PHARMACOLOGY AND TOXICOLOGY

Analysis of Bromantane Pharmacological Spectrum

S. B. Seredenin and A. G. Miramedova

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Bromantane (2[n-bromphenyl]aminoadamantane) in doses of 40-60 mg/kg had no effect on spontaneous motor activity of BALB/c mice in an Optovarimex apparatus and prevented freezing in the open field test, but stimulated motor activity in C57Bl/6 mice. It is concluded that psychostimulatory and anxiolytic effects are present in the spectrum of the pharmacological activity of bromantane.

Key Words: *bromantane; inbred mice; anxiolytic*

Bromantane (2[n-bromphenyl]aminoadamantane) was synthesized and tested at the Institute of Pharmacology by research group supervised by Prof. I. S. Morozov [2,5,8]. The drug was found to have adaptogenic, immunostimulating and detoxicating activity [2,3]. This study was aimed at investigation of psychostimulatory and anxiolytic effects of bromantane in animals with different emotional reactions to stress.

MATERIALS AND METHODS

Experiments were carried out on male BALB/c and C57Bl/6 mice weighing 20-22 g (Stolbovaya Breeding Center, Russian Academy of Medical Sciences). The animals were maintained in a vivarium for 2 weeks before experiments (10 mice per cage) on a standard diet with free access to water with normal 12h:12h light/dark schedule. All experiments were conducted from 9.00 to 13.00. Bromantane (10-200 mg/kg, aqueous suspension with Tween-80) was administered 1.5 h before the experiment. Different kinds of motor activity (MA) were studied in an Optovarimex apparatus [7] and open field [7,9,11]. The data were analyzed statistically using Student's *t* test [13].

Laboratory of Pharmacogenetics, Institute of Pharmacology, Russian Academy of Medical Sciences, Moscow

RESULTS

The combination of tests applied in our study allowed us to assess the effects of drugs under normal and stress conditions. C57Bl/6 and BALB/c mice showed similar spontaneous MA but different behavior in the open field: C57Bl/6 mice were characterized by high MA and low defecation rate, while freezing was typical of BALB/c [9,11]. It was previously shown, that benzodiazepine tranquillizers dose-dependently decreased MA of C57Bl/6 mice in the open field and in low doses activated behavior of BALB/c mice [1]. In the absence of emotional stress, standard tranquillizers depress behavioral activity in animals [1]. The standard psychostimulator sydnocarb dose-dependently increases MA in C57Bl/6 mice, but stimulates behavioral activity of BALB/c mice only in high doses [7]. Therefore, if an Optovarimex test reveals a stimulatory effect, the tested drug should be considered as a psychostimulator. The increase in activity of BALB/c mice in the open field test, but not in an Optovarimex test attests to an anxiolytic effect of test drug.

In the Optovarimex tests, bromantane in doses of 50 and 60 mg/kg stimulated MA of C57Bl/6 mice without affecting behavior of BALB/c mice. In a maximum dose of 200 mg/kg bromantane decreased spontaneous MA of BALB/c mice (Table 1). Therefore, bromantane was similar to sydnocarb, which in low doses stimulated activity of C57Bl/6 but not BALB/c

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TABLE 1. Effect of Bromantane on Spontaneous Motor Activity of BALB/c and C57Bl/6 Mice in Optovarimex Apparatus (*M±m*, *n*=30)

Dose, mg/kg	BALB/c		C57Bl/6	
	experiment	control	experiment	control
30	1415.2±316.0	1214.3±218.4	1176.1±248.3	1214.2±316.0
40	948.3±116.5	1003.7±125.3	1389.4±209.7	1216.0±128.3
50	1027.1±138.4	958.4±217.4	2908.4±107.6*	1214.3±308.4
60	1447.3±674.5	1318.4±316.7	2001.3±314.5*	1217.8±116.3
80	828.4±116.8	1016.7±318.4	1216.4±101.3	1014.4±216.7
100	1013.5±118.7	981.2±204.3	2417.1±316.7	2013.0±328.4
150	900.3±107.4	728.4±216.1	987.8±184.3	716.4±214.3
200	987.0±169.8*	568.0±144.3	804.3±166.7	713.5±105.4

Note: *$p<0.05$ in comparison with the control.

TABLE 2. Effect of Bromantane on Open Field Behavior in C57Bl/6 Mice (*M±m*)

Dose, mg/kg	MA					Defecation rate
	peripheral	central	the number of visits to the center	vertical	totall	
Control (*n*=50)	69±4.8	22.3±5.3	1.1±0.3	10.8±2.7	107.3±7.5	0.3±0.2
10 (*n*=10)	71.3±4.1	20.3±0.6	0.9±0.7	10.3±4.4	112.4±6.1	—
30 (*n*=10)	75.1±8.4	19.3±7.4	1.8±0.9	13.4±8.7	109.1±8.8	0.1±0.1
45 (*n*=15)	82.8±9.4	26.9±5.3	1.5±0.4	15.5±6.9	126.9±9.5*	0.4±0.2
50 (*n*=30)	93.7±5.8*	30.3±5.8	2.8±1.3	15.4±4.8	151.4±8.7**	0.4±0.3
60 (*n*=20)	88.3±6.8*	28.4±4.9	1.6±0.8	13.9±3.2	132.2±6.8**	0.3±0.1
80 (*n*=10)	78.2±8.7	23.3±4.8	0.8±0.3	12.4±2.9	104.7±8.7	—
100 (*n*=10)	71.1±3.8	20.8±7.6	1.3±0.8	9.4±5.1	122.6±7.8	0.5±0.2
150 (*n*=15)	68.8±5.1	20.9±8.3	0.7±0.4	10.1±4.3	100.5±8.3	0.3±0.1
200 (*n*=20)	60.0±3.4	28.9±4.3	1.5±0.8	9.1±3.8	99.0±4.8	—

Note: Here and in Table 3: *$p<0.05$, **$p<0.01$ in comparison with the control.

TABLE 3. Effect of Bromantane on Open Field Behavior in BALB/c Mice (*M±m*)

Dose, mg/kg	MA					Defecation rate
	peripheral	central	the number of visits to the center	vertical	totall	
Control (*n*=50)	20.3±5.1	0.3±0.4	—	—	20.3±5.1	0.4±0.1
10 (*n*=10)	26.4±3.5	0.9±0.8	—	—	25.5±3.4	0.5±0.2
30 (*n*=10)	29.4±6.8	0.9±0.5	—	0.1±0.1	30.4±6.8	0.3±0.2
45 (*n*=15)	30.3±6.7	8.7±1.4*	0.2±0.2	1.8±0.3*	40.0±6.7**	0.1±0.1*
50 (*n*=30)	42.5±6.7*	16.1±2.7**	0.1±0.1	2.4±0.6**	61.2±8.3**	0.1±0.1**
60 (*n*=20)	36.4±5.3*	7.6±2.8**	0.1±0.1	2.0±0.4	46.1±5.3*	0.3±0.2
80 (*n*=10)	30.9±8.7	1.0±0.6	—	0.3±0.3	32.2±8.7	0.4±0.1
100 (*n*=10)	24.0±3.8	0.8±0.4	—	—	24.8±3.8	0.5±0.2
150 (*n*=15)	18.0±2.6	0.5±0.3	0.2±0.1	—	18.7±2.8	0.1±0.1*
200 (*n*=20)	9.4±6.3	0.2±0.1	—	—	9.6±4.8*	0.9±0.2*

mice. However, in contrast to sydnocarb, the effect of bromantane showed no dose-dependence. Nevertheless, the data presented in Table 1 make it possible to conclude that bromantane exerts a psychostimulatory effect.

Under conditions of emotional stress in the open field test, the psychostimulatory effect of bromantane on C57Bl/6 mice was manifested in increased total, but not central MA (Table 2). In BALB/c mice, bromantane in doses of 45-60 mg/kg significantly increased all kinds of MA and decreased defecation rate (Table 3). The same doses of bromantane had no effect on behavior of BALB/c mice in the Optovarimex test. From these data it can be concluded that bromantane exerts a selective anxiolytic effect on animals with passive reactions to emotional stress. Similar effects have been previously described for low doses of the day tranquillizer gidazepam, atypical anxiolytic mexidol, and new original selective anxiolytic aphobasol [1]. Our data allow us to consider bromantane as a unique drug possessing psychostimulating and anxiolytic properties, which opens wide prospects for its clinical application.

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