EFFECT OF PHARMACOLOGICAL AGENTS ON INTRASPECIES AGGRESSION

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Aggressiveness arising in rats confronted with an unavoidable nociceptive stimulus is the result of overexcitation of the animals and can be used to detect the sedative effect of psychotropic drugs. A method of evoking motivated fighting in rats for their territory which is suitable for use for determination of the tranquilizing effect of psychotropic drugs is described. It was shown by means of this method that trifluoperazine, haloperidol, amitryptiline, imipramine, chloridazepoxide, diazepam, and benactyzine, in small doses, have a tranquilizing action whereas pentobarbital and chlorpromazine have a mainly sedative action.

KEY WORDS: social behavior of animals; aggression; psychotropic drugs.

To predict the ability of psychotropic drugs to prevent states of stress and hostility in man a number of experimental models combined under the general name of "experimental aggressiveness of animals" have been used [5, 10]. Experimental aggressiveness has various causes and it is often the result purely of excessive excitation of animals [13]. To detect substances with a specific antiaggressive action, it is therefore necessary to use aggressive responses determined by near-natural motives and characteristic of the species of animal studied. The writers previously studied the effect of psychotropic drugs on interspecies aggression with or without an emotional component [1, 2].

In the present investigation the effect of psychotropic drugs was studied on intraspecies aggression caused by a struggle for territory.

EXPERIMENTAL METHOD

Experiments were carried out on 1,260 male albino rats weighing 200-230 g in a chamber measuring $60 \times 55 \times 50$ cm, with a wooden stool in the center ($8 \times 8 \times 6$ cm – the minimal area holding two rats). Electric shocks 1 sec in duration, with a frequency of one shock every 3 sec and with a voltage of 60-70 V were applied to the electrode floor. A natural reflex of avoiding painful electrical stimulation of the feet by jumping onto the stool in under 5 sec, where it could sit for 15 sec, after which it was pushed off into an empty box, and the procedure was repeated 1 min later, was produced separately in each rat. The preservation of the avoidance reflex was tested next day, and the rat was used in the experiment 2 h later. In experiments with unavoidable stimulation (with no stool) the number of cycles of fights between two rats in 1 min was recorded. A cycle was taken as a period of fighting in the vertical posture (blows with the limbs, biting, and so on) until the animal came down onto all four limbs. In these experiments both rats trained to jump on to the stool and untrained rats were used. In experiments in which two rats jumped onto the stool, whether or not a pair of rats jumped together was recorded over a period of 1 min, using as the criterion the presence of the two rats together on the stool for 10 sec. To prevent training in combined occupation of the stool, each rat was used in the experiment once only. The results were subjected to disperson analysis [6].

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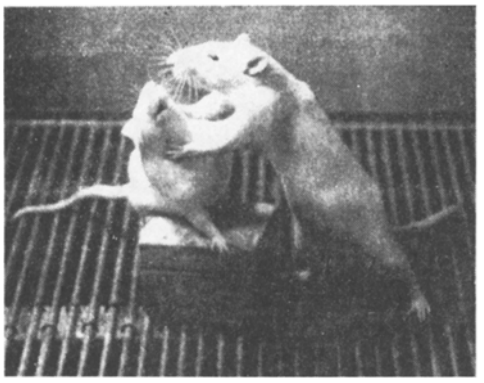

Fig. 1

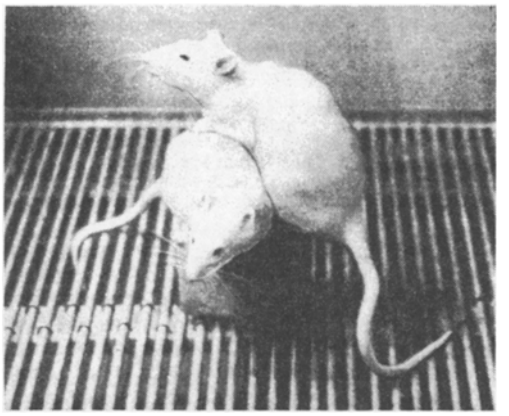

Fig. 2

Fig. 1. Rats fighting for possession of the stool.

Fig. 2. Sharing of the stool by two rats after administration of diazepam (0.5 mg/kg).

The pharmacological agents were injected intraperitoneally 30 min before the experiment in the following doses (in mg/kg): pentobarbital 0.25-4, chlorpromazine 0.25-3, trifluoperazine 0.1-2, haloperidol 0.1-5, amitryptiline 0.5-5, imipramine 0.5-5, chlordiazepoxide 1-20, diazepam 0.1-10, and benactyzine 0.1-5. Each subsequent dose was twice as large as its predecessor. With each dose two groups, each containing seven pairs of rats trained to jump on to the stool, were used. The rats of one group were placed in pairs in a chamber without a stool, the rats of the other group in a chamber with a stool.

EXPERIMENTAL RESULTS

In a situation of unavoidable stimulation the rats began to fight first after provocation by posture (getting up onto the hind limbs in response to a shock), and during subsequent stimulation, whenever the rats were brought together. Under these circumstances a rat could attack not only its partner, but also any convenient object (the feeding bowl, a wooden rod, and so on). In this situation 4.3 ± 0.6 cycles of fighting developed, but if the voltage was reduced by half (30-40 V) the number of cycles of fighting was reduced proportionally (1.8 ± 0.4). If the aggressiveness arising under these conditions was motivated, it might be expected that the number of cycles of fights between rats trained to jump on to the stool would differ in the chamber without the stool from the number among untrained rats, for frustration has a strong influence on motivated behavior [8]. However, this was not found (4.0 ± 0.5 cycles of fighting among untrained rats).

In a situation in which the stimuli could be avoided, no combined jumping by a pair of rats onto the stool was observed, and fighting began between the rat occupying the stool and the rat attempting to jump up alongside and continued throughout the experiment (Fig. 1). The possibility of provocation of aggression by posture in this situation (getting up on the hind limbs while jumping on to the stool) was tested by replacing the stool by a square stool of the same area, although in this case also no sharing of the stool took place and fights ensued. The characteristic similarity between these fights and the struggle for ownership of territory with a stranger under natural conditions is characteristic [7]. If the area of the stool was increased by 1.5 times or the strength of stimulation reduced by half, shared occupation of the stool took place in every case. Dispersion analysis showed that two factors influence shared occupation ($P < 0.01$): the strength of stimulation, an increase in which caused the aggressiveness of the rats to increase, and the area of the stool, a reduction in which was accompanied by fighting for territory.

Fighting between the rats, if stimulation was unavoidable, was not motivated (provocation by posture, no effect of frustration) and was determined by the strength of stimulation; the same situation could, however, evoke not fighting, but copulation, if rats of different sexes were used [9]. The aggressiveness arising in the chamber without the stool can thus be regarded as a distinctive type of response to extreme excitation of the rats. Fighting developing between rats jumping onto the stool, on the other hand, is clearly motivated. It was not provoked by posture, was directed purely against the partner, and only an increase in the area of the stool led to shared occupation.

The pharmacological agents studied differed in their effectiveness in preventing nonmotivated and motivated aggression. The values of ED_{50} (in mg/kg) for inhibiting fighting in the chamber without the stool were as follows for the various drugs: pentobarbital 2, chlorpromazine 1.1, trifluoperazine 1, haloperidol 3.2, chlordiazepoxide 17.5, diazepam 5.6, and benactyzine 3.6. Antidepressants in a dose of 5 mg/kg increased the number of cycles of fighting, but in smaller doses they had no effect. For restoring the number of joint occupations of the stool to normal (Fig. 2), the values of ED_{50} for these substances were (in mg/kg): pentobarbital 1.9, chlorpromazine 1, trifluoperazine 0.24, haloperidol 0.27, amitryptiline 0.58, imipramine 0.42, chlordiazepoxide 1.3, diazepam 0.16, and benactyzine 0.23. Pentobarbital and chlorpromazine thus inhibit both types of aggression in equal doses, the antidepressants abolished only motivated aggression, whereas the tranquilizers, as well as trifluoperazine and haloperidol, inhibited motivated aggression in much smaller doses than nonmotivated.

During the inhibition of fighting arising in response to unavoidable stimulation, the sedative effect of the pharmacological agents was exhibited, for aggressiveness under these circumstances was due to excessive excitation of the rats and was emotional in character. On this basis the absence of any effect on this form of aggressiveness, or even an increase in its intensity, by the action of antidepressants is understandable, although imipramine, for example, has an antiaggressive action in other tests [1, 12]. Considering the motivated character of the fighting for possession of the box, and also that the situation under these circumstances is one of conflict, the restoration of normal joint occupancy to avoid stimulation under the influence of the drugs studied can be regarded as a manifestation of their tranquilizing effect, not a general inhibition of emotions but correction of the motives of behavior inducing the fighting, provided that aggressiveness evoked by excessive excitation of the rats (fighting without the stool) was not suppressed in these same doses.

Complete restoration of normal joint occupancy of the stool to avoid stimulation was achieved by increasing the doses of the drugs to the following (in mg/kg): trifluoperazine 0.52, haloperidol 0.7, amitryptiline 4.6, imipramine 2.8, chlordiazepoxide 5, diazepam 0.46, and benactyzine 0.65. With an increase in the doses of pentobarbital and chlorpromazine above ED_{50} the number of cases of sharing the stool was reduced and the avoidance reflex was disturbed. In the same doses fighting was inhibited in the presence of an unavoidable stimulus, suggesting a predominantly sedative action of the pentobarbital and chlorpromazine [4, 11].

The results indicate that tranquilizers are effective in the case of intraspecies aggression. Previous investigations showed that tranquilizers are ineffective in the case of interspecies aggression [1, 2], so that the mechanisms of formation of intraspecies and interspecies aggression are presumably different. The model described above is more sensitive for the detection of the tranquilizing action of drugs than the method used previously [3] in which one individual runs away in response to nociceptive stimulation.

The effectiveness of the drugs tested in small doses indicates that the use of intraspecies relations between animals is a suitable technique with which to study psychotropic drugs.

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