

CHARACTERISTICS OF THE SPECTRUM OF PSYCHOTROPIC ACTIVITY  
OF SODIUM HYDROXYBUTYRATE

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It is concluded from data showing the effect of sodium hydroxybutyrate on conditioned motor defensive reflex behavior in a conflict situation, active avoidance without discriminative control in rats, and the side position test that the spectrum of psychotropic activity of the compound possesses certain qualitative distinguishing features. The action of sodium hydroxybutyrate in subnarcotic doses can be described as that of a sedative with manifestation of certain properties of neuroleptics and tranquilizers.

KEY WORDS: sodium hydroxybutyrate; psychotropic activity.

The neurotropic activity of sodium hydroxybutyrate has been studied in sufficient detail [1]. However, the effect of sodium hydroxybutyrate on various types of complex behavioral reactions and the position of this compound in a series of psychotropic drugs with sedative, tranquilizing, and neuroleptic types of action has so far received little investigation.

This paper describes the results of a study of the effect of sodium hydroxybutyrate on certain behavioral reactions in animals: the conditioned motor-defensive reflex, behavior in a conflict situation, and an operant continuous avoidance reaction. On the basis of the results an attempt was made to determine the position of sodium hydroxybutyrate among typical representatives of different classes of psychotropic drugs with a depriming type of action: sedatives, tranquilizers, and neuroleptics.

#### METHODS

Experiments were carried out on male albino rats weighing 180-220 g. To assess the tranquilizing action of the drugs the "conflict situation" method [2] was used. Activity of the drugs was compared by this method by calculating doses leading to a tenfold increase in the number of times the animals drank water compared with the control. To assess the effect of the drugs on conditioned-reflex activity the conditioned motor-defensive reflex method [3] was used. The effect of sodium hydroxybutyrate on the operant continuous active avoidance reaction was studied by Sidman's method [7]. The delay of the stimulating pulses was 20 sec, the interval between shocks was 5 sec, the duration of each stimulus 1 sec, and its amplitude 1 mA [5]. The animals' operant activity was recorded on an automatic ink-writer. Experiments were carried out on pretrained animals with a stable active avoidance skill. The effect of the drugs on the duration of intervals between pressing the lever by the animals in the course of 60 min was evaluated. Maximal doses of the various drugs not inducing a positive effect as shown by the "revolving rod" test were chosen for each series of experiments. The sedatives and muscle-relaxing effects of the drugs were determined by the "side position" test, followed by calculation of the index of tranquilizing action (ratio of the dose in which the drug leads to assumption of the side position to the dose giving a marked effect in the "conflict situation" test). The acute 24-h toxicity of the drugs also was determined. The drugs were injected intraperitoneally. The mean effective doses ( $ED_{50}$ ) were calculated by the method of Litchfield and Wilcoxon [6]. The action of sodium hydroxybutyrate in these tests was compared with the effects of phenobarbital, carbromal, chlordiazepoxide, meprobamate, and chlorpromazine.

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## RESULTS

Sodium hydroxybutyrate depressed the animals' conditioned-reflex activity in a dose of 12% of its LD<sub>50</sub>. Chlordiazepoxide, meprobamate, and carbromal had a similar action in doses equivalent to a much higher proportion of LD<sub>50</sub> (31, 42, and 47% respectively). By contrast with these drugs, chlorpromazine selectively depressed conditioned-reflex activity in a dose equivalent to 2% of LD<sub>50</sub>. In a conflict situation, sodium hydroxybutyrate in a dose of 350 mg/kg caused changes in the animals' behavior similar to those observed during the action of tranquilizers and sedatives, namely an increase in the number of times the animals drank water without any significant change in the level of motor activity or in the number of visits to the feeding bowl. However, the effect of sodium hydroxybutyrate was much less marked than that of tranquilizers and sedatives. Under the influence of chlorpromazine, motor activity was depressed and the animals made fewer visits to the feeding bowl and did not increase the number of times they drank water. With a further increase in the dose of sodium hydroxybutyrate to 400 mg/kg its tranquilizing effect did not increase, but its muscle relaxing action was exhibited more strongly. Sodium hydroxybutyrate caused the animals to adopt the side position in a dose equivalent to 28% of its LD<sub>50</sub>. Chlorpromazine had the same effect in a dose of 29% of LD<sub>50</sub>. The remaining drugs led to adoption of the side position in doses equivalent to a higher percentage of LD<sub>50</sub>. The index of tranquilizing action for sodium hydroxybutyrate, like that of the sedatives, was low: 2.2 for phenobarbital, 1.9 for carbromal, and 1.6 for sodium hydroxybutyrate. This index was considerably higher for tranquilizers (4.6 for meprobamate and 7.1 for chlordiazepoxide). The effect of sodium hydroxybutyrate (150 mg/kg) on the active avoidance reaction was compared with the effect of chlorpromazine (6.2 mg/kg), chlordiazepoxide (1 mg/kg), and phenobarbital (30 mg/kg). The effect of sodium hydroxybutyrate on the duration of the interval between pressing the lever was manifested as a decrease in the number of short (1-2 sec) intervals and in the total area of the histogram. Administration of phenobarbital led to an increase in the number of avoiding presses with an interval equal to the delay of the stimulating pulses (20 sec). The number of longer intervals also increased. Under the influence of chlordiazepoxide and, in particular, of chlorpromazine the decrease in the number of intervals measuring 1-2 sec was greater than under the influence of sodium hydroxybutyrate. Furthermore, after administration of these drugs the number of 20-sec intervals was reduced and the number of long intervals considerably increased. In this respect sodium hydroxybutyrate was similar to chlorpromazine as regards its selectivity in depressing the conditioned motor-defensive reflex. Features of antipsychotic action, incidentally, have been observed during clinical studies of sodium hydroxybutyrate also [4]. However, its effect on active avoidance differed essentially from the effects of chlorpromazine. In addition, with respect to its effect on the behavior of animals in a conflict situation hydroxybutyrate exhibits elements of a tranquilizing action. However, its action as a tranquilizer was weaker than that of phenobarbital and carbromal. The character of the effect of sodium hydroxybutyrate on active avoidance differs from that of all typical representatives of classes of psychotropic drugs with a depriming type of action.

The action of sodium hydroxybutyrate in subnarcotic doses can thus be described as sedative, with manifestation of certain elements characteristic of neuroleptics and tranquilizers.

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