# LACTATE DEHYDROGENASE ISOZYME SPECTRUM IN EXTRAMURAL GANGLIA OF THE AUTONOMIC NERVOUS SYSTEM, WORKING MYOCARDIUM, AND CONDUCTING SYSTEM OF THE RABBIT HEART IN ACUTE EXPERIMENTAL EMOTIONAL STRESS

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KEY WORDS: lactate dehydrogenase; working myocardium; conducting system of the heart; extramural ganglia of the autonomic nervous system.

The formation of the nonspecific resistance of the body to a stress-producing factor is known to be determined not only by changes in the level of adaptive hormones. Many systems of the body are involved in the stress responses.

Hence the importance of investigation of the degree of participation of individual cell formations of the autonomic nervous system in the formation and development of acute experimental emotional stress, and also the character of changes arising in a working organ (the heart) anatomically connected with these structures.

## EXPERIMENTAL METHOD

The relationship between aerobic and anaerobic pathways of carbohydrate metabolism was studied by determining the lactate dehydrogenase (LDH) isozyme spectrum [5] in rabbits with acute experimental emotional stress. Stress was induced by direct electrical stimulation of the negative emotiogenic zone of the hypothalamus (ventromedial nuclei) in conjunction with stimulation of different parts of the skin of the trunk, leading to the appearance of a marked response of passive fear. Rabbits kept in the animal house served as the control. In some experiments rabbits in a state of stress were placed in a modulated electromagnetic field (MEMF) with an intensity of 30 W/m and a carrier frequency of 39 MHz, modulation frequence 7 Hz, and depth of modulation 80%. The control for this group of animals consisted of immobilized intact rabbits placed in an MEMF with the same frequency and direction as in the experiments with stress.

The LDH isozyme spectrum was investigated in the superior cervical (SCG) and stellate (SG) sympathetic ganglia, at the level of the 4th to 6th thoracic segments, and the ganglion nodosum (GN) of the vagus nerve, the working myocardium, and the conducting system of the heart [the atrioventricular (AV) node and AV bundle with tissues of the right main branch of the bundle of His were isolated] [7].

## EXPERIMENTAL RESULTS

No changes in the ratio between the LDH isozymes compared with the control were found in homogenates of SCG and SG, the sympathetic chain, and GN of rabbits in a state of stress (Table 1; Fig. 1a, b). The LDH isozyme spectrum of the ganglia of the rabbit autonomic nervous system studied in these experiments can be classed as intermediate in type, suggesting that carbohydrate conversion in the nerve cells of these ganglia can take place both anaerobically, by glycolysis, and in aerobic reactions of the Krebs cycle. The results of these observations can be compared with those obtained by Grebenkina [1], who considers that acetylcholine synthesis in neurons of SCG depends on oxidative conversion of carbohydrates, whereas excitation of nerve cells during transsynaptic transmission of nervous impulses is associated

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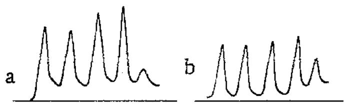


Fig. 1

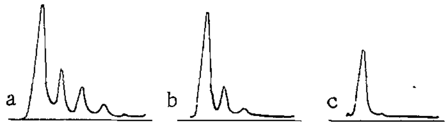


Fig. 2

Fig. 1. LDH isozyme spectrum in superior cervical ganglion: a) control rabbit; b) rabbit in state of stress.

Fig. 2. LDH isozyme composition in conducting system of the heart: a) control rabbit; b) rabbit in a state of stress; c) working myocardium of control rabbit.

more with processes of glycolysis. The absence of changes in the ratio between the basic processes supplying nerve cells of the ganglia with energy in rabbits in a state of stress does not rule out increased functional activity of structures of the autonomic nervous system in this case, but is evidence of the more balanced state of their metabolism. Only if stimulation of preganglionic fibers of SCG in the cat is prolonged (over 8 h) can it lead to a fall in its ATP concentration. During short-term stimulation of SCG a fall in the ATP concentration in it can be obtained only after removal of glucose from the perfusion solution [2].

The course of development of adaptive reactions in stress due to stimulation of negative emotiogenic zones of the hypothalamus can be traced by studying changes in cardiac activity. During stimulation of the ventromedial hypothalamic nuclei in rabbits disturbances of cardiac activity are caused by descending influences of the mesencephalic reticular formation, spreading with the aid of structures of the autonomic nervous system [6].

The study of the working myocardium of rabbits dying from acute cardiac failure in a state of stress revealed no changes in the ratio between activities of the LDH isozymes (Table 1). The LDH isozyme spectrum of the rabbit myocardium is evidence that carbohydrate conversion in heart muscle takes place by the aerobic route (Fig. 2c). The study of the biochemical mechanisms lying at the basis of the harmful effects of emotional stress on the heart, conducted in Meerson's laboratory, demonstrated the decisive role of glucocorticoids and catecholamines in these mechanisms. Meanwhile disturbances by myocardial metabolism of this sort are unconnected with the reactions providing the heart muscle with energy, and the ATP concentration in the myocardium of the animals was unchanged during stress; this fact is in good agreement with the results of observations showing preservation of the normal LDH spectrum in the working myocardium of the rabbits during emotional stress.

A marked tendency toward a change in the ratio between the LDH isozymes in the conducting system of the heart was noted in the animals which died during stress (Table 2; Fig. 2a, b). The new ratio between the isozyme fractions which developed brought the LDH spectrum of the conducting system more in line with the LDH spectrum of the working myocardium (Fig. 2c). The change in the LDH isozyme spectrum of the conducting system in stress indicates a close link between metabolic processes in the tissue and the functional state of the heart. Stimulation of the negative emotiogenic zones of the hypothalamus evoked changes in the LDH spectrum of the conducting system: Increased activity of the fast "cardiac" isozymes was observed. Emotional stress is thus accompanied by changes in the course of electrical processes in the tissues of the conducting system of the heart, and these changes must also affect its functional properties.

Placing rabbits in a state of emotional stress in an MEMF had a protective action against harmful effects due to stimulation of negative emotiogenic zones of the hypothalamus, interrupted stimulation of which for 3 h during exposure to the MEMF did not lead to the appearance of disturbances of cardiac activity. The LDH isozyme spectrum of the conducting system under these circumstances did not differ from normal.

How can the protective action of the MEMF on the animal be explained? According to Kholodov and Shishlo [9], an alternating electromagnetic field is a stressor which causes the development of a general adaptation syndrome. The increase in resistance of the body to the action of the emotiogenic factor can be explained by what is known as cross resistance, associated with the combined action of two stressors. Kositskii and Smirnov [3] explain the

TABLE 1. Correlation between Activity of LDH Isozyme Fractions in Ganglia of Autonomic Nervous System and Working Myocardium of Rabbits

| Fraction | Superior cervical ganglion | | | | Ganglion nodosum | | | | Stellate ganglion | | | | Sympathetic chain | | | | Working myocardium | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | control | stress | stress + MEMF | MEMF | control | stress | stress + MEMF | MEMF | control | stress | stress + MEMF | MEMF | control | stress | stress + MEMF | MEMF | control | stress |
| | (n = 7) | (n = 7) | (n = 6) | (n = 7) | (n = 6) | (n = 6) | (n = 6) | (n = 6) | (n = 6) | (n = 6) | (n = 6) | (n = 6) | (n = 7) | (n = 7) | (n = 6) | (n = 5) | (n = 4) | (n = 4) |
| $LDH_1$ | 21,3 | 20,8 | 27,9 | 24,8 | 25,1 | 23,4 | 28,2 | 27,9 | 20,2 | 24,6 | 28,1 | 24,8 | 23,2 | 24,2* | 27,1 | 26,6 | 90,1 | 90,3 |
| $LDH_2$ | 21,7 | 19,5 | 26,6* | 27,0* | 26,0 | 22,3 | 28,0 | 28,0 | 22,2 | 21,6 | 26,6 | 25,9 | 24,9 | 22,6 | 26,3 | 26,8 | 9,9 | 9,7 |
| $LDH_3$ | 21,7 | 23,0 | 27,6* | 26,1* | 20,5 | 23,4 | 26,0* | 24,9 | 21,6 | 25,0 | 25,2* | 27,5* | 27,4 | 30,7 | 25,2 | 26,4 | | |
| $LDH_4$ | 21,8 | 23,0 | 14,4* | 18,1 | 18,7 | 21,4 | 13, | 15,5 | 23,5 | 18,5 | 15,4 | 17,8 | 18,2 | 15,7 | 16,2 | 14,1 | | |
| $LDH_5$ | 13,5 | 13,7 | 3,5* | 4,0* | 9,7 | 9,5 | 4,4* | 3,7* | 12,5 | 10,3 | 4,2* | 4,0* | 6,3 | 4,8 | 5,2 | 6,0 | | |

*LDH fractions whose activity differs significantly from the control.

TABLE 2. Relative Activities of LDH Isozyme Fractions of Conducting System of the Rabbit Heart (M ± m)

| Fraction | Control (n = 8) | Stress (n = 10) | t | Stress + MEMF (n = 5) | t |
|---|---|---|---|---|---|
| $LDH_1$ | 64,16±3,2 | 70,97±2,1 | 1,82 | 67,2±4,5 | 0,55 |
| $LDH_2$ | 18,02±1,55 | 17,37±1,13 | 0,33 | 17,2±0,7 | 0,51 |
| $LDH_3$ | 11,95±1,18 | 9,6±1,1 | 1,46 | 12,2±2,1 | 0,1 |
| $LDH_4$ | 4,07±1,22 | 1,5±1,0 | 1,66 | 2,64±1,7 | 0,68 |
| $LDH_5$ | 1,78±0,56 | 0,57±0,38 | 1,77 | 0,74±0,7 | 1,1 |

Note: t) Student's criterion of significance.

increase in resistance of animals to the action of an additional stimulus not only by the effect of adaptive hormones during the development of "crossed resistance," but also by excitation of the CNS. The additional focus of excitation thus arising changes the character of the animal's response. In experiments on rabbits in which activity of the mediator systems was increased during stress, additional stimulation caused it to decrease [8]. Comparison of the results of the present experiments with data in the literature suggests that the changes arising in the ganglia of the autonomic nervous system during exposure to the combined effect of MEMF and stimulation of the negative emotiogenic zones of the hypothalamus can be interpreted as the result of the development of "crossed resistance" by the rabbits.

Changes in the LDH spectrum of immobilized animals during exposure to an MEMF can also be explained by this phenomenon (Table 1). The animals placed in the MEMF were securely fixed, and this was an additional stress-producing factor. The results of the investigation show that structures of the autonomic nervous system are an important component in the response of the body to the combined action of two stress-producing factors.

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