ilar changes also took place in the erythrocyte membranes (Table 1). Depression of NDLPO was observed, but the intensity of ADLPO varied within limits close to the control level, except when investigated on the 7th day (Fig. 1B). The plasma cholesterol level also fluctuated, with a marked tendency for the TCh level to fall on account of both FCh and ECh (Fig.2B). Similar changes also were observed in the erythrocyte membranes: a marked decrease in the TCh concentration, due mainly to FCh (Fig. 3B).

The results thus demonstrate changes in the LPO system, the TP level, and the cholesterol fractions in the plasma and erythrocyte membranes during prolonged exposure to noise with an intensity of 91 dB. Administration of TPA had a regulating influence on the parameters studied.

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EFFECT OF LITHIUM SALTS ON NEUROPATHOLOGICAL SYNDROMES OF SPINAL ORIGIN

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KEY WORDS: lithium chloride; lithium hydroxybutyrate; sodium hydroxybutyrate; generator of pathologically enhanced excitation; spinal cord; myoclonus and pain syndrome of spinal origin.

Lithium salts are being used on an ever-increasing scale in neurologic practice. One of them which deserves special attention is lithium hydroxybutyrate, because both the cation (lithium) and the anion (hydroxybutyrate) possess definite pharmacological properties, and their combined action determines the specific effects of the compound [4, 5, 7].

The aim of this investigation was to study the effect of lithium hydroxybutyrate on two forms of spinal cord pathology: generalized myoclonus and a pain syndrome of spinal origin. Their distinguishing pathogenetic feature is that generators of pathologically enhanced excitation (GPEE) are created in various sytems of the spinal cord [3]. Consequently, it was important, first, to discover whether hydroxybutyrate is effective in both forms of pathology,

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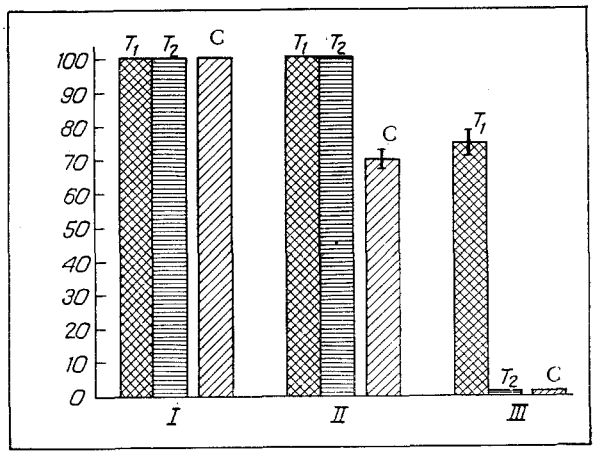

Fig. 1

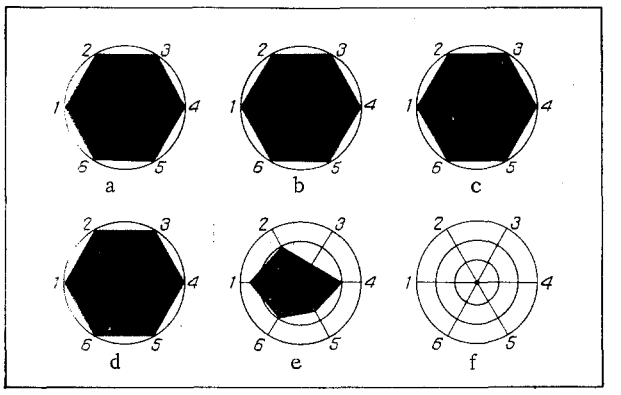

Fig. 2

Fig. 1. Action of lithium chloride (I), sodium hydroxybutyrate (II), and lithium hydroxybutyrate (III) on EA of muscles in generalized myoclonus of spinal origin. Ordinate, amplitude of EA (in % of original). Each compound was used in a dose of 300 mg/kg. T_1) Tonic EA in muscles innervated by segments of spinal cord in which GPEE was created (muscles of left hind limb). T_2) Tonic EA in muscles innervated by segments remote from GPEE (spinal muscles). C) Clonic EA.

Fig. 2. Action of lithium chloride, sodium hydroxybutyrate, and lithium hydroxybutyrate on pain syndrome of spinal origin. Components of pain syndrome recorded: 1) vocalization, 2) motor activity, 3) frequency of seizures, 4) response to provocation of painful episode (represented as vectors). Severity of individual components (i.e., degree of their depression) indicated on 3-point scale: 0) absence of components, 1 point) mild, 2 points) moderately severe, 3 points) severe degree of manifestation. Dark regions of circle along vectors indicate degree of manifestation of individual components and of pain syndrome as a whole. a) Pain syndrome, b) lithium chloride (300 mg/kg), c) sodium hydorxybutyrate (300 mg/kg), d, e, f) lithium hydroxybutyrate in doses of 100, 200, and 300 mg/kg, respectively.

bearing in mind the common feature of their pathogenetic mechanisms, namely the GPEE, and second, to determine features of the action of the compound associated with the specific character of the two syndromes (involvement of spinal motor and nociceptive systems). To determine the role of each of these components of lithium hydroxybutyrate, effects of lithium chloride and sodium hydroxybutyrate were studied for comparison.

EXPERIMENTAL METHOD

Noninbred albino rats weighing 200-220 g were used. A syndrome of generalized spinal myoclonus was induced by creation of a GPEE in the system of propriospinal connections with the aid of tetanus toxin (TT), an agent which disturbs different kinds of inhibition [10]. Creation of the model of the syndrome and its clinical manifestations were fully described previously [1]. The GPEE was activated by stimulation (pinching the skin of the toes) of the limb into which TT was injected. Electrical activity (EA) was recorded in the spinal and sacral muscles and the posterior group of thigh muscles on both sides.

A pain syndrome of spinal origin was evoked by creation of a GPEE in the system of the posterior horns of the spinal cord by means of penicillin, deposited in 1% agar [1]. An agar disk with incorporated penicillin (2500 U) was applied to one side of the dorsal surface of the spinal cord in region L_2-L_6. Observations were made on the animals' behavior, and individual symptoms of the pain syndrome were noted: vocalization, motor response, local response, duration of one seizure, frequency of seizures, the "guarding" phenomenon, and the response to provocation. The intensity of the pain syndrome was estimated on a 3-point system. The doses used in the experiments were: lithium hydroxybutyrate 50-300 mg/kg, lithium chloride 100-300 mg/kg, and sodium hydroxybutyrate 300-750 mg/kg. The compounds were injected intraperitoneally as aqueous solutions.

EXPERIMENTAL RESULTS

Generalized seizures consisting of tonic and clonic phases developed spontaneously in the animals 96 h after injection of TT in response to stimulation of the limb into which TT had been injected (the side of formation of the GPEE). The tonic phase was recorded on the electromyogram as a long burst of EA, consisting of high-amplitude and high-frequency discharges; the clonic phase was expressed as synchronized potentials, whose frequency and amplitude depended on the severity of the syndromes.

Intraperitoneal injection of lithium chloride in doses of 100 to 300 mg/kg did not cause weakening of the convulsions: the compound did not abolish spontaneous or evoked seizures and did not change the character of EA in the muscles (Fig. 1, I). Lithium hydroxybutyrate, in a dose as low as 50 mg/kg, led to a small decrease in the frequency of clonic EA with no change in tonic EA. With an increase in the dose to 200 mg/kg lithium hydroxybutyrate completely abolished the clonic phase of the seizure syndrome. Evoked tonic EA was reduced mainly in the spinal muscles on both sides and the sacral muscles on the right side. Injection of lithium hydroxybutyrate in a dose of 300 mg/kg caused deeper inhibition of tonic EA: EA was preserved only in muscles of the hind limb (the side of formation of GPEE) and, partly, in the left sacral muscles (Fig. 1, III). The effect began 10 min after injection of the drug. In special experiments lithium hydroxybutyrate was used in a dose of 400 mg/kg. Only in this case was EA inhibited in muscles of the left hind limb. Sodium hydroxybutyrate was less effective than lithium hydroxybutyrate: in a dose of 300 mg/kg sodium hydroxybutyrate led only to a small decrease in frequency of clonic EA (Fig. 1, II). To achieve an effect similar to that of lithium hydroxybutyrate (300 mg/kg) it was necessary to give sodium hydroxybutyrate in a dose of 750 mg/kg.

The animals developed a pain syndrome 10-15 min after cessation of anesthesia. It was characterized by paroxysmal seizures of high intensity, accompanied by a cry, by motor excitation, by flexion of the hind limb, and by attempts to bite the affected region (the projection zone of the pain). A similar seizure could be provoked in the interictal period by stimulation of the trigger region (the projection zone of the pain). The pain syndrome lasted 3-3.5 h.

Lithium chloride and sodium hydroxybutyrate were ineffective (did not abolish the pain syndrome) in all doses used (100-300 mg/kg). Lithium hydroxybutyrate had no analgesic action in a dose of 100 mg/kg, but if the dose of the drug was increased to 200 and, in particular, to 300 mg/kg, it weakened the pain syndrome or suppressed it completely (Fig. 2). The effect of the drug began to appear after a long latent period (50-60 min) and it continued for 2-2.5 h.

The spectrum of pharmacological activity of lithium hydroxybutyrate includes several properties attributable to lithium and to hydroxybutyrate: both cation and anion exhibit their own activity, mutually potentiating each other's effect [5]. Lithium (the cation) itself depresses increased activity of catecholaminergic structures, inhibits the synthesis and release of catecholamines, and stimulates their reuptake [8, 12]. Lithium exerts its action on the excited neuronal membrane through the Na-channel and inhibits entry of Ca^{++} [13]. At the synaptic level lithium inhibits the excitatory effects of glutamate and aspartic acid, increases the sensitivity of α-adrenoreceptors, and reduces the sensitivity of β-adrenoreceptors [14]. The hydroxybutyrate anion also has a multiple action: it potentiates GABA-ergic inhibitory processes, increases the reserves of high-energy compounds in the cell, has marked antihypoxic activity, and induces a tranquilizing effect [5, 6, 9, 11].

These investigations showed that lithium hydroxybutyrate is more effective against the forms of spinal cord pathology investigated: in a dose of 300 mg/kg it abolished the pain syndrome and seizure activity (spontaneous and provoked) in myoclonus, whereas lithium chloride and sodium hydroxybutyrate were ineffective in the same dose. The results are in agreement with those of investigations by several workers which showed that lithium chloride does not prevent the development of seizures due to camphor, metrazol, or thiosemicarbazide, but in other tests, to give the same effects, its doses had to be 20 times greater than those of lithium hydroxybutyrate [2]. Sodium hydroxybutyrate also was ineffective in doses comparable with lithium hydroxybutyrate. Only by increasing the dose to 750 mg/kg, i.e., by $2^1/_2$ times, did it abolish clonic and reduce tonic activity in regions remote from GPEE, while having no effect on tonic EA of muscles innervated by segments of the spinal cord containing the GPEE. Lithium hydroxybutyrate exerted its action even against pathological pain, suppressing GPEE and abolishing the pain syndrome. According to some evidence [7] lithium hydroxybutyrate blocks conduction of nociceptive impulsation in the center and raises the threshold of pain sensitivity.

Lithium hydroxybutyrate can thus exert an inhibitory action of GPEE irrespective of where the GPEE was created, on conduction of excitation provoked by the GPEE, and on structures receiving this excitation, or in other words, on all stages of the pathological system.

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EFFECT OF CHRONIC PSYCHOGENIC STRESS ON CHARACTERISTICS OF SOME RAT BRAIN SYNAPTIC MEMBRANE RECEPTORS

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KEY WORDS: rats; chronic stress; depression of behavior; brain receptors.

To discover the cellular and molecular mechanisms of the chronic action of psychotropic drugs an important step is to study their effect on the neurochemical characteristics of the brain in animals with appropriate pathology of behavior, which can be corrected by the drugs concerned [2]. In the present investigation characteristics of α- and β-adrenoreceptors, and also of imipramine and benzodiazepine receptors in brain synaptic membranes of rats were studied after exposure to combined stress for 15 days by a modified Hecht's method [7].

EXPERIMENTAL METHOD

Noninbred male albino rats weighing 180-200 g were used. Stress was induced in September-October, 1983, daily for 15 days by means of chronic reinforcement by painful electric shocks of a conditioned stimulus (flashes) according to a stochastic program, with probability of electric shocks of 0.5. The rats' behavior before and after the beginning of stress was assessed on the basis of their activity in an open field test, in a maze, and in a shuttle box [7].

On the 16th day the stressed and control (intact) animals were decapitated, the brain was quickly washed free from blood in 0.32 M sucrose solution, after which it was homogenized in the same solution (10% homogenate) in a glass homogenizer with Teflon pestle in 0.32 M su-

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