Psychotropic Effects of Sidnocarb and Ladasten in Inbred Mice with Different Reaction to Emotional Stress

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Dose-dependent relationship of the effects of sidnocarb and Ladasten on open field behavior and free motor activity was studied in inbred C57Bl/6 and BALB/c mice differing by emotional stress reaction phenotype. Ladasten in a dose of 10 mg/kg produced activating and anxiolytic effects on BALB/c mice in the open field test. Combined injection of Ladasten (10 mg/kg) and sidnocarb (6 or 12 mg/kg) activated animal behavior in both tests.

Key Words: *psychostimulators; stress; inbred mice; open field test; free motor activity*

Genetic determination of the psychostimulator effects was described not once [3,4,7,8]. Inbred animals in these experiments differently reacted to emotional stress. Evaluation of the psychostimulating effect of new compounds with consideration for the stress response phenotype attracted our attention.

We compared the psychostimulating effects of sidnocarb, Ladasten, and their combinations on C57Bl/6 and BALB/c mice with hereditary controled "active" and "passive" behavioral strategy in the open field (OF) test.

TABLE 1. Effects of Ladasten, Sidnocarb, and Their Combination on FLA of C57Bl/6 and BALB/c Mice ($M \pm m$)

Drug, dose	BALB/c		C57Bl/6	
	control	experiment	control	experiment
Ladasten, 10 mg/kg	1030.2±385.8 *n*=5	977.5±169.1 *n*=6	296.8±50.6 *n*=6	474.8±197.9 *n*=4
Sidnocarb, 6 mg/kg	1062.6±118.4 *n*=12	1302.4±103.7 *n*=11	277.7±46.7 *n*=6	988.3±46.7* *n*=4
Sidnocarb, 12 mg/kg	1227.5±62.6 *n*=11	1911.0±120.0* *n*=11		2838.8±411.6* *n*=5
Ladasten, 10 mg/kg+sidnocarb, 6 mg/kg	1354.2±320.9 *n*=6	2705.2±395.3*+ox *n*=6	304.8±54.2 *n*=6	2341.2±438.3*+ox *n*=6
Ladasten, 10 mg/kg+sidnocarb, 12 mg/kg		5485.0±587.2*+ox *n*=6		5839.7±684.1*+ox *n*=6

Note. *n*; number of groups of animals (3 per group); $p<0.05$ compared to: *control, +Ladasten, °sidnocarb in a dose of 6 mg/kg, ˣsidnocarb in a dose of 12 mg/kg.

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MATERIALS AND METHODS

Experiments were carried out on male C57Bl/6 and BALB/c mice (18-22 g) from Stolbovaya Breeding Center, Russian Academy of Medical Sciences. The animals were kept under standard conditions in laboratory vivarium at 12/12 h day/night regimen, 10 per cage, for 2 weeks before the experiment.

The behavior of mice in OF test and their free locomotor activity (FLA) were studied as described previously [1,2].

Sidnocarb and Ladasten as suspensions with Twin-80 were injected intraperitoneally 60 min before testing. Controls were injected with Twin-80.

The results were statistically processed using Student's *t* test.

RESULTS

Control results, characterizing OF behavior and FLA of C57Bl/6 and BALB/c mice (recorded using Opto-Varimex device), are in line with previous data [4,5,8] (Tables 1, 2). Sidnocarb dose-dependently increased FLA of C57Bl/6 mice in the Opto-Varimex test and caused a negligible effect in BALB/c mice in a dose of 12 mg/kg (Table 1).

Sidnocarb in a dose of 12 mg/kg activated OF behavior of C57Bl/6 mice and had practically no effect on BALB/c mice (Table 2).

These data agree with previous results [4,8], this giving grounds for comparative evaluation of phenotypical effects of sidnocarb with the effect of Ladasten, a new drug.

Ladasten in a dose of 10 mg/kg did not modify FAL of BALB/c mice and only slightly increased it in C57Bl/6 mice in the absence of emotional stress in the Opto-Varimex test (Table 1); this attested to low psychostimulating effect of Ladasten in this dose. It was previously shown that FLA stimulation in the Opto-Varimex was attained with the drug dose of 50 mg/kg [3]. Ladasten in a dose of 10 mg/kg markedly stimulated motor activity of BALB/c, but not C57Bl/6 mice, in the OF test.

These data, demonstrating the absence of FLA stimulation by Ladasten in a dose of 10 mg/kg in mice of both strains in the test involving no stress exposure for FLA recording, and activation of behavior of BALB/c (characterized by pronounced anxiety reaction) but not of C57Bl/6 mice (with active phenotype of behavior in OF) in the OF test, indicate that the drug effect in this dose was anxiolytic, but not psychostimulating, which is in line with previous data [5,6].

Combined treatment with sidnocarb and Ladasten markedly stimulated the behavior of BALB/c and

table 2. Effects of Ladasten, Sidnocarb, and Their Combination on OF Behavior Test of C57Bl/6 and BALB/c Mice (*M±m*)

Drug	BALB/c					C57Bl/6				
	FLA	PA	CA	VA	Em	FLA	PA	CA	VA	Em
Control	34.1±3.3 *n*=64	32.9±31.0 *n*=64	1.1±0.5 *n*=64	0.08±0.20 *n*=64	0.9±0.1 *n*=64	108.9±11.1[a] *n*=20	66.0±6.3[a] *n*=20	31.3±4.7[a] *n*=20	11.1±1.6[a] *n*=20	0.3±0.1[a] *n*=20
Ladasten, 10 mg/kg	60.9±9.5* *n*=21	60.7±9.4* *n*=21	0.3±0.1* *n*=21	0.0±0.0 *n*=21	0.3±0.1* *n*=21	125.7±11.8 *n*=10	78.6±10.2 *n*=10	38.9±5.8 *n*=10	7.2±1.3 *n*=10	0.2±0.1 *n*=10
Sidnocarb, 6 mg/kg	33.3±6.0 *n*=12	32.3±6.0 *n*=12	1.0±0.7 *n*=12	0.0±0.0 *n*=12	2.0±0.3 *n*=12	127.9±13.5 *n*=10	76.6±8.8 *n*=10	40.3±9.2 *n*=10	11.0±1.9 *n*=10	0.0±0.0* *n*=10
Sidnocarb, 12 mg/kg	40.7±9.2 *n*=21	36.8±7.6 *n*=21	3.6±2.7 *n*=21	0.3±0.2 *n*=21	1.0±0.3 *n*=21	163.7±12.8* *n*=10	133.1±9.0* *n*=10	17.7±3.0* *n*=10	12.9±1.8 *n*=10	1.2±0.3* *n*=10
Ladasten, 10 mg/kg+ sidnocarb, 6 mg/kg	86.1±8.1*[+ox] *n*=12	84.8±8.2[+ox] *n*=12	1.3±0.8 *n*=12	0.0±0.0 *n*=12	0.3±0.2* *n*=12	172.8±11.8*[+o] *n*=9	124.8±6.7*[+o] *n*=9	30.5±8.0 *n*=9	15.5±2.3 *n*=9	0.6±0.3 *n*=9
Ladasten, 10 mg/kg+ sidnocarb, 12 mg/kg	67.3±12.4* *n*=12	61.4±9.8*[ox] *n*=12	5.2±1.4* *n*=12	0.7±0.1* *n*=12	0.0±0.0* *n*=12	138.1±15.1* *n*=10	102.3±12.4* *n*=10	24.8±4.0 *n*=10	11.1±2.4 *n*=10	0.1±0.1 *n*=10

Note. *n*: number of animals; FLA: total motor activity; PA: peripheral; CA: central; VA: vertical activity; Em: number of defecations. $p<0.05$ compared to: *control, [+]Ladasten, [o]sidnocarb in a dose of 6 mg/kg, [x]sidnocarb in a dose of 12 mg/kg, [a]BALB/c mice.

C57Bl/6 mice in the Opto-Varimex test (Table 1). Increasing the dose of sidnocarb in the combination intensified the effect (Table 1). The combination of sidnocarb and Ladasten activated OF behavior of both mouse strains in comparison with controls (Table 2).

Thus, combined treatment with sidnocarb and Ladasten in the studied doses stimulated the behavior of animals with active response to emotional stress and animals responding to stress by a freezing reaction.

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