EFFECT OF PSYCHOTROPIC DRUGS ON CONDITIONED REFLEXES IN CATS AFTER EMOTIONAL EXCITATION

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After emotional responses of fear and rage differential inhibition and short-term memory are disturbed in cats. Trifluoperazine, haloperidol, amitriptyline, imipramine, chlordiazepoxide, diazepam, and benactyzine prevent the development of these disturbances. Chlorpromazine, as well as trifluoperazine and haloperidol in large doses (1 and 2 mg/kg), intensify the disturbances taking place. Unlike neuroleptics, the tranquilizers and antidepressants tested restore normal higher nervous activity over a wider range of doses; consequently, their use is to be preferred for the elimination of adverse sequelae of powerful emotional responses.

KEY WORDS: *emotional stress; conditioned reflex; psychotropic drugs.*

Emotional stress in man causes elevation of thresholds of perception [7], disturbs the objective assessment of time intervals [11, 12], and impairs occupational activity [11, 14].

The writer showed previously that after responses of fear and rage, attention in cats is weakened and tranquilizers (chlordiazepoxide, diazepam, and benactyzine), neuroleptics (trifluoperazine and haloperidol), and antidepressants (amitriptyline and imipramine) can restore attention to normal again [3].

The object of this investigation was to study the effect of psychotropic drugs on the disturbances of conditioned reflexes produced in cats by responses of fear and rage.

EXPERIMENTAL METHOD

Experiments were carried out on 19 cats with electrodes implanted into the anterior hypothalamus [13]. The parameters of stimulation and the manifestations of the responses of fear and rage evoked by threshold stimulation were described earlier [3]. A conditioned avoidance reflex was produced in 10 cats in a chamber measuring 75 X 50 X 55 cm with an electrode floor. The conditioned stimulus was the ringing of a bell, and 15 sec after it started, a painful electric shock was applied to the cat's paws. By pressing on a pedal the cat could prevent or stop this stimulation. The differential stimuli were a tone of 100 Hz and clicks (frequency 10/sec). A delayed conditioned food reflex was produced in seven cats in the same chamber. The conditioned stimulus in this case was light acting for 10 sec. Food reinforcement was given if the cats pressed on the pedal not before 6 sec and not later than 30 sec after stopping the conditioned stimulus. A conditioned reflex coinciding with the

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food reflex, consisting of pressing on the pedal during the action of the conditioned stimulus, was produced in two cats under the same conditions. Short-term memory was deemed not to be disturbed if the delayed conditioned reflex was restored after emotional excitation at the same times as the coincident reflex.

The drugs for testing were injected intraperitoneally 1 h before the experiment in doses (mg/kg body weight) of: chlorpromazine 0.1-1, trifluoperazine 0.25-2, haloperidol 0.25-2, amitriptyline 0.5-5, imipramine 0.5-5, chlordiazepoxide 1-5, diazepam 0.1-1, and benactyzine 0.25-1. Each consecutive dose was twice the one that preceded it. Significance of the difference between sample means was assessed by Fisher's criterion [8].

EXPERIMENTAL RESULTS

The conditioned avoidance reflex was not disturbed after a response of fear and rage. Its latent period in the control series was 5.6 ± 3.3 sec, falling after emotional excitation to 4.3 ± 2.9 sec. Differentiation to clicks was preserved but differentiation to the tone was disturbed: in 70% of presentations of the tone the cats pressed on the pedal.

Trifluoperazine and haloperidol, in doses of up to 0.5 mg/kg, and chlorpromazine, amitriptyline, imipramine, chlordiazepoxide, and diazepam, in all doses studied, had no effect by themselves on the conditioned avoidance reflex. Trifluoperazine and haloperidol, in doses of 1 and 2 mg/kg, inhibited the avoidance reflex so that it appeared in response to 70 and 30% of presentations respectively. Benactyzine in doses of 0.5 and 1 mg/kg disturbed differentiation to the tone.

After responses of fear and rage, the test drugs restored differentiation to the tone to normal in the following doses (in mg/kg): trifluoperazine 0.5, haloperidol 0.5, amitriptyline 2.5 and 5, imipramine 2.5 and 5, chlordiazepoxide 2.5 and 5, diazepam 0.25, 0.5, and 1, and benactyzine 0.5 and 1. Chlorpromazine, in doses of 0.5 and 1 mg/kg, had no effect on the avoidance reflex, whereas trifluoperazine and haloperidol in doses of 1 and 2 mg/kg, which inhibited the avoidance reflex only partially, completely suppressed that reflex in the period after emotional excitation: the cats pressed on the pedal only if unconditioned reinforcement by the electric current was given.

After responses of fear and rage the delayed and coincident conditioned food reflexes were lost, as also was the natural food response. Eating food was restored 2.0 ± 0.7 min after stimulation ceased, and the coincident conditioned reflex was restored after 8.4 ± 2.8 min. The delayed conditioned reflex began to recover after 1 min (i.e., after restoration of the coincident reflex to normal), and it was fully restored 22.1 ± 4.3 min after hypothalamic stimulation.

The substances used, except benactyzine, had no effect by themselves on the delayed conditioned reflex. Benactyzine, in doses of 0.5 and 1 mg/kg, inhibited both the delayed reflex and the natural food response. After emotional excitation, however, administration of benactyzine in these doses led the cats to eat the food and in 30% of cases a delayed reflex appeared. Trifluoperazine and haloperidol, in a dose of 0.5 mg/kg, amitriptyline in doses of 2.5 and 5 mg/kg, imipramine in doses of 2.5 and 5 mg/kg, chlordiazepoxide in doses of 2.5 and 5 mg/kg, and diazepam in doses of 0.25. and 5 mg/kg restored the delayed reflex to normal in the course of the same period as the coincident reflex, i.e., in the course of 2-3 min.

Subthreshold hypothalamic stimulation which did not evoke emotional responses had no effect on the conditioned reflexes in the cats.

The disturbances of internal inhibition and short-term memory observed in these experiments are characteristic of nervous overstrain [1-12] and are similar to those found in neurosis and the postneurotic period [4, 5]. The psychotropic drugs studied, except chlorpromazine, prevent the onset of these disturbances possibly by strengthening internal inhibition [2, 9, 10]. This effect appeared on the administration of the

same doses as those preventing the weakening of attention after emotional excitation [3]. Chlorpromazine (0.5 and 1 mg/kg), and also trifluoperazine and haloperidol with an increase in dose up to 1 and 2 mg/kg, increased the severity of the disturbances.

Unlike neuroleptics, tranquilizers and antidepressants restore higher nervous activity to normal after emotional excitation within a wider range of doses and exert a stimulant action on the CNS in approximately the same doses [6]; this makes them the drugs of preference for use to eliminate the adverse sequelae of strong emotional responses.

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