CHANGES IN CARBOHYDRATE-PHOSPHORUS METABOLISM IN THE BRAIN FOLLOWING SEVERE MECHANICAL TRAUMA

I. R. Petrov and B. I. Krivoruchko

UDC 617-001-07:616.831-008.939.15

Few attempts have been made to study the changes in tissue metabolism lying at the basis of the functional disturbances in the central nervous system in traumatic shock, and indeed only the first steps have been taken in this direction.

Kovach [8], for instance, found that in shock caused by freezing the hind limbs of rats in liquid air, the concentration of creatine phosphate in the brain increases until the agonal state is reached. In contrast to this, in tourniquet shock and also in shock caused by rotation in a drum [9], traumatic shock [6], and pleuropulmonary shock [3], an early decrease was found in the creatine phosphate concentration with disturbance of the processes of oxidative phosphorylation. These results were confirmed by studies of coupled phosphorylation in the mitochondria of the brain tissue in tourniquet and traumatic shock [4, 5]. However, in all these investigations, no account was taken of the severity of the process and the functional state of the nervous system.

In the present investigations, in which these factors were considered, an attempt was made to analyze the functional and biochemical processes developing in the higher levels of the nervous system (the brain) following severe mechanical trauma.

EXPERIMENTAL METHOD

Experiments were carried out on 28 rabbits. The severe mechanical trauma took the form of crushing of the soft tissues of both hind limbs by the method described previously [2]. The behavior of the animals, their arterial pressure, electrocorticogram (ECoG), respiration, pressor vascular reflexes, body temperature, and the concentrations of creatine phosphate (CP), adenosinepolyphosphates (ATP + ADP), inorganic phosphate (IP), and lactic acid the brain were studied. The phosphorus of all the fractions was determined by the method of Fiske and Subbarow [7] and the lactic acid by iodometric titration with precipitation of the proteins by zinc hydroxide [1].

In the investigations of series I the concentration of high-energy phosphates and of lactic acid was determined in normal conditions in 7 intact rabbits (see Table).

In series II the concentration of high-energy compounds and lactic acid was determined in 21 rabbits in various stages of shock produced by crushing the soft tissues. The animals of this series were subdivided into four groups depending on the severity of the shock, taking into account the general condition, the character of the ECoG and the level of the arterial pressure.

EXPERIMENTAL RESULTS

In the erectile phase of shock the rabbits exhibited violent motor excitation and the electrical activity of their cerebral cortex was intensified. At this period a marked decrease was observed in the concentration of CP and ATP + ADP in the brain. The IP concentration rose by 53% and the lactic acid concentration by 10.7 times. When the erectile phase changed into the torpid phase, the concentration of adenine polynucleotides rose above the control level and the IP level fell. With deepening of the torpid phase of traumatic shock, the differences between the control and the experimental rabbits were no longer significant, apart from the lower concentration of CP and the higher level of lactic acid in the brain tissue (see Table). The arterial pressure of the animals in torpid phase II was much lower than in torpid phase I (54±6 and 70±15 mm respectively) and, judging by the animals' behavior and the ECoG, the inhibition of the central nervous system was more marked.

Research Institute of Blood Transfusion and Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 63, No. 3, pp. 58-60, March, 1967. Original article submitted June 26, 1965.

Concentration of Phosphorus Compounds and Lactic Acid in the Brain of Rabbits Subjected to Severe Mechanical Tranuma (M±m)

Phase of shock	Number of rabbits	Phoshates and lactic acid (in mg%)								Arterial pressure (in mm)			
		CP	P	ATP+ ADP	P	IP	P	Lactic acid	P	Initial	At the beginning of trauma	At the end of the experiment	P
Control . .	7	5,4±0,3		21,0±0,5		12,8±0,8		18±1		—	—	—	
Erectile .	5	0,8±0,2	<0,001	15,0±1,1	<0,01	19,6±2,3	<0,02	304±17	<0,001	102±4,5	135±3,5	114±8,1	—
Torpid . .													
I	5	3,6±0,6	<0,025	23,2±0,8	<0,05	10,4±0,4	<0,025	152±16	<0,001	100±7,7	135± 9,5	70±6,8	<0,01
II	5	2,6±0,5	<0,001	23,2±1.2	>0,2	10,7±0,6	>0,05	146±13	<0,001	100±2,7	136± 5,4	54±2,7	<0,05
III	6	1,9±0,8	<0,5	16,3±1,2	<0,002	19,9±1,7	<0,001	177±21	>0,25	100±5,0	136±11,7	39±5,8	<0,05

Note. The significance of the differences of P was calculated relative to the control.

In the deep torpid phase of traumatic shock (see Table, torpid phase III), the rabbits did not react to tactile and nociceptive stimuli. Their ECoG at the time the brain was taken for biochemical analysis was considerably flattened. The arterial pressure at this time was 39±14 mm. Biochemical analysis of the brain showed that the CP concentration had fallen by 68% and that of ATP+ADP by 23% compared with normal, while the IP concentration had risen by 58% and the lactic acid by 6.2 times. Comparison of these results with those obtained with the animals in the torpid phase II showed a more marked and statistically significant decrease in arterial pressure ($P<0.05$) and a lower concentration of ATP+ADP. On the whole the concentration of phosphates was at the same level as in the erectile phase.

Analysis of the results of the functional and biochemical investigations in animals with traumatic shock due to crushing of the soft tissues showed that marked changes of carbohydrate-phosphorus metabolism took place in the brain of the rabbits in the phase of generalized exciation, characterized by intensive breakdown of high-energy phosphate and stimulation of glycolysis. In the erectile phase of traumatic shock, a primary exhaustion of the energy resources of the central nervous system thus was already apparent, and was due to the flow of nociceptive impulses and the hypoxia of the brain. The protective inhibition arising in these conditions led to temporary stabilization of ATP+ADP at a fairly high level at the expense of breakdown of CP and increased glycolysis.

With deepening of the torpid phase of shock the adaptive reaction—inhibition of the central nervous system—became inadequate to prevent breakdown of the high-energy phosphates. The increasing circulatory disturbances aggravated the hypoxia and hypoxemia, thus producing further disturbances of oxidative phosphorylation and exhaustion of the energy resources of the central nervous system.

The results of the these investigations thus confirmed and extended the findings concerning the disturbance of oxidative phosphorylation in traumatic shock and demonstrated that when the animal organism is subjected to severe mechanical trauma, besides functional changes in the brain, changes develop in carbohydrate-phosphorus metabolism, leading to disturbance of the functions of other organs and systems and to death of the organism.

LITERATURE CITED

1. G. E. Vladimirov, G. A. Dmitriev, and A. P. Urinson, Lab. Praktika, No. 8, 11 (1932).
2. B. I. Krivoruchko, Pat. Fiziol., No. 3, 26 (1963).
3. I. D. Kudrin, Voen.-med. Zh., No. 7, 38 (1961).
4. L. F. Panchenko, Ukr. Biokhim. Zh., No. 2, 283 (1965).
5. L. F. Penchenko and N. N. Bogolepov, Doklady Akad. Nauk SSSR, 160, No. 6, 1401 (1965).
6. I. R. Petrov, Pat. Fiziol., No. 5, 12 (1962).
7. C. H. Fiske and J. Subbarow, J. Biol. Chem., 81, 629 (1929).
8. A. G. B. Kovách, Fed. Proc., 20, Suppl. 9, 1222 (1961).
9. G. A. LePage, Am. J. Physiol. 146, 267 (1946).