INFLUENCE OF THE SODIUM SALT OF γ-HYDROXYBUTYRIC ACID ON INHIBITION OF THE KNEE REFLEX

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In 1960 Laborit [7, 8] investigated and introduced into medical practice the sodium salt of γ-hydroxybutyric acid (GHBA). Subsequently this compound was produced at the Institute of Pharmacology and Chemotherapy, Academy of Medical Sciences USSR, by A. P. Skoldinov and A. P. Arendaruk and experimentally studied by L. A. Serebryakov [1] and A. E. Uspenskii [2].

The purpose of this investigation was to study the influence of GHBA on the segmentary inhibiition of the monosynaptic reflex arc of the spinal cord.

EXPERIMENTAL METHOD

The experiments were conducted on cats under spinal narcosis, immobilized by decerebration. The cutting of the spinal cord and decerebration were performed under ether narcosis, which was stopped 2 h before the beginning of the basic experiment. Activation of the segmentary inhibitory mechanism was accomplished by stimulating the cutaneous branch of the peroneal nerve and the muscular nerve to the flexors of the femur, i.e., the afferents of the flexor reflex. Rectangular pulses from a GRAKh generator, applied in the form of a series lasting 20 sec through immersed Sherrington electrodes, filled with liquid petrolatum, were used for the stimulation. The state of inhibition in the extensor reflex arc was evaluated according to the degree of reduction of the amplitude of the ipsilateral knee reflex. The latter was induced by continuous rhythmic (2 sec interval) impacts of an induction hammer on the operated and distally cut tendon of the musculus quadriceps femoris, contraction of which was recorded mechanographically under the conditions of an isotonic system.

The test preparation was injected intravenously.

EXPERIMENTAL RESULTS

GHBA exerts a distinct influence upon the inhibition of the knee reflex induced by stimulation both of the cutaneous branch of the peroneal nerve (Fig. 1) and of the muscular nerve of the femoral extensors (Fig. 2). A distinct increase in the depth of inhibition is observed 5 min after injection of small doses of the preparation (25 and 50 mg/kg). The effect of GHBA increases distinctly with time. The inhibition becomes complete approximately 60 min after administration of the preparation in a dose of 25 mg/kg and 15-30 min after injection of a dose of 50 mg/kg. The inhibition induced by GHBA in the indicated doses develops against a background of a certain decrease in the amplitude of the testing knee reflex; however, this decrease is too small (10-30%) to consider it as a possible cause of the intensification of the inhibitory effect.

The use of GHBA in doses higher than 50 mg/kg leads to a more pronounced decrease in the amplitude of the test reflex, in view of which the further increase in the effect of inhibited stimulation observed cannot be considered as the result of intensification of the inhibition process itself under the influence of GHBA.

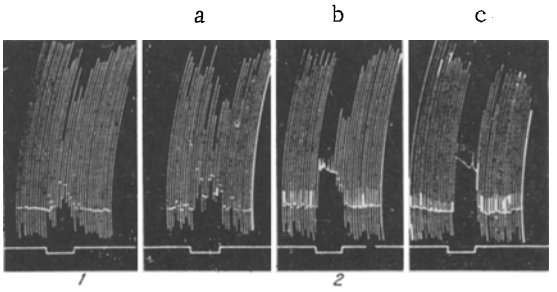

Fig. 1. Inhibition of the knee reflex after stimulation of the cutaneous branch of the ipsilateral peroneal nerve. 1) Before injection of GHBA; 2) after injection of GHBA in a dose of 25 mg/kg: a) after 5 min; b) after 30 min; c) after 60 min.

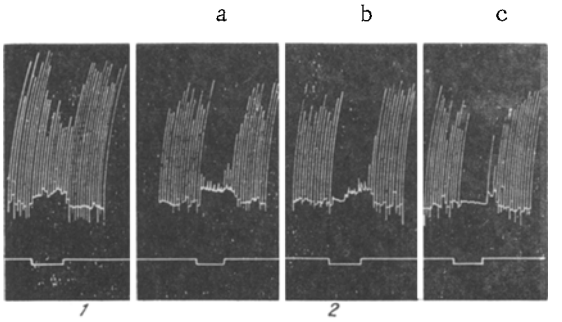

Fig. 2. Inhibition of the knee reflex after stimulation of the ipsilateral muscular nerve to the femoral flexors. 1) Before injection of GHBA; 2) after injection of GHBA in a dose of 25 mg/kg: a) after 5 min; b) after 30 min; c) after 60 min.

According to the widespread hypothesis, the inhibiting influence of γ-aminobutyric acid (GABA) upon the nervous system is due to intensification of the processes of inhibition. It has been hypothesized that GABA is an inhibiting mediator. However, no sufficiently convincing experimental data confirming this viewpoint [3, 4] have been obtained. An analysis of the central action of GABA is greatly hindered by the poor permeability of the hemato-encephalic barrier for this substance and by the need to be limited to methods of its local application. In view of this, it is of interest to investigate GHBA, a close analog of GABA, which penetrates well through the hemato-encephalic barrier. According to the available data, GHBA is one of the products of GABA metabolism; an interconversion of these substances under the action of a number of enzymes has been demonstrated [6, 9]. GHBA, in contrast to GABA, induces pronounced damping central effects under conditions of resorptive action [1, 2, 7, 8].

In the experiments described above, it was established that GHBA, introduced intravenously in relatively small doses, intensifies the inhibition of the knee reflex in the case of stimulation of the cutaneous and muscular nerves. The data obtained confirm the hypothesis of the existence of a relationship between GABA (or its metabolic products) and the processes of central inhibition. However, the nature of this relationship is not yet clarified.

SUMMARY

The object of study was the influence of the sodium salt of γ-oxybutyric acid (GHBA) on the segmental inhibition of the monosynaptic reflex arc of the spinal cord. The experiments were staged on nonanesthesized spinal cats immobilized by means of decerebration. The state of the inhibition of the monosynaptic reflex arc was estimated by the degree of decrease in the amplitude of the knee-reflex during activation of the segmental inhibitory mechanisms. GHBA in a dose of 25-50 mg/kg raises the degree of inhibition of the knee-reflex. The effect of GHBA attains a maximum within from 30 to 60 min after its intravenous injection. The effect lasts 2.5-3 h.

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