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Modulation of Orientation and Exploratory Behavior of (CBA×C57Bl/6)F1 Mice by Immunocompetent Cells

V. V. Abramov, E. V. Markova, N. A. Korotkova, and V. A. Kozlov

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The present investigation develops a previously published concept on integration of the immune, endocrine, and nervous systems in a universal structural and functional block (IMEN system). Splenocytes from donor (CBA×C57Bl/6)F1 mice characterized by specific behavior in the open field test modified the behavior of syngeneic recipient mice after intravenous infusion.

Key Words: *splenocytes; behavior; mice*

Recent data on the mutual regulatory effects of the neuroendocrine and immune systems [1,2,8,10,12] provide the basis for the concept of the immuno-endocrine nervous (IMEN) system [4,5]. According to this concept integration relationships exist between the neuroendocrine and immune systems. The cells of these two systems are characterized by pronounced phenotypical and functional similarity. This implies, among other things, that immunocompetent cells can participate in the regulation of higher nervous activity. However, this aspect of integration of these systems remains poorly studied.

We investigated the role of immunocompetent cells in modulation of behavioral reactions of experimental animals: our aim was to demonstrate the capacity of splenocytes of donor mice (CBA×C57Bl/6)F1, characterized by specific behavior, to modulate the behavior of syngeneic recipient mice. Demonstration of such a capacity was expected to confirm the integration relationships between the immune and nervous systems.

Laboratory of Neuroimmunology, Institute of Clinical Immunology, Siberian Division of Russian Academy of Medical Sciences, Novosibirsk. ***Address for correspondence:*** Valery_abramov@mail.ru. Abramov V. V.

MATERIALS AND METHODS

Male (CBA×C57Bl/6)F1 mice (18-20 g) from Tomsk Breeding Center were used in the study. Before the experiment the animals were kept in a laboratory vivarium (10 per cage) for at least 2 weeks on a standard diet with free access to food and water and normal 12-h day-night regimen.

The orientation exploratory activity of animals was tested in the open field test [6]. All experiments were carried out from 10.00 to 15.00. The test field was a 100×100 cm chamber (100 squares) with 40-cm plastic walls illuminated with a shadow less 100 W bulb placed at a height of 100 cm above the center of the field. An animal was placed into the corner of the chamber and its minute-by-minute motor activity was recorded for 5 min. The number of crossed central and peripheral squares, rearings (free and with wall support, manege running), and total exploratory activity were evaluated. (CBA×C57Bl/6)F1 mice were divided into 3 groups depending on their behavior in the open field: with high (HA), medium, and low (LA) exploratory activity [7,13].

Splenocytes (1.5×10^7 in 0.5 ml RPMI-1640) were transferred from LA animals to HA recipients (LA→HA transfer) or vice versa from HA animals to LA recipients (HA→LA transfer) intravenously and the

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TABLE 1. Transfer of Orientation and Exploratory Behavior in the Open Field Test between Groups of (CBA×C57Bl/6)F1 Mice with Splenocytes (*M*±*m*)

Total orientation and exploratory activity		Transfer			
		LA→HA (*n*=30)		HA→LA (*n*=50)	
		control	experiment	control	experiment
Horizontal	day 5	160.3±3.2 158.3±17.5	118.3±15.0** 79.4±13.3*	10.3±5.5 11.8±6.4	115.6±12.6* 99.1±4.6*
	day 14	210.8±29.3 181.3±20.5	78.3±14.4* 47.4±1.2*	9.7±5.1	103.3±8.1*
Vertical					
	day 5	12.8±1.1 17.5±2.7	2.6±0.7* 4.0±1.1*	0.0±0.0 0.6±0.4	10.6±1.8* 10.7±1.7*
	day 14	20.0±0.8 16.8±5.1	1.8±1.2* 1.2±0.7*	0.0±0.0 —	8.4±1.2 —

Note. Numerator and denominator: results of 2 repeated experiments on different animals at different time. Dash: no experiments because of technical reasons. *p<0.01, **p<0.05 compared to the control.

parameters of orientation and exploratory activity of recipients were tested on days 5 and 14 after cell transfer. LA→LA or HA→HA transfer (1.5×10^7 in 0.5 ml RPMI-1640) served as the control. The amount of transplanted splenocytes (1.5×10^7 cells) was chosen in previous experiments. The basic condition was the absence of the effect after cell transfer between mice with identical behavioral parameters.

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

RESULTS

The LA→HA transfer significantly decreased behavioral parameters of the recipient mice in the open field on days 5 and 14 after transfer, while HA→LA transfer significantly increased these parameters (Table 1). Splenocyte transfer between mice with identical behavioral parameters had no effect on exploratory activity of recipients (Table 1).

Hence, splenocytes can modulate orientation and exploratory behavior of animals, which suggests the involvement of immunocompetent cells in the regulation of higher nervous activity. Immune cells produce cytokines possessing neuroregulatory properties [3,10-12]. Injection of tactivin (a complex of peptides produced in the thymus) to August rats significantly improved avoidance conditioning in a shuttle box [3]. Presumably, cytokines produced by immunocompetent cells are responsible for the modulating effect of splenocytes on orientation and exploratory behavior of (CBA×C57Bl/6)F1 mice in the open field test. If so, we can assert that splenocytes of animals with different levels of the above-mentioned behavioral reactions produce different sets of cytokines. In other words, bidirectional and mutual relationships between immunocompetent cells and CNS can exist in mice characterized by certain behavioral features. CNS regulates production of some cytokines by immune cells, while immune cells determine behavioral characteristics of animals [1,2,4,5,8,9,11].

Hence, we demonstrate the possibility of purposeful modification of orientation and exploratory behavior of (CBA×C57Bl/6)F1 mice in the open field test by injection of splenocytes from syngeneic donors with different behavior pattern.

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