Lactate and Succinate Dehydrogenase Activity in Blood Lymphocytes of Aggressive and Submissive Male Mice

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The influence of social status on some immunological characteristics in experimental animals was studied (sensory contact model). Lactate dehydrogenase activity in blood lymphocytes changed similarly in aggressive and submissive mice probably due to social stress. The activity of succinate dehydrogenase changed differently and correlated with the type of social behavior.

Key Words: *lactate dehydrogenase; succinate dehydrogenase; lymphocytes; immune state; antagonistic behavior*

The mechanisms of integration of the nervous and immune systems are now extensively studied. Peripheral manifestations of this integration are well studied, while the dependence of the immune state on brain functions associated with mental activity and behavior needs further examination. There is practically no data on the relationship between the energy metabolism in lymphocytes and specific characteristics of higher nervous activity.

A correlation between activities of principal enzymes of energy metabolism [8], lactate and succinate dehydrogenases (LDH and SDH, respectively) in blood and brain lymphocytes was previously reported [5, 11]. This explains the interrelation between these parameters and behavior revealed in a number of studies. Thus, in outbred rats brain SDH activity correlates positively with characteristics of active behavior and negatively — with characteristics of passive behavior (the time of passive swimming under inescapable conditions) [10]. We found low SDH activity in blood lymphocytes from rats with passive behavior genetically predisposed to catalepsy [2]. It was revealed that shifts in brain metabolism and behavior caused by pharmacological manipulations modulated some characteristics of blood lymphocytes, in particular, LDH and SDH activities [1]. These data suggest the existence of a close correlation between behavior, LDH and SDH activity in blood lymphocytes and functioning of the immune system.

We analyzed blood cells and LDH and SDH activities in lymphocytes from animals with opposite types of social behavior (aggressive and submissive), formed as a result of successive victories and defeats in daily aggressive interactions between males. These animals exhibited different changes in brain neurotransmitter systems [4] and immune resistance [9,13].

MATERIALS AND METHODS

The experiments were carried out on mature 2.5-3-months-old C57Bl/6J male mice weighing 22-25 g. The model of sensory contact was used to form aggressive and submissive behavioral patterns. The experience of victory or defeat acquired in the first conflicts was reinforced during repeated fighting between males of opposite behavioral types. The following

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TABLE 1. Dehydrogenase Activity in Blood Lymphocytes and Differential Blood Count in Mice with Different Types of Social Behavior

Experiment	Activity		Lymphocyte count, %	SN count, %
	SDH	LDH		
Confrontation period				
control	12.56	16.48	89	9.17
A10	11.8**	20.24**	80.67**	15.44**
A20	12.69	20.66**	76*	21.6*
V10	12.91	20.13**	77.43*	20.43*
V20	16.98**,x	19.15	86.4x	12.4x
Rest				
control	15.74	14.56	81.8	14.8
aggressors	15.48	16.39	88.4**	8.8**
victims	13.54**	18.19**	87.6**	10

Note. SN: segmented neutrophils. *$p<0.01$, **$p<0.05$ in comparison with the control, x$p<0.05$ in comparison with V10 mice.

groups of mice with the experience of consecutive victories and defeats after 10 and 20 daily fightings were formed: aggressors (A10 and A20, respectively) and victims (V10 and V20, respectively). Some males from both A20 and V20 groups were placed in cage with females, *i. g.* under socially comfortable conditions without conflicts for 14 days. The controls for both groups were the animals housed individually for 5 days. On the next day after the last confrontation or after 2 week rest, the experimental and control animals were decapitated. Blood smears were stained for the cytochemical analysis of SDH and LDH activity in lymphocytes [6]. Differential blood count was determined on Romanowsky-stained smears [6]. The data were analyzed statistically using a nonparametric Wilcoxon—Mann—Whitney *U* test.

RESULTS

The formation of aggressive and submissive social behavior changed the proportion of lymphocytes and segmented neutrophils in the blood (Table 1). After rest these indices changed in a pendulum-like manner. Thus, lymphocyte count significantly reduced in group A10 and, especially, in group A20 after rest returned to the normal value, and even exceeded it. On the contrary, neutrophil count gradually increased with each session and after rest decreased below the control. After 10 consecutive confrontations, the changes in lymphocyte and neutrophil count in submissive mice were similar to those in aggressors, but after 20 sessions these parameters did not differ from the control, which suggests some adaptation to social conflicts. After rest lymphocyte count in victims surpassed the control, while the neutrophil count remained unchanged, which can be explained by infection and inflammation of inflicted wounds. The count of other leukocytes changed insignificantly. In general, these changes in differential blood count caused by social experience were similar in victims and aggressors and can be considered as nonspecific. LDH activity increased in aggressors and victims, although to a different degree (Table 1). These changes can be associated with inevitable social stress, in both participants of a social conflict. However, in aggressors, LDH activity after a 2-week rest returned to the control level, while in the victims it remained considerably elevated.

SDH activity in blood lymphocyte of aggressive and submissive mice changed in different ways: it decreased in A10 mice and increased in V20 mice. The formation of opposite behavior was found to exert diverse effects on the immune response to sheep erythrocytes: activation in aggressive and decrease in suppressive males [13]. The authors explain this by the formation of different neurochemical spectrum in the brain: aggressive behavior is associated with the predominance of dopamine, while submissive with the predominance of serotonin.

Our findings indicate that changes in the immune state during long-lasting social conflicts include shifts in the energy metabolism of lymphocytes and that neurochemical spectrum of the brain correlates with the enzyme spectrum of immunocompetent cells. We believe that the peculiarities of lymphoid cell energy metabolism can be used as a marker of neurochemical shifts in the central nervous system accompanying psychoemotional and behavioral pathologies. On the other hand, complex correction of psychoemotional and immune disorders should probably include modulation of the redox processes in cells.

REFERENCES

1. N. I. Gryazeva, M. V. Robinson, and V. A. Trufakin, *Byull. Sib. Otd. Ros. Akad. Med. Nauk.*, No. 4, 45-47 (1994).
2. N. I. Gryazeva, M. V. Robinson, N. N. Barykina, *et al.*, *Byull Eksp. Biol. Med.*, **125**, No. 5, 555-557 (1998).
3. G. V. Idova, T. A. Pavina, E. L. Al'perina, and L. V. Devoino, *Ros. Fiziol. Zh.*, **84**, No. 4, 380-384 (1998).
4. N. N. Kudryavtseva amd I. V. Bakishtanovskaya, *Zh. Vyssh. Nervn. Deyat.*, **41**, No. 5, 459-466 (1991).
5. M. E. Margolina, *Pediatrie* [in Russian], No. 2, 24-27 (1981).
6. V. V. Men'shikov, L. N. Delektorskaya, R. P. Zolotnitskaya, *et al.*, *Laboratory Techniques in Clinics* [in Russian], Moscow (1987).
7. R. P. Nartsissov, *Arkhive Anat.*, **56,** No. 5, 89-91 (1969).
8. *Neurochemistry*, Eds. I. P. Ashmarin and P. V. Stukalov [in Russian], Moscow (1996).
9. N. A. Popova, S. I. Il'nitskaya, L. A. Kolesnikova, *et al.*, *Ros. Fiziol. Zh.*, **82**, No. 12, 14-19 (1996).
10. K. Yu. Sarkisova, L. V. Nozdracheva, and M. A. Kulikov, *Zh. Vyssh. Nervn. Deyat.*, **41,** No. 5, 963-972 (1991).
11. M. I. Chikovani., A. A. Arkhipova, S. V. Petrichuk, and R. P. Nartsissov, *Pediatriya*, No. 11, 17-18 (1981).
12. V. M. Shishchenko, G. F. Suslova, and R. P. Nartsissov, *Arkhive Anat.*, **66,** No. 3, 90-92 (1974).
13. L. V. Devoino, E. L. Alperina, N. N. Kudryavtseva, and N. K. Popova, *Brain Behav. Immun.*, No. 7, 91-96 (1993).