses of amizil (1 mg/kg) and spasmolytin (10 mg/kg), a value of the same order as the result of comparative assessment of the muscarine-like cholinolytic activity of the central cholinolytics [1]. The purpose of the next experiments was to discover the point of application of the action of these drugs, or in other words, to determine the localization of cholinergic systems in the central nervous system. Chronic experiments were performed on rabbits with transection of the spinal cord at the level of the 12th thoracic vertebra. Under these conditions neither amizil (1 mg/kg) nor spasmolytin (5 mg/kg) altered the latent period of the flexor reflex. No clear decrease in tone or characteristic motor response of the hind limbs was observed after injection of the central cholinolytics, as was constantly observed in intact rabbits. Consequently, the muscarine-like cholinergic structures responsible for inhibition of the flexor reflex are located above the site of transection.

To determine the effects of the central cholinolytics on descending influences, experiments with interoceptive inhibition were carried out. Interoceptive stimulation is known to inhibit the reflex activity of the spinal cord.

In control experiments with interoceptive inhibition it was found that distension of the stomach of the intact rabbit led in 65 of 106 cases to an increase in the latent period of the flexor reflex. After injection of the central cholinolytics amizil (0.1 mg/kg) and spasmolytin (5 mg/kg) into rabbits, interoceptive inhibition of the flexor reflex was observed in all 14 experiments (Fig. 2). This observation demonstrates an increase in interoceptive inhibition by central cholinolytics. The inhibition under these circumstances becomes sustained in character.

When the stomach was distended in rabbits with a transected spinal cord the latent period of the flexor reflex was unchanged. Assuming that an increase in interoceptive inhibition would take place following administration of the cholinolytics, as in intact animals, amizil and spasmolytin were injected in similar experiments on spinal animals. However, distension of the stomach in rabbits with a transected spinal cord, against a background of the action of amizil (1 mg/kg) or spasmolytin (5 mg/kg) did not alter the latent period of the flexor reflex.

Contraction of the flexors of the hind limb, the effectors of the flexor reflex arc, may be obtained by stimulation of the corresponding points of the motor cortex. The mean latent period of the cortical motor response in our experiments was 39.5 ± 2.4 msec. Amizil, in doses of 1 and 3 mg/kg, and spasmolytin in doses of 5, 10, and 30 mg/kg, did not change the time of the cortical motor response.

Distension of the stomach did not change the latent period of the cortical motor response. No change likewise was observed in the latent period of the cortical motor response after distension of the stomach against the background of the action of amizil (1 mg/kg) or spasmolytin (5 mg/kg). This result may probably be explained by the low sensitivity of the structures of the central nervous system controlling the course of the cortical motor response to central cholinolytics.

It may be concluded from the results of these experiments that muscarine-sensitive cholinergic systmes are mainly responsible for the transmission of descending influences to the segmental apparatus of the spinal cord, because mainly the central muscarine-like cholinolytics (amizil and metamizil) have an inhibitory influence on the flexor polysynaptic reflex.

LITERATURE CITED

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