EFFECT OF PSYCHOTROPIC DRUGS ON THE FORMATION OF THE AVOIDANCE REACTION IN ALBINO RATS TO NOCICEPTIVE ELECTRICAL STIMULATION OF ANOTHER ANIMAL

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The effect of amphetamine, imipramine, haloperidol, and droperidol administered daily for 10 days on the formation of the avoidance reaction was studied in albino rats in response to nociceptive electrical stimulation of another rat. All the drugs stimulated the formation of this reaction especially during the period of their administration. In some rats the reaction persisted after withdrawal of the psychotropic drugs. Imipramine was the most active in this respect. The stimulant effect could be connected with the adrenopositive properties of the drugs tested.

A study of the effects of psychotropic drugs on the avoidance reaction in one rat to nociceptive stimulation of another showed that butyrophenone derivatives (haloperidol, droperidol, and triperidol) differ qualitatively from phenothiazine derivatives (chlorpromazine, trifluoperazine) [2]. Whereas chlorpromazine and trifluoperazine inhibit this reaction, butyrophenone derivatives, by contrast, exacerbate it and lead to the appearance of aggressiveness of the animals in that situation. Similar effects are produced by imipramine and amphetamine.

This paper describes a more detailed study of the activating effects of haloperidol, droperidol, imipramine, and amphetamine on the responses of animals evoked by the behavior of another rat subjected to nociceptive stimulation.

EXPERIMENTAL METHOD

Experiments were carried out on 87 female albino rats weighing 270-300 g. The method used was essentially as follows [2, 5]. The "observer" rat, under the influence of the response of the "victim" rat to nociceptive stimulation, leaves one compartment of the experimental chamber in which it closes electrical contacts and enters another compartment, thereby breaking the electrical circuit and thus stopping the nociceptive stimulation of the "victim." The response was regarded as positive if the observer rat remained not less than 3 min in the "breaking" compartment out of a total exposure of 5 min.

Animals chosen for the experiments were those which, after 10 exposures or more (one exposure daily), never once entered the "breaking" compartment or spent less than 3 min in it.

Amphetamine (1 mg/kg), imipramine (15 mg/kg), haloperidol, and droperidol (1 mg/kg) were injected intraperitoneally 1 h before the experiment daily for 10 days. Each substance was tested on 10 rats, and the number of animals in which an avoidance reaction appeared was counted. Observations were continued for 10 days (while the drugs were being given) and for the next 10 days after their withdrawal.

Control rats received isotonic sodium chloride solution under the same conditions.

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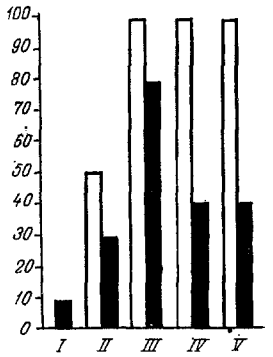

Fig. 1. Effect of psychotropic drugs on formation of avoidance reaction in rats during nociceptive stimulation of another rat: I) control; II) amphetamine 1 mg/kg; III) imipramine 15 mg/kg; IV) haloperidol 1 mg/kg; V) droperidol 1 mg/kg. Unshaded columns represent positive reaction during administration of drugs, shaded columns the same after their withdrawal. Ordinate, percentage of animals giving a positive reaction.

EXPERIMENTAL RESULTS AND DISCUSSION

Imipramine had the strongest activating action (Fig. 1). The avoidance reaction to nociceptive stimulation of the partner appeared in all the rats during the administration of the drugs and persisted for the next 10 days in 80% of the animals. The general behavior of the rats remained unchanged, and only during attempts to push them toward the entrance into the "closing" compartment did they run to the opposite end of the "breaking" compartment.

During the period of their administration haloperidol and droperidol had the same action as imipramine; i.e., they caused all the animals to stay for a long time in the "breaking" compartment. However, the effect was less stable and it persisted for the next 10 days in only 40% of the rats. Another characteristic feature of the rats' behavior during the action of both the neuroleptics was their active resistance to pushing into the "closing" compartment. This was seen particularly clearly after administration of droperidol, when, in addition to the marked evidence of muscular relaxation, the rats responded to pushing by turning away from the entrance into the "closing" compartment, stepped back from it, squeaked, hissed, and tried to bite the tongs. Under the same conditions the intact animals usually ran freely from one compartment into the other.

The muscle relaxants themselves were not a factor preventing the animals from going into the "closing" compartment for after administration of haloperidol and droperidol in larger doses, depressing the avoidance reaction, the rats still crossed into this compartment [2].

After administration of amphetamine a positive effect was observed in only 50% of the rats during the period of administration and in 30% during the next 10 days.

Attempts to reach the "victim" through the partition (by jumping or climbing over it) were characteristic of most animals which did not leave the "closing" compartment after receiving amphetamine.

The results thus show that all the drugs tested stimulated the formation of the avoidance reaction in rats to nociceptive stimulation of other rats.

The mechanism of the activating effect of amphetamine and imipramine is connected with the influence of these substances on noradrenalin metabolism in the brain [3, 7, 9, 12, 13]. The stimulant effect of amphetamine and imipramine on the avoidance reaction is presumably based on the changes in noradrenalin metabolism induced by the drugs. Considering that butyrophenone derivatives (haloperidol, droperidol) have a similar effect on the reaction described, and taking into account also data in the literature on the excitatory effects of haloperidol [1, 8, 11] and its interference with dopamine and noradrenalin metabolism [4, 8], it can be postulated that adrenopositive components play a role in the mechanism of action of butyrophenones on this response. It is evidently the adrenopositive properties of the butyrophenone derivatives which explain the stimulant effects of this group of neuroleptics (by contrast with neuroleptics of the phenothiazine series) observed under clinical conditions [6, 10].

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