

EFFECT OF PSYCHOTROPIC DRUGS ON FIGHT AND FLIGHT REACTIONS EVOKED BY ELECTRICAL STIMULATION OF THE ANTERIOR HYPOTHALAMUS

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In experiments on cats, administration of chlorpromazine, trifluoperazine, perphenazine, haloperidol, imipramine, and meprobamate inhibited the motor components of the fight and flight reactions evoked by electrical stimulation of the anterior hypothalamus and paraventricular nucleus. Benactyzine and librium considerably raised the threshold of electrical stimulation for development of the fight reaction, while haloperidol completely blocked the flight reaction. It is considered that one region on which benactyzine, librium, and haloperidol exert their action on the manifestation of emotional responses of fight and flight may be the anterior hypothalamus and paraventricular nucleus.

One of the principal properties of psychotropic drugs is their ability to modify emotional manifestations in both man and animals. At the same time, the specific effects of these drugs on different emotional responses, and more especially the localization of this action in the central nervous system, remain unknown. A possible point of application of this action of the psychotropic drugs is the hypothalamus, because among the structures participating in the formation of outward manifestations of the emotions a leading role is ascribed to the hypothalamus [1, 2, 4].

The object of this investigation was to study the action of a group of different classes of psychotropic drugs on the fight and flight reactions developing at the level of the anterior hypothalamus.

EXPERIMENTAL METHOD

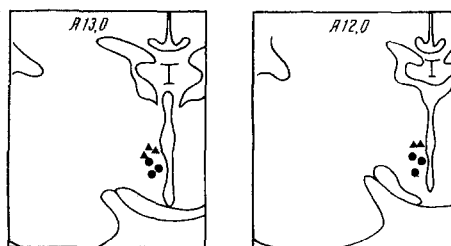


Fig. 1. Location of electrodes in anterior hypothalamus. Circles denote regions electrical stimulation of which evoked a fight reaction, triangles region from which a flight reaction was evoked.

Nichrome electrodes, 0.3 mm in diameter, were permanently inserted into the anterior hypothalamus and paraventricular nucleus (A 13.0-A 12.0 according to the stereotaxic atlas [5]) of 21 cats weighing 3-3.5 kg. For monopolar electrical stimulation, monophasic pulses (100/sec, 0.5 msec, 10 sec) were generated by a Sanei electronic stimulator with isolation output unit. The cathode was the stimulating electrode. In different experiments the amplitude of the pulses varied from 1.5 to 5 V and was controlled by means of an SI-1 oscilloscope. The amplitude of the pulse which, if applied 4 times in succession at intervals of 4 min, evoked a uniform response of the animal, was taken as the threshold value. During the experiment the cats were kept in a room where they could move freely. The tested drugs (chlorpromazine, trifluoperazine, perphenazine, haloperidol, imipramine, meprobamate, librium, benactyzine, and morphine) were injected intraperitoneally 1 h before the beginning of stimulation.

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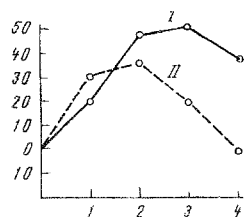


Fig. 2. Effect of librium in a dose of 10 mg/kg (I) and benactyzine in a dose of 3 mg/kg (II) on threshold of flight reaction. Abscissa, time (in h); ordinate, mean increase in threshold, in percent.

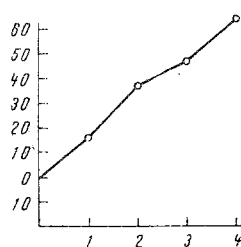


Fig. 3. Effect of haloperidol on threshold of flight reaction. Abscissa, time (in h); ordinate, mean increase in threshold, in percent.

tion for estimation of the threshold (Fig. 2). Benactyzine and librium, given in smaller doses, gave a weaker effect.

With the exception of haloperidol, none of the tested drugs altered the threshold amplitude of the stimuli for evoking a flight reaction. During electrical stimulation the animals got up, walked to the wall of the room and tried to get out of it, but their movements were slow and sluggish, and the sympathetic effects (erection of the hair and dilatation of the pupils) also were absent. After administration of large doses of chlorpromazine (6-8 mg/kg) the muscular relaxation became so marked that the animals could not get up in the period of stimulation, and simply waved their paws helplessly. Haloperidol (4 mg/kg) completely blocked the flight reaction, although the manifestations of ataxis or catatonia were not so clearly defined (Fig. 3). With a considerable increase in the strength of stimulation over threshold, instead of a flight reaction, elements of the fight reaction were produced in the cats: purring and hissing.

Morphine (1-6 mg/kg) in all the animals caused dilatation of the pupils but had no marked effect on the fight and flight reactions evoked by electrical stimulation of the hypothalamus.

In these experiments the outward signs of the fight and flight reactions (motor and autonomic) developed as the result of direct electrical stimulation of the region forming these manifestations (the hypothalamus), and consequently, they developed independently of the external environment. The course of the fight reaction resembled the "sham rage" described by Masserman [3], for during the reaction the cat could be stroked; after the end of stimulation, the reaction immediately disappeared and the animals showed no signs of restlessness. The flight reaction was different in character. During stimulation, the animals' actions were completely purposeful: the cat looked for somewhere in the room where it could escape, and having found the place, tried to get into it as quickly as possible. After stimulation, if the door of the room was opened, the cat immediately tried to get out. This fact, in the writer's opinion, indicates that during stim-

After the experiments the location of the electrodes was determined histologically. Their positions are indicated in Fig. 1.

EXPERIMENTAL RESULTS AND DISCUSSION

In response to electrical stimulation of the anterior hypothalamus and paraventricular nucleus of the cats in these experiments, two diametrically opposite reactions developed: a fight reaction and a flight reaction. The fight reaction consisted of lowering the head, curving the spine and tail, a dull rumbling turning into hissing, and associated autonomic components such as dilatation of the pupils, erection of the hair, and urination.

The flight reaction had the following appearance. Immediately after the beginning of stimulation the cat began to look around restlessly, then got up and ran quickly toward one wall of the room, climbing up on its hind paws, and clambering upward in an attempt to get out of the room. This reaction was accompanied by dilatation of the pupils, erection of the hair, and sometimes by hissing and urination.

After administration of chlorpromazine (1-8 mg/kg), trifluoperazine (1-4 mg/kg), perphenazine (1-5 mg/kg), haloperidol (1-4 mg/kg), imiprazine (10 mg/kg), and meprobamate (80-100 mg/kg), electrical stimulation of the animals no longer evoked motor responses, apart from raising of the head, or sympathetic effects (dilatation of the pupils, erection of the hair). In addition, under the influence of these drugs, the tone of the cats' nictitating membrane was lowered, and remained unchanged even during stimulation. At the same time, no changes were observed in the characteristic components of the fight reaction: purring and hissing.

Benactyzine (3 mg/kg) and librium (10 mg/kg) completely blocked the flight reaction — the animals remained quiet during threshold stimulation. With an increase in amplitude of the stimulating pulses, the flight reaction in these animals was reproduced, although against the background of benactyzine the motor components and erection of the hair were absent, although the purring and hissing were clearly defined and could be used as a crite-

ulation the animal experienced some unpleasant sensations which it tried to avoid. In the case of the fight reaction, this was a purely motor reaction and only that part of the hypothalamus responsible for this motor function was involved. In the case of the flight reaction, this was more highly integrated and associated with a particular emotional feeling. On the basis of these experiments it can be considered that the behavioral responses described are not the result of sensations of pain, because morphine, in analgesic doses, did not modify these reactions.

All the psychotropic drugs studied in these experiments, except morphine, depressed the motor components of the fight and flight reactions, but the specific components of the fight reaction – purring and hissing – were unaffected by the tranquilizers imipramine and meprobamate.

The fact that benactyzine and librium raise the threshold for manifestation of all components of the fight reaction, while haloperidol completely blocks the flight reaction, is evidence that a probable site of application of the action of these drugs on the emotional reactions described is probably the region of the anterior hypothalamus and the paraventricular nucleus.

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