EFFECT OF PSYCHOTROPIC DRUGS ON ORIENTING AND INVESTIGATIVE BEHAVIOR AFTER FRIGHT INDUCED BY ACOUSTIC STIMULATION

R. M. Salimov

UDC 615.214.015.4:612.833.9

After frightening acoustic stimulation a state of alertness and anxiety arises and leads to weakening of attention to the new situation and intensification of the orienting reaction toward the source of sound. Defensive motivation arising under these conditions does not change with an increase in loudness of the sound. The tranquilizers diazepam (Seduxen), benactyzine, and chlordiazepoxide (Librium), the antidepressants amitriptyline and imipramine, and the neuroleptics trifluoperazine and haloperidol, in small doses, prevent these disturbances. Pentobarbital, chlorpromazine, and also trifluoperazine and haloperidol in large doses, do not prevent these consequences of emotional excitation.

KEY WORDS: psychotropic drugs; emotional stress; orienting-investigative behavior.

In the period after fright, the consequent defensive motivation persists [1], the orienting reaction relative to the stimulus inducing the emotional response is intensified [6], and attention to the situation, as manifested in investigative behavior, is weakened [9]. As a result, behavior adequate to the situation may be impaired [3]. It is therefore interesting to study the effect of certain members of the neuroleptic, tranquilizer, and antidepressant groups of drugs on investigative behavior and the orienting reaction after frightening acoustic stimulation.

EXPERIMENTAL METHOD

Experiments were carried out on 95 male Wistar rats weighing 180-200 g and 11 cats weighing 2-3 kg. For 2 h the rats were accustomed to being lifted by hand and placed in a chamber measuring 38 × 30 × 30 cm, lined inside with white foam plastic, and which also contained a wood block measuring 6 × 5 × 4 cm. After exposure to acoustic stimulation (a tone of 200 Hz, 20 dB) for 10 sec the rats were allowed to investigate the situation for 3 min. The duration of visually assessed episodes of contact investigation of the surroundings with the vibrissae on their head was recorded by activating an SSESh-63 counter for the corresponding time. The interval between successive placings of the rats in the chamber was 3 min. The duration of the period of immobility during action of the acoustic stimulus served as the index of alertness, whereas the number of defecations during 3 min of investigations served as the index of fear [7].

Cats were placed in a chamber measuring 75 × 55 × 65 cm with a viewing window 7 cm in diameter. Acoustic stimulation (a tone of 200 Hz, 20 or 40 dB) was applied 5 min later through a telephone mounted in the ceiling of the chamber for 5 sec. The sound was applied four times during the experiments at intervals of 6 min. Before and after application of the sound the orienting reactions were recorded every 5 sec for 2.5 min as rotations of the head toward the source of sound and indrawing of the ears, reflecting a state of alarm [8]. To make the indices recorded comparable, changes in them were expressed as ratios of their initial level: $f' = (f_i - f_k)/f_k$, where f_k is the number of episodes before acoustic stimulation and f_i the number after stimulation. The drugs were injected intraperitoneally into the rats 30 min, and into the cats 1 h, before the experiments in doses of (mg/kg): pentobarbital 2, chlorpromazine 1, trifluoperazine 0.5 and 1, haloperidol 0.5 and 1, diazepam 0.5, benactyzine 0.5, chlordiazepoxide 5, amitriptyline 5, and imipramine 5. The mean values of the recorded indices and their confidence limits for $P = 0.05$ and the significance of the difference by Fisher's method were calculated [2].

Institute of Pharmacology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 84, No. 11, pp. 579-582, November, 1977. Original article submitted May 13, 1977.

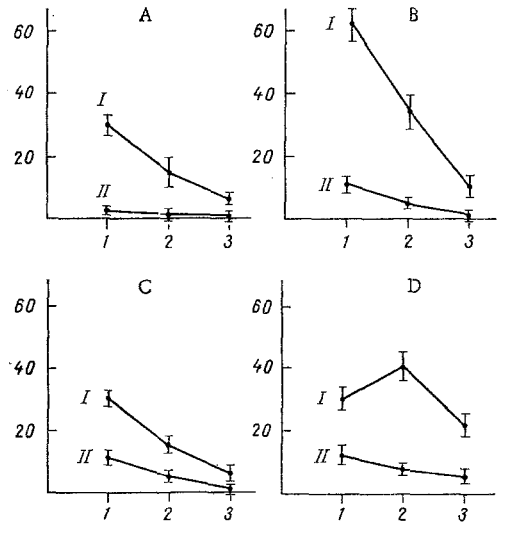

Fig. 1

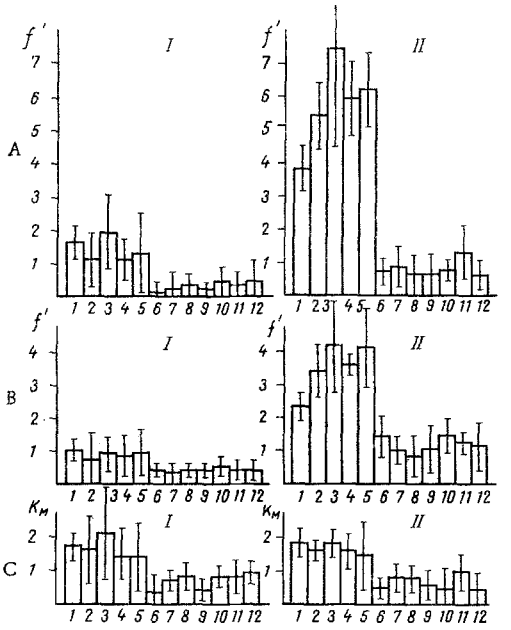

Fig. 2

Fig. 1. Effect of experimental conditions on investigative behavior in rats. A) Empty chamber; B) chamber with wooden block; C) chamber with wooden block after acoustic stimulation; D) chamber with wooden block, acoustic stimulation before first session of investigation only. I) Investigation of chamber; II) investigation of wooden block or of central part of floor corresponding to it. Abscissa, No. of session of investigation; ordinate, duration of investigation (sec).

Fig. 2. Effect of psychotropic drugs on increase in number of episodes of pressing in of the ears (A) and orienting reaction (B) relative to initial level (f') and on coefficient of defensive motivation (C) of cat after acoustic stimulation (K_M). I) After stimulation at 20 dB; II) at 40 dB. 1) Without drugs; 2) pentobarbital; 3) chlorpromazine; 4) trifluoperazine 1 mg/kg; 5) haloperidol 1 mg/kg; 6) trifluoperazine 0.5 mg/kg; 7) haloperidol 0.5 mg/kg; 8) diazepam; 9) benactyzine; 10) chlordiazepoxide; 11) amitriptyline; 12) imipramine.

EXPERIMENTAL RESULTS

The time during which the rats investigated the floor and walls of the chamber in which the block of wood was placed was twice as long as in an empty chamber ($P < 0.001$) (Fig. 1A, B), and this can be interpreted as a manifestation of attention to the situation and not merely as a response to its novelty. This difference disappeared as the investigative reaction was extinguished. During acoustic stimulation the period of immobility lengthened from 1.0 ± 0.9 to 4.3 ± 1.9 sec and the number of defecations increased from 0.3 ± 0.3 to 2.2 ± 1.5 ($P < 0.05$). After acoustic stimulation the investigation of the empty chamber was unchanged but the period of investigation of the floor and walls of the chamber containing the wooden block was reduced (Fig. 1C), indicating a weakening of attention to the surroundings. If acoustic stimulation was applied only once, before the first session of investigation, during the second session the duration of investigation of the floor and walls of the chamber with the block was increased ($P < 0.05$) (Fig. 1D).

The drugs used differed in their effect on investigative behavior in the chamber with the wooden block after acoustic stimulation (Table 1). Pentobarbital, chlorpromazine, and also trifluoperazine and haloperidol in doses of 1 mg/kg, reduced the number of defecations but did not affect the immobility or weakening of attention to the situation. The possibility cannot be ruled out that they themselves could disturb the investigative reaction, for trifluoperazine and haloperidol in doses of 0.5 mg/kg prevent this weakening of attention. Chlorpromazine, in a larger dose, can actually intensify the disturbance of investigative behavior caused by emotional stress [7]. The tranquilizers diazepam, benactyzine, and chlordiazepoxide and the antidepressants amitriptyline and imipramine prevented immobility, defecations, and weakening of attention to the situation after fright.

TABLE 1. Effect of Psychotropic Drugs on Disturbance of Investigative Behavior in Rats after Acoustic Stimulation (M ± m)

Experimental conditions (drug and dose, mg/kg)	Duration of immobility during acoustic stimulation, sec	Number of defecations during 3 min of investigation	Duration of investigation, sec	
			of walls and floor of chamber	of wooden block in center of chamber
Control (without acoustic stimulation)	1,0±0,9	0,3±0,3	60,2±5,2	9,8±2,2
Control (after acoustic stimulation)	4,3±1,9	2,2±1,5	29,6±3,0	10,6±2,4
Pentobarbital, 2	5,0±3,1	1,0±0,9	28,2±4,3	10,0±2,7
Chlorpromazine, 1	4,2±2,2	0,4±0,8	26,0±4,0	9,8±2,1
Trifluoperazine:				
1	6,0±2,7	0,6±0,8	25,0±4,0	8,0±2,0
0,5	0,6±0,8	0,2±0,4	56,6±2,8	9,6±1,9
Haloperidol:				
1	4,8±2,7	0,4±0,8	25,6±5,0	7,0±1,9
0,5	0,4±0,8	0,0	55,8±4,3	8,8±2,3
Diazepam, 0.5	1,0±1,3	0,3±0,5	57,6±4,6	10,2±2,1
Benactyzine, 0.5	0,6±0,8	0,6±0,8	56,4±2,6	10,6±3,1
Chlordiazepoxide, 5	0,6±0,8	0,6±0,8	54,8±2,9	7,8±2,2
Amitriptyline, 5	0,6±0,8	0,4±0,8	57,0±3,2	11,2±2,7
Imipramine, 5	0,4±0,5	0,8±0,7	52,8±4,0	10,2±1,4

At the moment of acoustic stimulation the cats "froze" on the spot, pressed in their ears, and looked in the direction of the source of sound (manifestations of fright) [8]. After acoustic stimulation with an intensity of 20 dB the number of episodes of the orienting reaction and pressings in of the ears increased from 4.1 ± 1.2 to 7.2 ± 1.8 and from 2.2 ± 0.7 to 4.8 ± 1.3, respectively ($P < 0.01$) and after acoustic stimulation at 40 dB to 12.2 ± 3.2 and 9.2 ± 2.4, respectively. This intensification of alarm and of the orienting reaction toward the source of sound after fright probably reflects the cat's assessment of the situation as potentially dangerous.

Pentobarbital, chlorpromazine, and also trifluoperazine and haloperidol in doses of 1 mg/kg, did not affect the number of episodes of the orienting reaction or of pressing in the ears in cats before acoustic stimulation and after stimulation at 20 dB, but after acoustic stimulation at 40 dB the number of episodes of these reactions increased. Diazepam, benactyzine, chlordiazepoxide, amitriptyline, imipramine, and also trifluoperazine and haloperidol in doses of 0.5 mg/kg, reduced the number of episodes of the orienting reaction and of pressing in of the ears after acoustic stimulation (Fig. 2A, B) although they did not affect them before stimulation.

In a situation of anticipation of possible punishment, Simonov [4] demonstrated the following relationship between an index reflecting the degree of emotional stress (P_{en}) and the index of deficiency of information for removing the indeterminacy of the situation ($P_{\Delta i}$), namely: $P_{en} = K_M \cdot P_{\Delta i}$, where K_M is a coefficient reflectng the magnitude of the corresponding motivation. In the present case, P_{en} is f' for pressing in of the ears [8], and $P_{\Delta i}$ is f' for the orienting reaction [5]. In that case, the value of the coefficient of defensive motivation can be determined as follows: K_M = f' for pressing in of the ears/f' for the orienting reaction. As Fig. 2C shows, K_M had the same value after acoustic stimulation of different loudness, and consequently it evidently reflects the discrete character of the change in the corresponding motivation. Diazepam, benactyzine, chlordiazepoxide, amitriptyline, imipramine, and also trifluoperazine and haloperidol in doses of 0.5 mg/kg reduced the defensive motivation arising as a result of fright (Fig. 2C). Pentobarbital, chlorpromazine, and also trifluoperazine and haloperidol in doses of 1 mg/kg, had no effect on the magnitude of the resulting defensive motivation.

The data indicate that defensive motivation persisting after fright leads to weakening of attention to the situation and strengthening of the orienting reaction directed toward the source of the frightening sound. These disturbances can be prevented by the tranquilizers and antidepressants used, and also by the neuroleptics trifluoperazine and haloperidol in small doses.

LITERATURE CITED

1. A. V. Val'dman, in: The Experimental Neurophysiology of Emotions [in Russian], Leningrad (1972), pp. 108-123.
2. N. A. Plokhinskii, Biometrics [in Russian], Moscow (1970), p. 130.
3. R. M. Salimov, Byull. Éksp. Biol. Med., No. 8, 61 (1975).
4. P. V. Simonov, The Theory of Reflection and the Psychophysiology of Emotions [in Russian], Moscow (1970), p. 24.
5. O. G. Chorayan and T. A. Petrosova, Vopr. Psikhol., No. 3, 133 (1976).

6. G. Bohlin, Psychophysiology, 13, 345 (1976).
7. S. E. File, Psychopharmacologia (Berlin), 32, 193 (1973).
8. S. Norton and E. J. De Beer, Ann. N. Y. Acad. Sci., 65, 249 (1956).
9. D. I. Williams, Anim. Behav., 19, 365 (1971).

EFFECT OF PHENTOLAMINE AND OBSIDAN ON MORPHOMETRIC INDICES OF THE ISLETS OF LANGERHANS IN RATS RECEIVING ALLOXAN

T. G. Anishchenko and O. V. Artemenko

UDC 612.349.7.014.2.014.46 : 547.854.6].014.46 :615.217.24

Chronic administration of phentolamine and obsidan to rats previously treated with alloxan alleviated the destructive action of alloxan on the B cells and promoted new islet formation. It is suggested that phentolamine and obsidan block one of the possible mechanisms of the destructive action of alloxan on the islet tissue, connected with the intensification of adrenalin secretion.
KEY WORDS: islets of Langerhans; alloxan; adrenoreceptors; phentolamine; obsidan.

Both the parasympathetic and the sympathetic nervous systems participate in the regulation of the endocrine function of the pancrease [6]. An inhibitory effect of sympathetic nerves on B cell function has been found in experiments with sympathetic denervation of the pancreas [4, 7] and administration of α- and β-adrenoreceptor-blocking drugs. In the last case hyperemia of the islet-cell apparatus, an increase in the Zn concentration in the cytoplasm of the B cells, and the formation of new islets of Langerhans are observed, evidence of an increase in insulin-forming function during adrenoreceptor blockade [5].

The question naturally arises whether this stimulating action of chemical desympathization is manifested after injection of alloxan and whether administration of blocking agents would alleviate to some extent the action of alloxan on the islets of Langerhans.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats with an initial mean weight of 250 g. Diabetes was produced by subcutaneous injection of alloxan in a dose of 15 mg/100 g body weight. In a high proportion of the animals the first injection of alloxan did not cause the development of diabetes, as reflected in the level of the diuresis and the appearance of sugar in the urine. Alloxan was injected again into these animals in the same dose on the 12th day of the experiment. The total duration of the experiment was 24 days.

Phentolamine and obsidan were injected intramuscularly throughout the period of the experiment in doses of 2 mg/100 g body weight and 2-3 mg per rat, respectively, daily. On the days when alloxan was injected, phentolamine and obsidan were injected intramuscularly 2 h before the alloxan.

Sections through the pancreas 5 μ thick were stained with aldehyde–fuchsin by Gomori's method in Dyban's modification. The following morphometric indices were used: the relative percentage of islet tissue, the number of islets per 10 mm^2 area of section, the mean area of an islet, the number of B and A cells per islet, the ratio between the numbers of B and A cells, and the area of the nuclei of the B and A cells.

The pancreases of intact rats served as the control.

Department of Human and Animal Physiology, N. G. Chernyshevskii Saratov University. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 84, No. 11, pp. 582-584, November, 1977. Original article submitted June 7, 1977.

 0007-4888/77/8411-1606$07.50