Genetic Catalepsy and Ultralow Dose Antibodies to S-100B Antigen

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 146, No. 12, pp. 679-681, December, 2008
Original article submitted March 5, 2008

We studied consumption of 20% sucrose solution by rats genetically predisposed to catalepsy (GC strain) during training. The consumption of sucrose solution by GC rats was lower in comparison to that in Wistar rats. "Potentiated" antibodies to S-100B antigen administered orally after training sessions increased the number and duration of subsequent contacts of rats with sucrose solution.

Key Words: *catalepsy; training; ultralow doses; antibodies; S-100B*

The GC rats (genetic cataleptics) selected from outbred Wistar rat population for predisposition to catalepsy are characterized by behavioral and neurochemical parameters similar to those observed in depression [4]. One of the key symptoms of depression is anhedonia manifesting in animals in reduced consumption of sucrose [10,11]. Antidepressants remove this disorder. Antidepressant effects of ultralow-dose antibodies to S-100 antigen were described [3,5,6].

We studied the levels of 20% sucrose consumption during training of GC rats and the effects of ultralow-dose antibodies to S-100B antigen on this consumption.

MATERIALS AND METHODS

Experiments were carried out on adult male Wistar rats from Breeding Center of Novosibirsk State Medical Academy and on GC rats from Breeding Center of Institute of Cytology and Genetics [1]. The animals were kept 2 per cage with free access to water and food and 12:12 h light:darkness regimen. Training was carried out in a organic glass box with metal floor. Two drinking bowls with 20% sucrose solution were located at each of the lateral walls of the box.

Before training, the animals were adapted to the box 10 min per day for 4 days. Sucrose consumption was evaluated by the duration of animal contacts with the bowls. During the first 3 sessions, yellow bowls on the left were replaced with black bowls with water. Two right bowls remained yellow and contained 20% sucrose solution. Acoustic signals and electrostimulation were used in subsequent experiments. Stimulation and registration of rat reactions were realized with a PC.

Acoustic signal (800 Hz) combined with switching on the electric current (0.15 mA) [7] connected to the bowls was used for training of the avoidance reaction during three 15-min sessions. Conditioned signal (CS) was presented in 50% contacts of the animals with 20% sucrose solution. Then the animals were trained to differentiate between the acoustic signals. During two sessions, CS with current were alternating with differentiation stimulation (DS) of 200 Hz frequency without electric current. In two other sessions, the DS frequency was increased to 400 Hz, while 800-Hz signal was combined with electric current as before.

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0007-4888/08/1466-0779

Affinity-purified antibodies to S-100B antigen, prepared by serial dilutions and activation were used in experiments. These antibodies form the active principle for Proproten-100 neurotropic drug (Materia Medica Holding). Immediately after each training session, Wistar (n=8) and GC rats (n=6) received antibody solution (0.5 ml); controls (9 Wistar and 9 GC rats) received water (0.5 ml). The effects of antibodies were analyzed by comparing the summary groups consisting of Wistar or GC rats.

The number of animal contacts with drinking bowls separated by intervals of at least 5 sec and duration of each contact with sucrose solution were evaluated. The data for two latest sessions were summed up for the choice of drinking bowl and each combination of acoustic signals. The results were statistically processed using bifactorial analysis of dispersions.

RESULTS

Significantly lower consumption of sucrose by GC rats in comparison with Wistar was detected during training to choose the bowls with sucrose solution and water ($F_{1.27}$=9.90, p<0.005).

The duration of sucrose consumption in experiments with acoustic signals was lower in GC rats during CS in comparison with Wistar rats during CS and DS of 200 Hz ($F_{1.27}$=5.50, p<0.05) and 400 Hz ($F_{1.27}$=8.13, p<0.01). Glucose consumption decreased also during DS of 200 Hz ($F_{1.27}$=6.29, p<0.05) and 400 Hz ($F_{1.27}$=7.61, p<0.01; Fig. 1).

Treatment of animals with potentiated antibodies to S-100B antigen led to a significant increase in the number of contacts with drinking bowls during CS alone ($F_{1.27}$=21.18, p<0.001) and its alternation with DS of 400 Hz ($F_{1.27}$=8.41, p<0.01). The

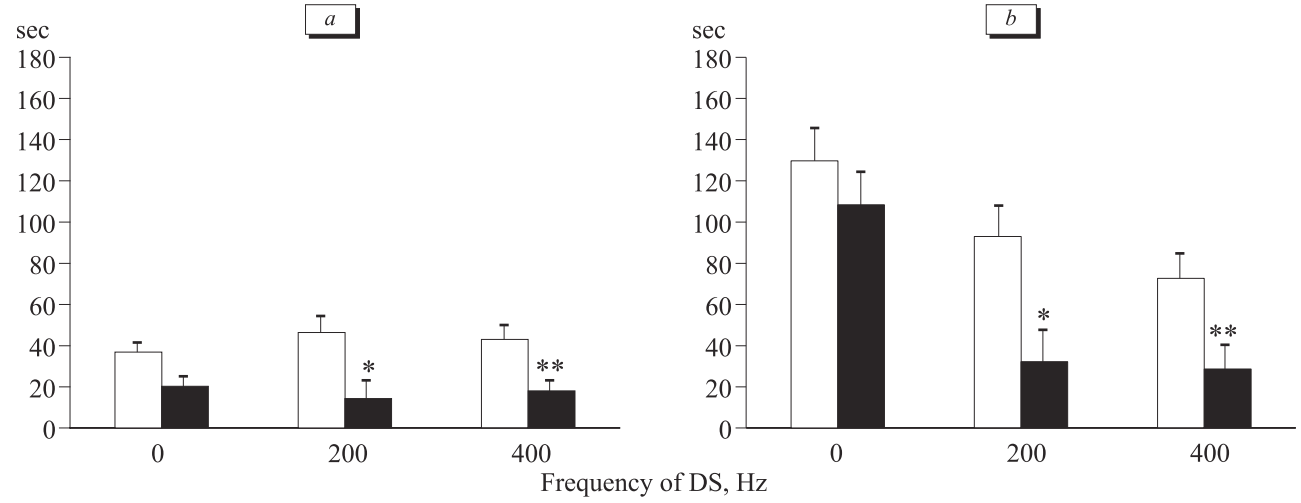

Fig. 1. Time of contact with drinking bowls for Wistar (light bars) and GC rats (dark bars) during CS and DS. *a*) alternation of CS (800 Hz) and DS; *b*) DS. *p<0.05, **p<0.01 compared to Wistar rats.

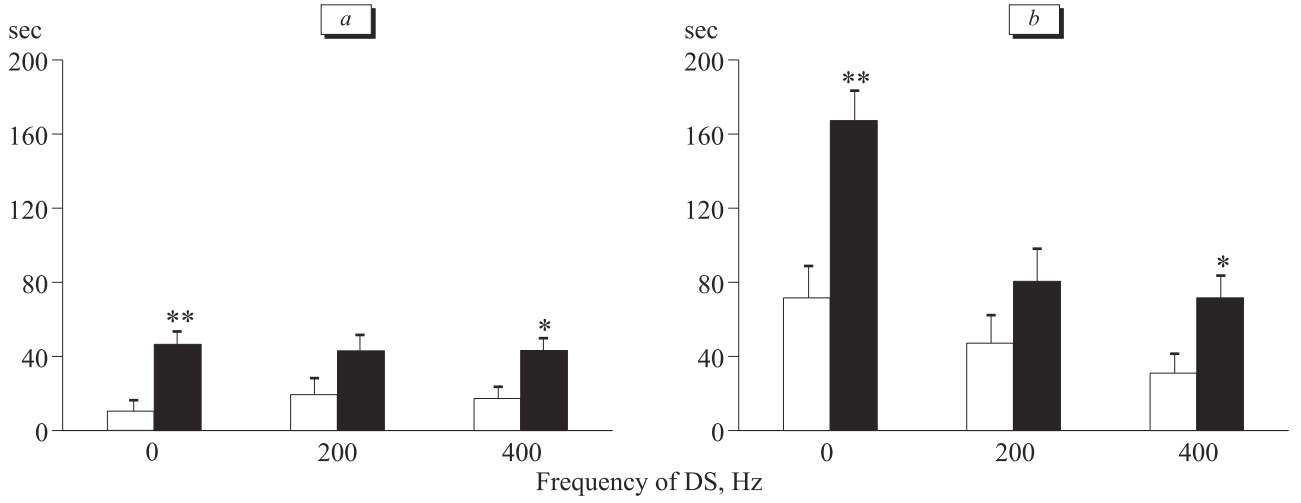

Fig. 2. Effects of potentiated antibodies on the duration of contact with drinking bowls during CS and DS. *a*) alternation of CS (800 Hz) and DS; *b*) DS. Light bars: control (potentiated water); dark bars: antibody solution. *p<0.05, **p<0.001 compared to the control.

total duration of contacts with sucrose increased under the effect of the drug during CS of 800 Hz without DS (F=15.18, p<0.001) and with DS of 400 Hz ($F_{1.27}$=7.28; Fig. 2). Moreover, antibodies to S-100B antigen increased sucrose consumption without CS ($F_{1.27}$=16.27, p<0.001) or during DS of 400 Hz ($F_{1.27}$=7.16, p<0.01).

These data suggest that treatment with antibodies to S-100B directly after training sessions modulating memory mechanisms [9] promotes better memorization of unpunished contacts with sucrose in comparison with those associated with aversive exposure. Increased sucrose consumption after antibody treatment can also be due to disorders in learning of passive avoidance of electric current by animals of both strains, though this behavioral reaction was more pronounced (drinking suppression during CS) and more generalized (reaction to DS) in GC compared to Wistar rats. This disturbed avoidance under the effect of antibodies to S-100B is in good agreement with their anxiolytic effect [8].

The efficiency of ultralow-dose antibodies to S-100B protein in rats with depression and anxiety was demonstrated previously [6]. The data obtained on GC rats also confirm the antidepressant effect of these antibodies.

The study was supported by the Russian Foundation for Basic Research (project No. 06-04-49003).

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