Modulation of Exploratory Behavior in Mice during Activation of Cell Immune Response

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We revealed a modulating effect of cell immune response on exploratory activity of (CBA× C57Bl/6)F_1 mice depending on their initial behavioral profile. The formation of BCG-induced delayed-type hypersensitivity was accompanied by stimulation of the exploratory behavior in animals with initially low or intermediate activity, but did not change this parameter in behaviorally active mice.

Key Words: *exploratory behavior; delayed-type hypersensitivity; immune response*

Recent biological and medical studies revealed functional relationships between the nervous and immune systems [1,2,5,6,9,11]. We study the effects of the immune system on behavioral reactions in mice. Previous experiments showed that (CBA*C57Bl/6)F_1 mice differ in exploratory activity, which is directly related to the intensity of cell-mediated immune reactions [7,15]. Here we evaluated the effects of immunostimulation with bacillus Calmette-Guerin (BCG) vaccine on exploratory behavior of mice.

MATERIALS AND METHODS

Experiments were performed on 150 male (CBA× C57Bl/6)F_1 mice aging 3 months (Institute of Pharmacology, Tomsk). Two weeks before the start of the experiments the animals were kept in cages (10 mice per cage) under standard vivarium conditions (12-h light-dark cycle and *ad libitum* food and water supply). Experiments were performed at 10.00-15.00. Delayed-type hypersensitivity reaction was induced with dry BCG vaccine (Allergen). The mice were divided into groups with high, intermediate, and low exploratory activity (EA) depending on their behavior in the open field test [15]. The animals were vaccinated intraperitoneally (0.5 mg in 0.5 ml RPMI-1640 medium). Control animals received an equivalent volume of RPMI-1640 medium. Two weeks after vaccination EA was studied in an open field [4]. The open field was a large rectangular chamber (100×100 cm, 100 squares) surrounded by plastic walls (40 cm in height) and illuminated with a 100-W shadow-free lamp (1 m above the center of the area). The mouse was placed to the corner, and locomotor activity was recorded minutely for 5 min. We recorded the number of crossed central and peripheral squares, count of central (free) and peripheral (manege running) rearing postures, and total locomotor activity. Emotional strain was estimated by the number of fecal boluses. The results were analyzed by Student's *t* test (Jandel Sigma Plot software).

RESULTS

BCG-vaccinated mice displayed different behavioral patterns in the open field test (Table 1). Vaccination stimulated horizontal peripheral and central locomotor activity in animals with initially low or intermediate EA ($p<0.01$). These mice also demonstrated increased central ($p<0.05$) and peripheral vertical activity ($p<0.01$), which indicated stimulation of the motor and exploratory behavioral components. BCG vaccine did

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TABLE 1. Effects of BCG Vaccine on Exploratory Behavior of (CBA×C57Bl/6)F_1 Mice with Different Initial EA in the Open Field Test (*M*±*m*)

Parameter	High EA		Intermediate EA		Low EA	
	control	BCG	control	BCG	control	BCG
Horizontal locomotor activity						
peripheral	224.7±8.8	203.5±9.6	127.2±6.1	214.5±11*	35.6±7.6	117.9±15.7*
central	35.4±5	21±9.6	13.2±2.6	27.2±8.9*	0.7±0.6	7.1±3.4*
Vertical locomotor activity						
free	13.5±2.1	12.0±4.4	8.7±1.5	12.4±2.3**	0	2.5±1.2*
manege running	25.0±2.8	17.1±5.3	11.3±2.3	20.8±2.4*	0	12.1±2.2*

Note. *p<0.01 and **p<0.05 compared to the control.

not modulate EA of mice with initially high activity (Table 1).

BCG vaccination causes delayed-type hypersensitivity, which is manifested in selective activation of macrophages and $CD4^+$ lymphocytes (Th1 cells) [14]. Production of interferon-γ, tumor necrosis factor-α, and interleukin-12 by these cells is the key element of BCG-induced immune response [12,13]. These cytokines are probably responsible for modulation of EA in experimental animals. The fact that interferon-γ inhibits humoral immune response after BCG vaccination [10] confirms our assumption that exploratory behavior is closely associated with cell-mediated immune reactions [7,15].

Changes in the total locomotor activity of (CBA×C57Bl/6)F_1 mice during stimulation of the cell-mediated immune response confirm their dependence on the initial EA: the lower is initial EA, the more pronounced is the effect (Fig. 1).

Our findings attest to a relationship or parallelism between behavioral and immune reactions in mice during BCG vaccination. Changes in these parameters caused by BCG-induced delayed-type hypersensitivity depend on the initial behavioral profile of experimental animals.

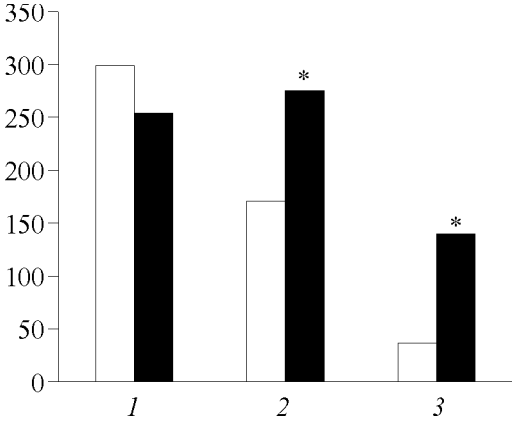

Fig. 1. Effect of BCG vaccination on total locomotor activity of (CBA×C57Bl/6)F_1 mice with different initial exploratory activity in the open field test. Ordinate: number of crossed squares over 5 min. Low (*1*), intermediate (*2*), and high (*3*) initial exploratory activities. Light bars: control; dark bars: BCG vaccination. *p<0.01 compared to the control.

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