GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

Effect of Experimental Neurotic Stimulus on Behavior and Learning Ability of Mice

N. I. Suslov, A. M. Dygai, E. G. Skurikhin, A. A. Churin, N. V. Provalova, and E. D. Gol'dberg

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The effects of conflict situation and deprivation of REM sleep and their successive combination on behavior, learning, and memory of CBA mice were studied. It was found that these interventions induce transient disturbances of emotional reactions and of orientating and exploring behavior and sustained disturbances of zoosocial behavior (increased aggressiveness and changed nature and intensity of communication) as well as impair the development and consolidation of conditioned reflex, without any effect on a previously developed reflex.

Key Words: *experimental neurotic stimulus; zoosocial behavior; aggressiveness; learning ability; memory*

Changes in social relations are an important component of the stress-induced behavioral shifts [2]. Neurotic influences alter zoosocial contacts and increase aggressiveness, particularly toward intruders [2,4]. However, the literature data on this issue are controversial.

Previously, we showed that conflict situation and deprivation of REM sleep induce contralateral changes in the blood of experimental animals. In this study we investigated the behavior of mice exposed to neurotic influences.

MATERIALS AND METHODS

Experiments were performed on 400 male CBA mice weighing 18-20 g. The effects of conflict situation (CS) [3], deprivation of REM sleep (DRS) [6] for 48 h, and their successive combination (CS—DRS) on orientating and exploring behavior in the open field test [7], emotional reaction [5], development and reproduction of the passive avoidance reflex (PAR) [1] were studied. In order to assess changes in zoosocial behavior, after neurotic influence a mouse was placed in a plastic cage (10×25 cm) for 1 h (resident). Then an intact outbred male mouse (intruder) was placed in this cage, and the animals were observed for 10 min. The duration of the first communication with the intruder, the number and duration of subsequent communicative episodes, the total number of aggressive incidents (fights and threatening postures) initiated by the resident were recorded. The passive avoidance reflex was developed immediately before, 24 h, and 7 days after neurotic influence. The retention of the reflex was tested 1 h, 1, 3, 7, 10, 14, 21, and 30 days after its development. Intact mice with PAR served as a control. Special control (mice tested for PAR 7 days after its development) was used for mice in which neurotic stimuli were applied 7 days after the development of PAR. Statistical analysis was performed using Student's *t* test.

Institute of Pharmacology, Tomsk Research Center, Siberian Division of the Russian Academy of Medical Sciences

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RESULTS

Neurotic stimuli caused considerable behavioral changes in male CBA mice. A sharp increase in the intensity of emotional response was observed 2 h after stimulation, the increase being particularly high in mice subjected to CS—DRS. An increase in motor activity and a decrease in exploring activity in the open field test were observed in all mice exposed to CS, DRS, and CS—DRS. In CS—DRS mice, the intensity of all tested behavioral reactions increased, the increase in motor activity being the highest. Changes in exploring and orienting activities and in emotional reactions occurred within several hours after neurotic stimulation. Then behavioral reactions of stimulated mice did not differ from the control.

Changes in zoosocial behavior were prolonged and varied depending on neurotic stimulus (Table 1). A decrease in the duration of the first and subsequent communications with an increase in this parameter on day 3 and the absence of aggressiveness were observed in mice exposed to CS. The same held true for DRS mice; however, by the 3rd day this parameter and aggressiveness increased. By contrast, after exposure to CS—DRS a sharp increase was observed in the duration and number of communications within the first hours and a decrease in these parameters after 24 h with subsequent increase on the 3rd day. On day 3 after neurotic stimulation, the number of episodes of aggressiveness increased in DRS and CS—DRS mice, while in control mice it decreased. It should be noted that in the control group the resident attacked the intruder after actively approaching it, while in DRS and CS—DRS groups approaching intruder was attacked.

Thus, neurotic stimulation produces ambivalent effects on the behavior of CBA mice. We think that increased orientating and exploring activities are indicative of anxiety due to asthenization within the first hours after stimulation. Changes in zoosocial behavior point to profound disturbances in the sphere of individual contacts and territorial behavior. Based on complex dynamics of these changes, it can be suggested that they are associated primarily with impaired processing of new information and weakening of motivation mechanisms. The shortening of the first communication implies a reduced informational capacity of the short-term memory, while its prolongation indicates impaired primary processing of information. Different periods and intensity of behavioral alterations may result from phasic shifts of the corresponding changes due to profound disturbances that were observed in the CS—DRS model.

Neurotic stimulation produced a negative effect on the development of PAR (Table 2) particularly in mice exposed to CS—DRS. Neurotic stimulation at longer

TABLE 1. Parameters of Zoosocial Behavior of Mice after Neurotic Simulation ($X \pm m$)

Time after stimulation, h	Duration of the first communication, sec	Total communication time, sec	Number of communication episodes	Number of aggressiveness episodes	Number of aggressive residents, %
Control group					
2	37.6±5.2	54.0±8.7	7.0±1.3	0.0±0.0	0
24	32.4±4.3	38.8±5.6	4.4±0.6	5.0±1.0	30
72	18.2±1.2	32.2±3.9	3.8±0.3	3.0±0.9	20
Conflict situation					
2	9.8±1.5**	28.2±4.0*	5.8±0.7	0.0±0.0	0
24	22.4±3.1	38.8±5.2	5.6±0.5	0.0±0.0	0
72	28.8±3.3*	41.6±5.6*	5.0±0.4	0.0±0.0*	0
Deprivation of REM sleep					
2	10.0±1.9**	41.0±6.3	3.8±0.7*	0.0±0.0	0
24	21.0±2.7*	71.4±6.6*	7.2±0.9	5.0±0.2	40
72	6.8±0.7**	24.4±2.9	4.6±0.3	6.0±0.5	40
Combined stimulation					
2	93.6±7.1**	133.0±7.3**	9.4±0.7	0.0±0.0	0
24	11.6±0.7*	44.2±2.9	11.6±0.8**	12.0±1.2*	40
72	41.2±5.4**	63.4±7.1**	6.0±0.3*	16.0±1.9**	60

Note. *$p<0.05$, **$p<0.01$ compared with the control.

TABLE 2. Effect of Neurotic Stimulation on Reproduction of Passive Avoidance Reflex (PAR)

Modeled situations	Time after PAR development, days							
	1 h	1	3	7	10	14	21	30
Control	86.6	91.6	91.6	75	83.3	50.0	66.6	16.6
PAR after 7 sec: test	56.2	62.5	68.7	81.2	18.7	18.7	18.7	6.2
DRS	100	90	90	90	90	80	80	60
CS	62.5	68.7	100	81.2	50	49	50	12.5
CS—DRS	100	84.6	92.3	92.3	92.3	69.2	69.2	46.1
PAR immediately after: DRS	83.3	83.3	18.1	18.1	0	0	0	0
CS	0	50	71.4	62.5	62.5	87.5	25	0
CS—DRS	0	0	0	0	0	0	0	0
PAR after 24 h: DRS	23	100	92.3	100	46.2	23	0	0
CS	0	53.8	100	15.3	7.6	0	0	0
CS—DRS	40	30	0	0	0	0	0	0
DRS immediately after PAR	0	37.5	12.5	0	0	0	0	0
CS immediately after PAR	0	75	33.3	16.6	0	0	0	0
CS—DRS immediately after PAR	0	70	40	0	0	0	0	0
CS—DRS after 24 h REM sleep	10	10	0	0	0	0	0	0

periods after development of PAR had no effect on the reflex reproduction and even facilitated it in comparison with the control. This may be associated with specificity of the chosen experimental conditions.

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