EFFECT OF PSYCHOTROPIC DRUGS ON MOTIVATIONAL COMPONENTS AND ON RESULTS OF OPERANT ACTIVITY IN RATS

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UDC 615.214.015.4:612.821.1/.3].076.9

KEY WORDS: motivation; operant activity; action of psychotropic drugs.

A little-studied aspect of the mechanism of action of psychotropic drugs is their effect on motivational components of goal-directed behavioral acts. The study of this problem in experiments on animals presents definite technical difficulties due to the lack of any reliable and specific physiological parameters to characterize the intensity of the dominant motivation and to enable the levels of motivational and emotional excitation to be assessed separately [3]. One possible technical approach to the solution of this problem is the use of previously established views on the close connection between the intensity of the dominant motivation and accuracy of correction of the results of current activity [11].

In the present investigation an attempt was made to use the method of determining the zone of uncorrectable results to assess the intensity of a dominant avoidance motivation and to estimate the influence of a number of psychotropic drugs on it in rats during operant activity aimed at avoiding painful electrical stimulation, in the absence of exteroceptive warning [14].

EXPERIMENTAL METHOD

Experiments were carried out on 98 noninbred male albino rats weighing 220-350 g, previously trained in active avoidance (by pressing a lever) of painful electrical stimulation applied to the electrode floor of the chamber. Details of the technique were described previously [8, 9]. Achievement of the final results of this type of operant activity is determined by accuracy of reproduction of intervals between pressing the lever, which should not exceed 20 sec (the delay time of the stimulating pulses after a single pressing of the lever). With the formation of the functional system of this behavioral act the interval between pressings of the lever will be corrected if disagreement develops between the results achieved and its model in the action acceptor [1]. The use of the correlation matrix method enables the zone of uncorrected (i.e., corresponding to parameters of the model formed in the action acceptor) results at the various stages to be determined. This zone is closely linked with the level of motivation of achievement and characterizes it [10]. On the basis of analysis of the correlation matrix of results at consecutive stages (the duration of intervals between pressings on the lever) it can be determined whether this result is corrected in subsequent attempts. This analysis is based on comparison of all the events in a given line of the correlation matrix corresponding to the duration of the interval studied, the number of corrections — whether a decrease or an increase, and the so-called zero corrections when the previous result is repeated on pressing the lever the next time, and also of random deviations from the value of the time interval studied. The theoretical basis and mathematical procedure of this method were fully described previously [10].

To study the effect of the level of avoidance motivation of the size of the zone of uncorrected results, operant activity was carried out with the usual strength of painful electrical reinforcement (1 mA) and with a strength reduced to values just above the threshold (0.3 mA). The experiments of this series were conducted on the same animals (23 rats). The effect of members of several classes of psychotropic drugs on the size of the zone of uncorrected results was investigated: the drugs included tranquilizers (diazepam — 0.5, 2, and 5 mg/kg; fenibut — β-phenyl-γ-aminobutyric acid — 10, 30, and 50 mg/kg), neuroleptics (chlorpromazine 0.1, 0.5, and 1 mg/kg; haloperidol — 0.25, 0.5, and 1.5 mg/kg), sedatives (pheno-

Laboratory of Action Protectors, Institute of Pharmacology, Academy of Medical Sciences of the USSR. (Presented by Academician of the Academy of Medical Sciences of the USSR A. V. Val'dman.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 95, No. 6, pp. 65-68, June 1983. Original article submitted December 31, 1982.

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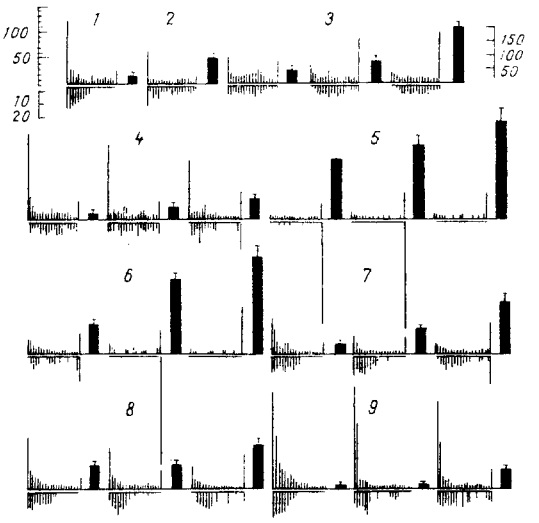

Fig. 1. Effect of test procedures on zone of uncorrected results (bottom histograms), character of operant activity (top histograms — distribution based on number of intervals between pressings on lever), and number of shocks allowed to get through (columns on the right). 1) Initial operant activity (strength of reinforcing stimuli 1 mA); 2) activity against a background of depressed motivation (strength of reinforcing stimuli 0.3 mA); 3) after injection of diazepam (in doses of 0.5, 2, and 5 mg/kg — histograms from left to right); 4) fenibut (10, 30, and 50 mg/kg); 5) haloperidol (0.25, 0.5, and 1.5 mg/kg); 6) chlorpromazine (0.1, 0.5, and 2 mg/kg); 7) phenobarbital (1, 5, and 25 mg/kg); 8) sodium hydroxybutyrate (80, 150, and 350 mg/kg); 9) amphetamine (0.5, 5, and 10 mg/kg). Scale on left: top — for interval histogram, bottom — for histogram of position composition of zone of uncorrected results (in % of total number of positions included in the specified zone for the given group). Scale on right — for number of shocks allowed through.

barbital — 1, 5, and 25 mg/kg; sodium hydroxybutyrate — 80, 150, and 350 mg/kg), psychostimulants (amphetamine — 0.5, 5, and 10 mg/kg). In the above-mentioned doses the drugs exhibited their characteristic pharmacological activity. The pain threshold (as shown by the appearance of vocalization) was determined in control experiments on separate groups of rats receiving electric shocks of stabilized amplitude applied to the electrode floor of the chambers in which operant activity was performed. All drugs for testing (or physiological saline, in the control) were injected intraperitoneally 40-60 min before the beginning of the experimental session lasting 1 h. Each dose was tested on 16-18 experiments. The experiments were repeated not before 7-8 days after the last dose of the drug had been given.

EXPERIMENTAL RESULTS

The experiments showed (Fig. 1) that a reduction in the strength of negative reinforcement (operant activity in response to application of electric shocks of amplitude just above the threshold level to the electrode floor) caused widening of the zone of uncorrected results, to judge from the histogram of frequency of incorporation of the various positions in it (as percentages of the total number of positions occurring in the zone of uncorrected results for the given group of animals). If electric shocks of the usual amplitude at which learning and training of the animals took place (1 mA) were applied to the electrode floor, this zone included intervals of 1 to 11 sec between pressings on the lever. Longer intervals during subsequent pressing were corrected by reduction of their length. During activity of reinforcing stimuli with reduced amplitude (0.3 mA) the zone of uncorrected results included intervals from 1 to 20 sec, i.e., not even pressings on the lever leading to avoidance underwent subsequent correction (interval 20 sec, when the first shock was applied to the electrode floor).

With a reduction in strength of the arousing stimulus (and, consequently, in the strength of the motivation for its avoidance) the character of operant activity showed very little change — only a small decrease was observed in the number of short (1-2 sec) intervals between pressings on the lever. However, the final result of operant activity under these circumstances was substantially worsened, to judge from the increase in the number of electric shocks allowed to get through.

After injection of diazepam (0.5-5 mg/kg) and fenibut (10 mg/kg) widening of the zone of uncorrected results also was observed. Activity under these circumstances took place when the strength of the reinforcing stimuli was 1 mA. Injection of large doses of fenibut (30-50 mg/kg) caused not only widening of this zone, but also exclusion of individual positions from it. The 20-sec interval increased significantly as a fraction of the total position composition of the zone of uncorrected results. A similar composition of the zone of uncorrected results was observed in animals poorly trained in this type of operant activity, when an adequate model was not formed in the action acceptor. That may be why in the initial stages of formation of operant skill the zone of uncorrected results could not be detected at all. After injection of the tranquilizers an increase in the number of electric shocks allowed to get through was observed. The character of the interval histogram in this case changed variously. In particular, after injection of fenibut in doses of 10 and 30 mg/kg the number of short intervals between pressings on the lever was increased compared with the control. Diazepam, within the dose range tested, caused a significant fall in this parameter. Diazepam and fenibut caused virtually no change in the threshold of pain sensitivity. Similar results for diazepam were obtained previously [4].

Phenobarbital and sodium hydroxybutyrate in small doses (1 and 80 mg/kg respectively) caused no change in size of the zone of uncorrected results. However, in the doses mentioned above, these drugs caused a decrease in the number of short intervals between pressings on the lever and an increase in the number of electric shocks allowed to get through, typical of psychodepressants [6, 12]. Phenobarbital and sodium hydroxybutyrate in larger doses (15-25 and 150-350 mg/kg respectively) caused widening of the zone of uncorrected results with the loss of individual positions from it. In small doses these drugs did not change the threshold of pain sensation. It should be pointed out that widening of the zone of uncorrected results was observed after administration of phenobarbital and sodium hydroxybutyrate in doses with a tranquilizing action in the conflicting situation test [4, 7]. Haloperiodol and chlorpromazine, within the dose range studied, caused a marked change in the position composition of the zone of uncorrected results (widening in the direction of longer intervals, exclusion of many positions, as has been described for the effect of large doses of fenibut and sedatives). Haloperidol and chlorpromazine, in doses of 1.5 and 2 mg/kg respectively, caused disappearance of this zone. Even in small doses the neuroleptics studied sharply reduced the number of short intervals between pressings of the lever and the total number of operant responses and increased the number of electric shocks allowed through. Haloperidol and chlorpromazine in doses of 0.25-0.5 and 0.1-0.5 mg/kg respectively did not change the threshold of pain sensitivity. Amphetamine in a dose of 0.5 mg/kg narrowed the zone of uncorrected results somewhat compared with the control (positions 1-9), whereas in doses of 5 and 10 mg/kg it led to widening of the zone and to the exclusion of several positions from it. In these doses amphetamine caused a marked increase in the number of short intervals between pressings on the lever and in the total number of operant reactions. In doses of 0.5 and 5 mg/kg it reduced the number of electric shocks passed through compared with the control, whereas in a dose of 10 mg/kg it increased that number. In doses of 0.5 and 5 mg/kg amphetamine did not change the threshold of pain sensation, but in a dose of 10 mg/kg it reduced it.

The results are evidence that the size of the zone of uncorrected results, with a formed model in the action acceptor, can reflect quantitatively the level of the dominant motivational excitation. It can be tentatively suggested that tranquilizers, in doses in which their specific action is manifested, and also sedatives in doses with a tranquilizing effect [4, 7] initially inhibit the formation of a dominant motivation at the stage of afferent synthesis, and this is reflected in the parameters of the model in the action acceptor. Neuroleptics, with no tranquilizing activity in the doses tested by the conflicting situation method [4], can give rise to disturbances in the coordinated inclusion of individual components of the functional system in its activity. Dopaminergic mechanisms, responsible for the transmission of information from the limbico-hypothalamic complex to the motor system in the process of formation of the behavioral act [13] could be among the targets for the action of these drugs. The mechanism of the similar action of tranquilizers and amphetamine (5-10

mg/kg) on the size of the zone of uncorrected results and on the intensity of avoidance motivation may perhaps be based on a similar stimulating effect on the positive reinforcement systems [2, 5].

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