Effect of Immunization with Sheep Red Cells on Rat Behavior

Yu. V. Burov, L. E. Davydova, and T. N. Robakidze

UDC 57.083.3:612.82

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 118, № 11, pp. 474-476, November, 1994
Original article submitted April 6, 1994

The changes of behavior of rats in the "open field" test and the conditioned reaction of passive avoidance during the humoral immune response to a conventional antigen - sheep red cells - are studied. The primary immune response is found to be accompanied by activation of the exploratory component of rat behavior and by a reduced capacity for the development of the passive avoidance reaction in the initial period of antibody production; the development of the secondary immune response led to a short-term increase in locomotor activity. The results point to the effect of the normal immune response on the physiology of rat behavior.

Key Words: *antibody production; sheep red cells; passive avoidance reaction; "open field" test*

The humoral factors generated during an immune response interfere with the functioning of the central nervous system. It has been shown, for instance, that interleukins and interferons induce slow-wave sleep, raise the body temperature, produce an analgetic effect, and affect locomotor activity, taste, and olfaction [5,7,9,11-13]. It is also known that the induction of a normal immune response modifies the electrophysiological parameters of the central nervous system and the production of hypothalamic and pituitary hormones, as well as changing the turnover rate of neurotransmitters [2,3,6,8]. However, the effect of the generation of the immune response upon the integral indices of higher nervous activity has not yet been studied in experimental animals.

Our goal, therefore, was an investigation of behavioral reactions of rats in the "open field" test and changes in the conditioned passive avoidance reaction (PAR) during the synthesis of antibodies against a conventional antigen - sheep red cells (SRC).

Department of Psychopharmacology, Russian Research Center for the Safety of Biologically Active Substances, Staraya Kupavna, Moscow Region. (Presented by Yu. A. Romanov, Member of the Russian Academy of Medical Sciences)

MATERIALS AND METHODS

The experiments were carried out using 30 pubertal outbred male white rats weighing 220-230 g purchased from the Kryukovo Breeding Center (Moscow Region). The animals were kept at 21-23°C, under the standard 12-h light regime, 10 rats per 21×45 cm cage. Food and water were given ad li-

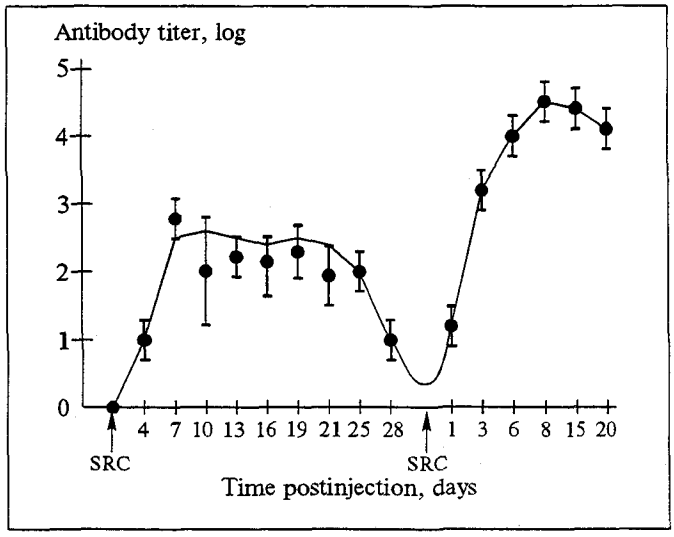

Fig. 1. Dynamics of antibody response to SRC.

0007-4888/94/0011-1170$12.50

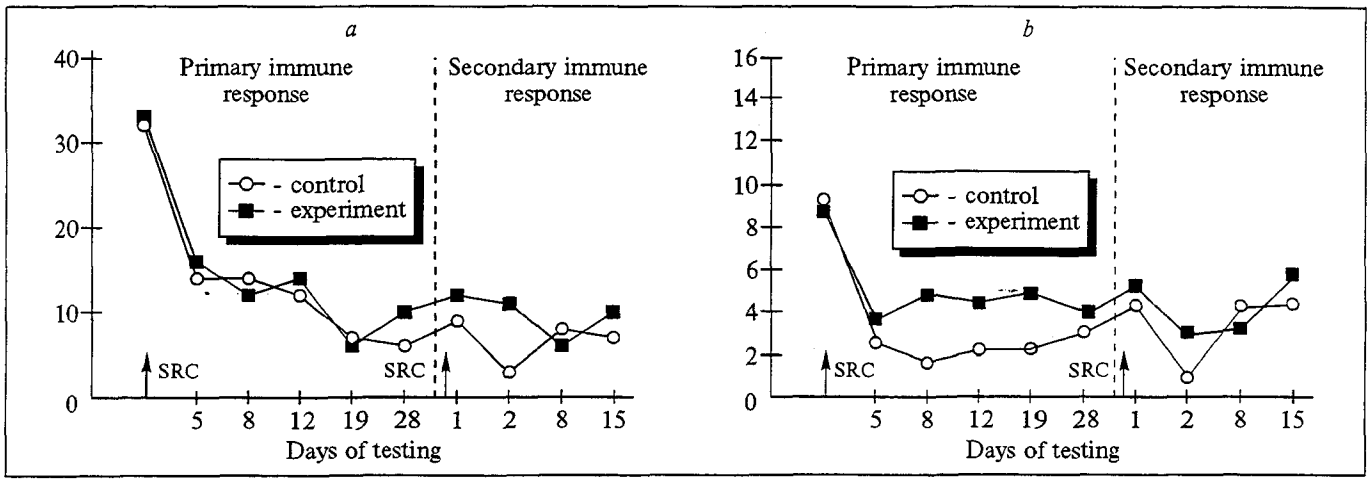

Fig. 2. Study of "open field" behavior. *a*) change in exploratory activity; ordinate: frequency of upright postures; *b*) change in locomotor activity; ordinate: number of sectors crossed.

bitum. The animals were immunized by intraperitoneal injection of 5×10^8 SRC. The second immunization was carried out 30 days later. Control rats received saline with the same schedule and by the same route. For a study of the dynamics of antibody response, blood was taken from the sublingual vein in animals of both groups before and every 3rd day after immunization. The antibody titers were estimated by the routine hemagglutination method [4].

The orientation-locomotor reaction was recorded in the "open field" test after Hall [10]. Twenty-four hours before the start of immunization the preliminary testing was performed and the animals were divided into statistically similar groups. Each animal was evaluated during 2 min for the following parameters: locomotor activity, according to the number of sectors crossed; exploratory activity, according to the number of upright postures; emotional state, according to the number of fecal pellets.

Animal behavior was followed up on the 5th, 8th, 12th, 19th, and 28th days after the first immunization and on the 1st, 2nd, 8th, and 15th days after the second. These time-points were chosen in order to cover all stages of the humoral response.

The conditioned-response activity of animals was estimated by the PAR method [1]. The animals were conditioned on the 8th day after the first antigen injection, the time corresponding to the initial stage of the plateau phase of antibody synthesis. The latent period needed for the escape of a rat from the illuminated to the dark part of the cage was recorded in seconds. The animals were tested 24 h and 7 days after conditioning.

RESULTS

The study of antibody production dynamics revealed (Fig. 1) that the inductive phase of the primary immune response lasted 1-6 days, followed by the productive phase, lasting from the 6th to the 25th day. A decline in the antibody titer was observed on the 28th day. The phase of logarithmic antibody increase during the secondary immune response was observed at days 1-4, while maximum antibody production (the plateau) occurred from the 6th to the 20th day. These results are in agreement with published data on the development of the normal immune response [14].

The observation of "open field" rat behavior revealed that the induction of the primary immune response causes a change in exploratory activity (Fig. 2, *a*). A statistically reliable increase of this component of the orientation-locomotor reaction (2.3-fold) was recorded on the 8th day after immunization. This period corresponds to the beginning of the plateau phase of antibody production. Figure 2, *b* demonstrates that in the case of the

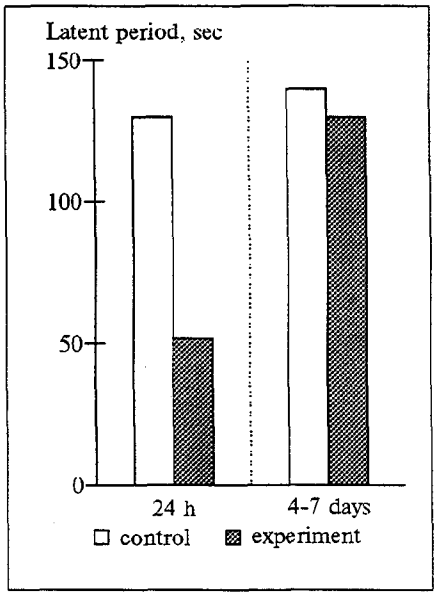

Fig.3. Study of conditioned – response activity of rats immunized with SRC.

secondary immune response on the 2nd day after antigen injection there occurs a statistically reliable increase in the locomotor activity of the experimental animals (2.5-fold). This behavior change corresponds to the inductive phase of antibody production. During the whole period of observation no differences in the emotional state were recorded between the control and experimental animals.

The study of conditioned-response activity of the rats (Fig. 3) revealed a statistically reliable (2.3-fold) reduction in the capacity for PAR learning on the 8th day of the primary immune response. However, examination of animals 7 days after conditioning showed no difference between immunized and control animals. Therefore, one can conclude that the immunization with conventional antigen (SRC) interferes with elaboration of the conditioned response but does not affect the preservation of the memory trace.

Thus, we are the first to establish that the primary immune response is accompanied by an activation of the exploratory component of rat behavior and a decreased capacity for PAR elaboration in the period corresponding to the beginning of the productive phase of antibody response, and that the development of the secondary immune response is accompanied by a short-term phase of increased locomotor activity. The findings present evidence of an influence of the normal immune response on the integral processes of higher nervous activity in rats.

REFERENCES

1. Yu. V. Burov, T. N. Robakidze, L. V. Kadysheva, and S. A. Sukhanova, *Byull. Eksp. Biol. Med.*, **111**, № 6, 612-614 (1991).
2. O. V. Galkina, E. L. Al'perina, O. V. Suslyakova, and L. V. Devoino, *Ibid.*, **110**, № 8, 178-180 (1990).
3. V. A. Grigor'ev, and V. M. Klimenko, *Fiziol. Zh. SSSR*, № 2, 221-230 (1984).
4. *Immunological Methods* [in Russian], Ed. G. Frimel, Moscow, (1987), pp. 127-130.
5. G. I. Chipens, V. E. Klusha, N. G. Ievinya, *et al.*, *Fiziol. Zh. SSSR*, № 5, 638-645 (1989).
6. H. Besedovsky, A. del Rey, E. Sorkin, *et al.*, *Science*, **221**, № 4610, 564-566 (1983).
7. J. E. Blalock and E. M. Smith, *Biochem. Biophys. Res. Commun.*, **101**, № 2, 472-478 (1981).
8. C. D. Breder, C. A. Dinarello, and C. B. Saber, *Science*, **240**, 321-324 (1988).
9. A. Fontana, E. Weber, and J. M. Dayer, *J. Immunol.*, **133**, 1696-1698 (1984).
10. C. S. Hall, *J. Comp. Psychol.*, **18**, 385-403 (1934).
11. P. G. Higgins, *J. Clin. Path.*, **37**, 109-116 (1984).
12. J. M. Krueger, J. Walter, C. A. Dinarello, *et al.*, *Amer. J. Physiol.*, **246**, R994-R999 (1984).
13. D. M. McCarthy, M. J. Kluger, and A. J. Vander, *J. Leukoc. Biol.*, **37**, 725-726 (1985).
14. Z. J. Urh, M. Finkelstein, and J. Bamann, *J. Exp. Med.*, **115**, № 3, 665-670 (1962).