THE EFFECT OF STIMULANTS AND DEPRESSANTS ON THE ACTIVITY OF SOLITARY NEURONS IN THE SPINAL CORD ASSOCIATED WITH STIMULATION OF THE CEREBELLUM

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The method of intracellular conduction of potentials from motor and internuntial neurons was used to study the effect of various neurotropic agents on the activity of spinal neurons, which were stimulated or depressed in association with stimulation of the anterior lobe of the cerebellum. We investigated compounds which stimulate neural activity(corasol, caffeine), and substances with an inhibitory type of action – narcotics (nembutal, hexenal, urethane) and the analgesic, promedol. Data characterizing the features of facilitation and inhibition in the motor and internuntial neurons subsequent to stimulation of the cerebellum were described earlier.

EXPERIMENTAL METHOD

The experiments were set up on cats, immobilized by relaxants. Potentials of the subject neurons were conducted off with the aid of intracellular microelectrodes of the usual type. We recorded the responses that arose in the motor and internuntial neurons of the seventh thoracic and first lumbar segments in the spinal cord during rhythmic stimulation of the anterior lobe of the cerebellum, and also of the posterior and anterior radicles. A similar experimental method was described earlier [3, 4]. The pharmacological materials under investigation were injected intravenously. The effect which they caused was judged from the change in the activity of the same cell which was under observation prior to injection of the preparation. A total of more than 60 units were studied. Some of the experiments (12 cells), in which we investigated the action of narcotics, were carried out on animals that were first injected with subconvulsive doses of strychnine.

EXPERIMENTAL RESULTS

Corasol and caffeine. Neural stimulants showed a distinct ability to intensify the facilitating influence of the cerebellum on the motor cells of the anterior horns. This effect was observed with injection of corasol in doses of 5-10 mg/kg, and was less clear with injection of caffeine in doses of 10-15 mg/kg.

Under the influence of corasol, there was an increase in the amplitude of the excitatory postsynaptic potentials (EPSP), caused by the cerebellar stimuli, and a shortening of the latent period for their arisal. The capacity of the cells to respond to rhythmic stimulation of the cerebellum rose sharply. While before the injection of corasol the motor neurons discharged with a constant rhythm that did not exceed 5-10 per sec, after injection of the preparation the frequency of the discharge rhythm reached 50-60 per sec. There was also an increase in the responses to tetanic stimulation of the cerebellum, using high frequency stimuli (300 per sec).

It is important to note that the described action of corasol appeared after its injection in doses which did not essentially change the responses of the motor neurons to afferent impulses [4].

Examples, illustrating the effect of corasol on the activity of the lumbar motor neurons during stimulation of the cerebellum and afferent pathways, are shown in Fig. 1. In Fig. 1 A, the motor neuron did not respond to cerebellar stimulation, but the cerebellum showed a marked facilitating action on the response of the cell arising from stimulation of the posterior radicle. After injection of corasol, the effect of cerebellar stimulation increased markedly. There was also an increase in the facilitating action of the cerebellum in the presence of afferent stimulation.

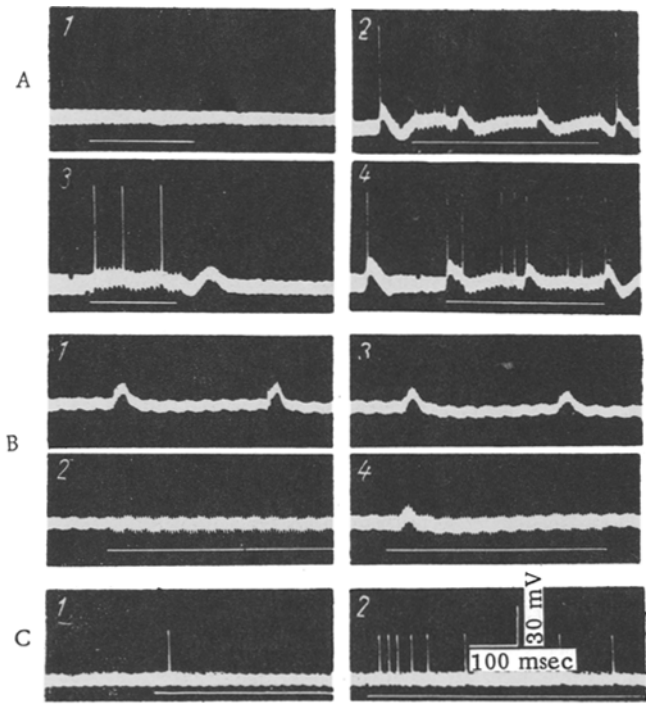

Fig. 1. The effect of corasol (A and B) and caffeine (C) on the activity of motor and internuntial neurons. A) Responses of a motor neuron to stimulation of the cerebellum (1) and the posterior radicles and cerebellum (2), before (3) and 3 min after (4) the injection of corasol in a dose of 10 mg/kg; B) polysynaptic EPSP of the motor neuron during stimulation of the posterior radicle before (1) and 4 min after (3) the injection of corasol in a dose of 7 mg/kg. Responses of the same cell to stimulation of the cerebellum before (2) and after (4) the injection of corasol; C) responses of an internuntial neuron to cerebellar stimulation before (1) and 3 min after (2) the injection of caffeine in a dose of 8 mg/kg. In all frames, stimulation of the cerebellum is noted by a horizontal mark.

At the same time, responses to stimuli applied to the posterior radicles remained practically unchanged. It is apparent from Fig. 1 B that corasol did not affect the amplitude and duration of the motor neuron's EPSP during stimulation of the afferent pathways, but caused the appearance of previously unobserved EPSP during cerebellar stimulation. Corasol also markedly heightened the activation of the internuntials subsequent to cerebellar stimulation, as manifested by an increase in the frequency and duration of the discharges. Analogous effects were observed for the action of caffeine (Fig. 1 C).

In contrast to the stimulatory influences, the inhibitory effects of the cerebellum remained unchanged (in 3 of the 4 experiments), or were even intensified (in 1 experiment). These observations coincide with the data on the capacity of corasol to increase the inhibitory postsynaptic potentials (IPSP) of the spinal cord motor neurons during stimulation of the segment pathways [4].

Hexenal, nembutal, and urethan. Even in small doses, the carcotic substances markedly depressed the excitatory influences from the cerebellum on the spinal cord motor neurons. This was predominantly manifested by a decrease in the responses to the second and subsequent stimuli of a rhythmic series. This action was noted with the use of slow stimulation rhythms (2-5 per sec), under the influence of quite small doses of the narcotic preparations (1-2 mg/kg for hexenal, 2-5 mg/kg for nembutal, and 50-70 mg/kg for urethan). When the doses of the narcotics were increased by 2-3 times, we observed a lowering of the EPSP and blockade of the arisal of action potentials, even at the very beginning of cerebellar stimulation. At the same time, there also began to appear signs of depression of the motor neuron responses to afferent stimuli. However, in the latter case the depression was chiefly exerted on the polysynaptic components of the afferent responses (Fig. 2 A). The different degree of urethan's influence on the responses of the motor neurons during supraspinal and afferent activation is also shown in Fig. 2 B.

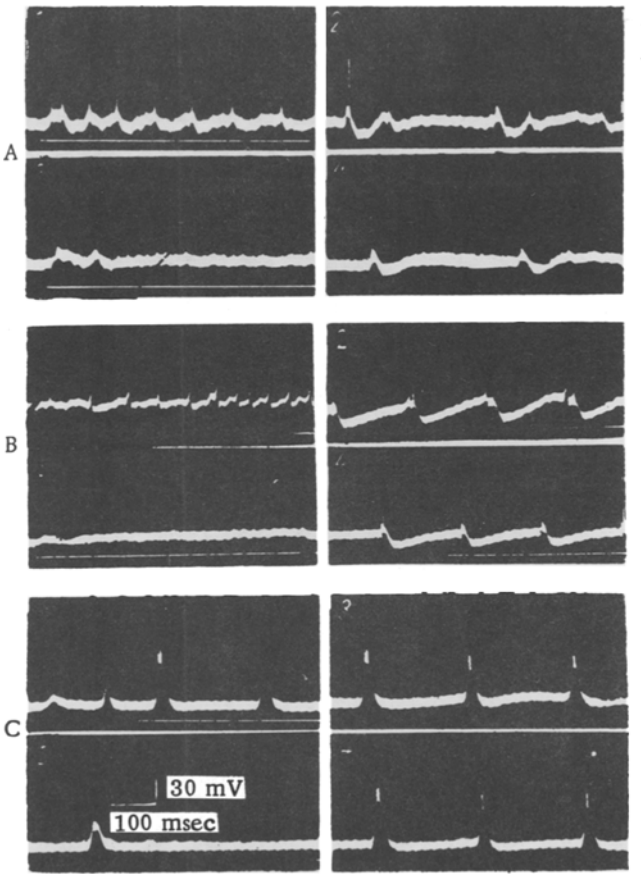

Fig. 2. The effect of urethan (A and B) and hexenal (C) on the activity of the motor neurons. A) Responses of the cell to stimulation of the cerebellum (1) and the posterior radicle (2), before (3) and 5 min after (4) the injection of urethan in a dose of 150 mg/kg; B) responses of the cell to stimulation of the cerebellum (1) and the posterior radicle together with the cerebellum (2), before (3) and 3 min after (4) the injection of urethan in a dose of 120 mg/kg; C) responses of a motor neuron in a strychninized animal to stimulation of the cerebellum (1) and the posterior radicle (3), before (2) and 2 min after (4) the injection of hexenal in a dose of 2 mg/kg. Stimulation of the cerebellum is denoted by a horizontal mark.

As was already noted earlier, under the influence of strychnine the responses of the motor neurons to cerebellar and afferent stimuli were often of the same character. In the experiments on preliminarily strychninized animals, it was found that, under these conditions, the responses of the cell to stimulation of the cerebellum are depressed by narcotics significantly more effectively (Fig. 2 C).

Promedol. This analgesic preparation possesses the ability to weaken the inhibition of the knee jerk reflex associated with stimulation of the cerebellum [1]. Starting from that, it may be postulated that promedol is capable of weakening the inhibitory influences of the cerebellum on spinal cord motor neurons. In the experiments in which we recorded the IPSP of the motor neurons caused by afferent and cerebellar stimuli, it was established that the latter are weakened by promedol in doses (3-7 mg/kg) which still do not essentially influence the inhibitory effects obtained during activation of the afferent pathways (Fig. 3 A). At the same time, the facilitating influences from the cerebellum on the motor neurons are altered in varying ways following the injection of the indicated doses of promedol. Out of 7 cells investigated, in 4 we observed a certain weakening of the facilitating effect, in 1 we did not note any changes, and in 2 the facilitating influences were even somewhat intensified. It should be noted that in all these cases the changes in activity of the motor neurons were not great (Fig. 3 B).

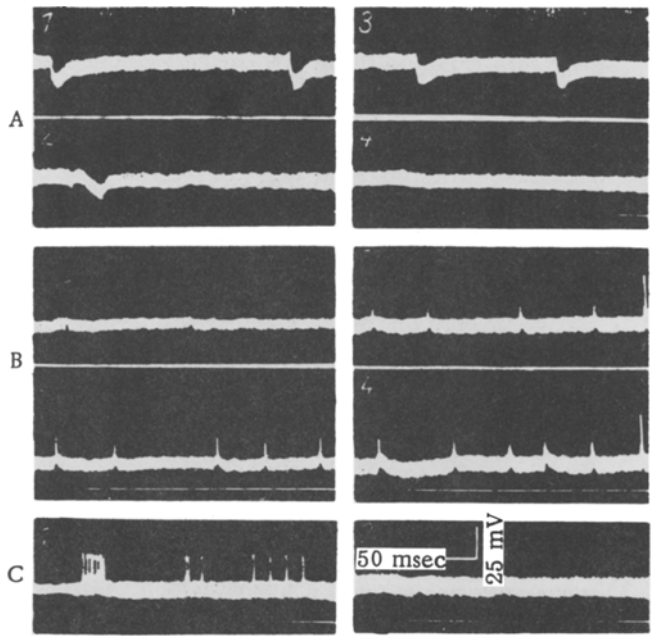

Fig. 3. The effect of promedol on the activity of motor and internuntial neurons. A) IPSP of a motor neuron, caused by stimulation of the posterior radicle (1.3) and the cerebellum (2,4), before (1,2) and 3 min after (3, 4) the injection of promedol in a dose of 6 mg/kg; B) responses of the motor neuron to stimulation of the posterior radicle (1,3) and the posterior radicle together with the anterior lobe of the cerebellum (2,4), before (1,2) and 4 min after (3,4) the injection of promedol in a dose of 5 mg/kg; C) responses of an internuntial neuron to stimulation of the cerebellum before (1) and 3 min after (2) the injection of promedol in a dose of 7 mg/kg. Stimulation of the cerebellum is denoted by a horizontal mark.

It was noted that promedol is capable of depressing the activation of the internuntial neurons associated with stimulation of the cerebellum. As can be seen in Fig. 3 C, after injection of the preparation the responses of the internuntial neuron were completely eliminated.

The obtained data show that a whole series of pharmacological substances with a stimulatory or depressant type of action is capable of effectively intensifying or eliminating the cerebellar influences on the motor and internuntial neurons of the spinal cord. All the investigated substances demonstrated their action on the cerebellar influences when used in doses significantly lower than those which alter the responses of spinal cord neurons to afferent stimulation. This may be based on the following facts.

1. The sensitivity of the cells in the spinal cord to a given pharmacological substance is significantly less than the sensitivity of the neurons in the suprasegmental formations, through which is accomplished the transfer of excitation from the cerebellum to the cells of the spinal cord. This explanation is quite probable in relation to the substances with an excitatory type of action – corasol and caffeine. According to the data in the literature [2], the action of these substances is primarily directed toward the centers of the brain. In experiments with intracellular conduction of potentials, investigators established [4] the minimal effect of even large doses of these substances on the motor neurons of the spinal cord.

2. High sensitivity of the cerebellar influences to pharmacological substances may be caused by the fact that the former are conducted through long, multisynaptic pathways, with the participation of a large number of internuntial neurons, both at the level of the mid-brain and medulla centers, where the switch occurs in the pathways leading to the spinal cord [5, 6], and at the segmental level. At the same time, the multisynaptic routes are the most easily depressed by various pharmacological substances, including narcotics. The facts obtained in this investigation also show that the activity of the internuntial neurons is the most easily altered after the injection of the pharmacological preparations.

The capacity of promedol to depress the IPSP caused by stimulation of the cerebellum , with retention of the IPSP caused by afferent impulsation, permits postulating that this preparation depresses the internuntial neurons of multisynaptic pathways, through which suprasegmental inhibition is accomplished.

SUMMARY

The method of intracellular conduction of potentials from motor and internuntial neurons of the spinal cord (7th thoracic and 1st lumbar segments) was used in cats to study the influence of various neurotropic substances on the facilitating and inhibitory effects secondary to the rhythmic stimulation of the anterior lobe of the cerebellum. Hypnotics (nembutal, hexenal, urethan) depressed the facilitating effects of the cerebellum, both in the motor and internuntial neurons, while analeptics (corasol, caffeine) considerably intensified them. Promedol decreased the activity of the motor neurons associated with cerebellar stimulation. All the compounds studied were capable of influencing the cerebellar effects in considerably smaller doses than those which changed the cellular response to afferent stimuli.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
