Neurotropic and Neurospecific Substances and Their Antibodies: Effects on Conditioned Activity of Rats

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We compared the effects of neurotropic and neurospecific substances and their antibodies on conditioned activity of rats. Single treatment produced the positive effect on the latency and number of conditioned responses. Repeated treatment with test compounds in the same dose improved conditioned activity of animals.

Key Words: *ultralow doses; antibodies; conditioned responses*

Here we compared the effects of substances and their antibodies synthesized by the method of potentiation and administered in ultralow doses on memory in rats. The conditioned avoidance response (CAR) served as the model of memory.

MATERIALS AND METHODS

Experiments were performed on 70 male outbred rats weighing 200-250 g. The animals were divided into 7 groups of 10 specimens each. Control rats were treated with distilled water. Experimental animals perorally received potentiated ethanol (PE, C1000), morphine (PM, C1000), brain-specific S100 protein (P-S100, C200), and potentiated antibodies to morphine (PAB-M, C30+C200), S100 protein (PAB-S100, C1000), and opiate μ-receptors (PAB-μR, C30) in a daily dose of 0.1 ml for 10 days. Test preparations were synthesized at the "Materia Medica Holding" Research-and-Production Company. The latency of CAR, number of conditioned responses, and associated behavioral reactions were assayed 30 min after treatment,

CAR was elicited with acoustic stimulation (300 bpm). The animals were placed in a shuttle box. Electrocutaneous stimulation of the limbs with suprathreshold current served as the unconditioned stimulus. CAR was considered to be elicited when the reaction developed in response to each or did not accompany only one of the conditioned stimuli presented 6 times at 2-3-min intervals [1].

The results were analyzed by Student's *t* test.

RESULTS

Single treatment with PE improved pre-elicited CAR. The latency of CAR decreased, while the number of conditioned reactions increased. Administration of PE in the same dose for 10 days had no effect on conditioned activity, which practically did not differ from that observed before treatment (Table 1).

Single treatment with PM did not change the latency of CAR and number of conditioned reactions. Administration of PM for 10 days had no effect on conditioned activity of rats. The latency and number of conditioned reactions tended to decrease up to day 10, but then did not differ from the baseline level (Table 1).

Qualitative and temporal characteristics of CAR remained unchanged after single administration of P-S100. Treatment with P-S100 for 9 days produced considerable changes in the latency of CAR. This stereotyped behavior was elicited in 100% trials. Administration of P-S100 on day 10 had no effect on conditioned activity of animals. The latency of CAR decreased, while the number of reactions surpassed that observed before treatment (Table 1). These results indicate that P-S100 improve plasticity and increase strength of nerve processes.

Single treatment with PAB-M markedly decreased the latency of CAR. The number of conditioned reactions increased insignificantly. After administration of PAB-M for 9 days the latency of CAR de-

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TABLE 1. Effects of PE, PM, P-S100, PAB-M, PAB-S100, and PAB-μR on CAR in Rats (Latency, sec, *M*±*m*, *n*=10)

Series	Single treatment		Tenfold treatment	
	before	after	before	after
Control	6.90±0.03 (89.0)	6.50±0.13 (89.0)	6.70±0.21 (95.0)	6.80±0.17 (90)
PE	6.70±0.27 (89.9)	5.50±0.29* (96.6)	6.50±0.28 (94.9)	6.40±0.28 (98.3)
PM	6.50±0.09 (93.3)	6.2±0.1 (98.3)	6.2±0.6 (88.1)	6.50±0.08 (96.6)
P-S100	6.60±0.15 (94.9)	6.30±0.16 (96.6)	5.70±0.15 (100.0*)	5.70±0.17 (100*)
PAB-M	6.40±0.08 (89.8)	5.10±0.08* (94.9)	5.60±0.08 (96.6)	6.00±0.06 (100)
PAB-S100	8.10±0.09 (88.3)	7.90±0.09 (85.0)	9.2±0.1* (94.9)	8.40±0.09 (100*)
PAB-μR	7.00±0.12 (91.5)	6.0±0.1* (93.2)	7.50±0.09 (100*)	7.20±0.06 (100*)

Note. CAR performance is shown in brackets (%). $p<0.05$: *compared to the baseline level; $^{+}$compared to parameter before the 10th treatment.

creased, while the number of reactions increased. Treatment with PAB-M on day 10 improved conditioned activity of animals. Therefore, repeated administration of PAB-M produced the cumulative effect.

Single administration of PAB-S100 practically did not affect parameters of CAR. The latency and number of reactions increased after treatment with PAB-S100 for 9 days. On day 10 the latency of CAR did not differ from that observed before treatment (Table 1). These changes indicate that the process of excitation was variable, while its strength increased.

Single treatment with PAB-μR decreased the latency and slightly increased the number of CAR. The latency of CAR increased after administration of this preparation in the same dose for 9 days. However, performance of the reaction reached 100% and significantly differed from the baseline level.

Our results indicate that single treatment with ultralow doses of test substances and distilled water (statistically insignificant) having different chemical structure and producing various effects on the central nervous system improves conditioned activity of animals. They produce the nonspecific effect, which is probably related to mobilization of adaptive reactions in response to novel stimuli affecting homeostasis of the internal environment.

Administration of test substances for 10 days improves CAR by facilitating closure of the conditioned relationship. Unstable plasticity of excitation is manifested in the varying latency of CAR and reflects the "search" for optimal functions of memory as a unit of integrative activity. It should be emphasized that homeostasis (CAR) is equalized without increasing the dose of potentiated substances.

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