3. R. A. Brace et al., Am. J. Physiol., 227, 590 (1974).
4. B. Braveny, Arch. Int. Physiol. Biochem., 72, 553 (1964).
5. H. G. Glitch, H. Reuter, and H. Scholz, J. Physiol. (London), 209, 25 (1970).
6. S. Ito, Jpn. Cir. J., 39, 37 (1975).
7. S. Harigaya and A. Schwartz, Circulat. Res., 25, 781 (1969).
8. J. Koch-Weser and J. R. Blinks, Pharmacol. Rev., 15, 601 (1963).
9. I. Levy, Arch. Int. Physiol. Biochem., 76, 680 (1968).
10. R. Niedergerke and H. C. Luttgau, Nature, 179, 1066 (1957).
11. Z. I. Penefsky et al., in: Myocardial Biology, Baltimore (1974), pp. 31-39.
12. K. Prasad, S. Singh, and J. C. Collaghan, Fed. Proc., 27, 348 (1968).
13. A. Schwartz, in: Calcium and the Heart, New York (1971).
14. D. G. Teiger and A. Farah, J. Pharmacol. Exp. Ther., 164, 1 (1968).
15. H. Tritthart, R. Kaufmann, H. Volkmer, et al., Pflug. Arch. Ges. Physiol., 338, 207 (1973).

TISSUE RESPIRATION ENZYMES AND OXIDATIVE PHOSPHORYLATION IN THE MYOCARDIUM AFTER NEUROGENIC INJURY

V. V. Bul'on

UDC 616.127-009-092:612.26

After neurogenic injury to the myocardium caused by electrical stimulation of the aortic arch for 3 h a marked increase in succinate dehydrogenase activity, a sharp decrease in cytochrome oxidase activity, and uncoupling of oxidation and phosphorylation were observed (esterification of inorganic phosphate was reduced whereas the oxygen consumption was unchanged and the P/A ratio reduced). It is concluded that in neurogenic injuries to the myocardium the coordination of regulation of energy metabolism is disturbed, with the ultimate result that oxidative phosphorylation is uncoupled and the synthesis of high-energy compounds reduced.

KEY WORDS: neurogenic injury to the myocardium; respiratory enzymes; oxidative phosphorylation.

Previous investigations in the writer's laboratory have shown that the morphological changes in the myocardium resulting from neurogenic injury caused by the action of extremal factors are preceded by metabolic disturbances. These disturbances are manifested as stimulation of glycolysis, as shown by increased hexokinase and total lactate dehydrogenase activity and by the accumulation of lactic acid [3, 4]. Meanwhile an increase in the contribution of the pentose phosphate pathway of carbohydrate oxidation to the energy metabolism of the injured myocardium is observed, as shown by increased glucose-6-phosphate dehydrogenase activity [4].

It was accordingly decided to investigate the state of oxidative processes in the myocardium following neurogenic injury. For this purpose the activity of respiratory enzymes such as succinate dehydrogenase (SD) and cytochrome oxidase (CO) and the intensity of oxidative phosphorylation were studied.

EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 3.0-3.5 kg. Neurogenic injury to the myocardium was produced by electrical stimulation of the aortic arch for 3 h by means of an electrode introduced through the right common carotid artery [1]. The animals were killed immediately after the end of electrical stimulation. Intact animals served as the control. Activity of SD [8] and CO [7] was determined spectrophotometrically in mitochondria isolated from the heart by differential centrifugation. The activity of the enzymes was expressed in conventional ΔE units/mg protein/h. The intensity of oxidative phosphorylation was determined manometrically in a Warburg apparatus and the protein concentration by Lowry's method [9].

Laboratory of Experimental Pharmacology, Department of Pharmacology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR S. V. Anichkov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 86, No. 7, pp. 13-14, July, 1978. Original article submitted February 29, 1978.

TABLE 1. Activity of Oxidative Enzymes of Heart Muscle (in ΔE/mg protein/h) Following Its Neurogenic Injury

Group of animals	SD (n=7)	CO (n=6)
Control	13,7±0,6	43,0±4,4
Experimental	20,2±1,0	23,0±1,9

Legend. n) Number of experiments.

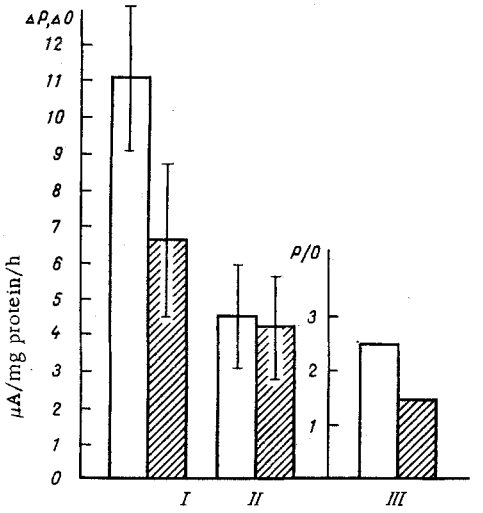

Fig. 1. Oxidative phosporylation in mitochondria of rabbit heart muscle after stimulation of aortic arch for 3 h. I) Esterification of inorganic phosphorus; II) oxygen consumption; III) P/O ratio. Unshaded columns – control; shaded columns – electrical stimulation.

EXPERIMENTAL RESULTS AND DISCUSSION

The activity of the respiratory enzymes of the myocardium following its neurogenic injury showed considerable changes (Table 1). For instance, 3 h after the beginning of electrical stimulation SD activity was increased by 47%. These results agree with those of investigation of SD activity in myocardial infarction [5, 6]. The authors cited observed a sharp increase in SD activity during the first hours of the disease and a marked decrease on the following days. The increase in SD (an enzyme which serves as indicator of metabolic processes in the Krebs' cycle) activity coupled with intensification of glycolysis [4] in neurogenic injury to the myocardium can evidently be regarded as a metabolic response aimed at maintaining the energy supply to the injured myocardium.

Investigation of CO activity, which reflects the intensity of metabolism as a whole and the aerobic pathway of oxidation, showed that, unlike SD activity, it was reduced. Compared with the control, CO activity was reduced almost by half. It can be concluded from these observations that the respiratory chain of the mitochondria is the most vulnerable stage in the energy metabolism of heart muscle tissue, and this is confirmed also by the results of investigations of the intensity of oxidative phosphorylation. These experiments showed that in neurogenic injuries to the myocardium caused by electrical stimulation of the aortic arch the esterfication of inorganic phosphate is reduced, whereas the level of oxygen consumption was unchanged and the P/O ratio reduced (Fig. 1). These results are evidence of uncoupling of oxidation and phosphorylation which, in turn, may lead to a decrease in the synthesis of high-energy compounds.

In previous investigations the writer showed that after neurogenic injury to the myocardium the content of ATP and creatine phosphate is reduced whereas the inorganic phosphate concentration is increased [2, 3].

The results of the present and previous investigations thus indicate that during the development of neurogenic injuries to the myocardium caused by electrical stimulation of the aortic arch for 3 h considerable disturbances in the energy metabolism of the heart muscle tissue take place. Comparison of the activity of certain enzymes of glycolysis, of the pentose phosphate pathway of carbohydrate oxidation [4], the Krebs' cycle, and the respiratory chain of the mitochondria shows disturbance of the coordinated regulation of energy metabolism, with the ultimate result that oxidative phosphorylation is uncoupled and the synthesis of high-energy compounds is reduced.

LITERATURE CITED

1. S. V. Anichkov, I. S. Zavodskaya, E. V. Moreva, et al., Neurogenic Injuries and Their Pharmacotherapy [in Russian], Leningrad (1969).
2. S. V. Anichkov, N. A. Novikova, V. B. Isachenko, et al., Pat. Fiziol., No. 2, 50 (1974).
3. I. S. Zavodskaya, E. V. Moreva, N. A. Novikova, et al., Byull. Éksp. Biol. Med., No. 4, 61 (1974).
4. N. A. Novikova, Byull. Éksp. Biol. Med., No. 10, 1205 (1976).
5. R. A. Frol'kis, in: Abstracts of Proceedings of the 2nd All-Union Conference on Biochemistry of the Muscular System [in Russian], Leningrad (1972), pp. 224-225.
6. Ya. B. Eidinov, in: Abstracts of Proceedings of the 2nd All-Union Conference on Biochemistry of the Muscular System [in Russian], Leningrad (1972), pp. 247-248.
7. S. J. Cooperstein and A. Lazarov, J. Biol. Chem., 189, 665 (1951).
8. S. J. Cooperstein, A. Lazarov, and N. J. Kurfess, J. Biol. Chem., 186, 129 (1950).
9. O. H. Lowry, N. J. Rosebrough, A. L. Farr, et al., J. Biol. Chem., 193, 265 (1951).

MECHANISM OF FORMATION OF COMPLEXES OF EPILEPTIC ACTIVITY IN THE CEREBRAL CORTEX UNDER THE INFLUENCE OF A DETERMINANT FOCUS

G. N. Kryzhanovskii,* R. F. Makul'kin, A. A. Shandra, and D. V. Boiko

UDC 616.831.31-009.24-031-092.9-07

Experiments on cats anesthetized with pentobarbital showed that when a hyperactive focus with a high level of excitation is formed in the temporal cortex and a series of foci with lower levels of excitation is formed in other parts of the neocortex, a functional complex with coordinated activity is created and is controlled by the activity of the hyperactive focus. The latter plays the role of a determinant structure. Depression of the determinant focus leads to disintegration of the epileptic complex. The nature of the foci is unimportant as regards the realization of these relationships: Both determinant and dependent foci could be created with the aid of strychnine and penicillin, which disturb different types of inhibition. The results confirm the general concept of the role of determinant structures in the activity of the nervous system.

KEY WORDS: determinant focus; epileptic complex; neocortex; strychnine; penicillin.

It has been shown [2] that a powerful focus of excitation created with the aid of strychnine in the cerebral cortex plays the role of determinant structure, determining the character of activity of other discrete foci of strychnine excitation, strengthens excitation in them, unites them into a single functional complex, and determines the behavior of the complex as a whole. This complex can be destroyed by suppression of the determinant focus, whereas blocking the other foci constituting the complex had no significant effect on its behavior.

*Corresponding Member of the Academy of Medical Sciences of the USSR.

Laboratory of General Pathology of the Nervous System, Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. Department of Pathological Physiology, N. I. Pirogov Odessa Medical Institute.

Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 86, No. 7, pp. 14-19, July, 1978. Original article submitted September 9, 1977.